<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>523</td>
<td>Chronic subdural haematoma: a retrospective 232 cases review - a comparison of a single centre between a population aged under 75 and above 75 years old</td>
<td>S. Leuce, H.D. Bade, H. Pleș - ROMANIA</td>
</tr>
<tr>
<td>552</td>
<td>Multidisciplinary approach to orbital fracture repair</td>
<td>V.V. Costan, M. Dabija - ROMANIA</td>
</tr>
<tr>
<td>563</td>
<td>Mirror, mirror on the wall, who’s the fairest of them all? Atypical meningioma associated with multiple meningiomas</td>
<td>A.I. Cucu, Claudia Florida Costea, Mihaela Dana Turliuc, Gabriela Florenta Dumitrescu, Anca Sava, I. Poeata - ROMANIA</td>
</tr>
<tr>
<td>573</td>
<td>Thoraco-lumbar spine injuries – a retrospective study on 651 cases</td>
<td>Ioana Viorela Jitaru, Al. Stan, Antonia Nita, C.E. Popescu - ROMANIA</td>
</tr>
<tr>
<td>583</td>
<td>Thrombectomy for ischaemic stroke in a young patient. Case presentation</td>
<td>A. Chiriac, Georgiana Ion, N. Dobrin, Z. Faiyad, I. Poeata - ROMANIA</td>
</tr>
<tr>
<td>589</td>
<td>Penetrating brain injury with 2 nails as an attempt of suicide</td>
<td>Anuța Negru, M. Angelescu - ROMANIA</td>
</tr>
<tr>
<td>593</td>
<td>Stent assisted coiling technique for anterior communicating artery aneurysms treatment</td>
<td>A. Chiriac, Giorgiana Ion, N. Dobrin, I. Poeata - ROMANIA</td>
</tr>
<tr>
<td>602</td>
<td>Combined treatment of a giant anterior skull base meningioma</td>
<td>Georgiana Ion, Z. Faiyad, I. Poeata, A. Chiriac - ROMANIA</td>
</tr>
<tr>
<td>607</td>
<td>Familial cerebral cavernous malformation syndrome in Serbian family</td>
<td>Aleksić Vuk, Mandarić Aleksandar, Mihajlović Miljan, Aleksić Nemanja, Rapaić Marko, Jovančević Miroljub, Stanić Milenko, Samardžić Marko, Popović Igor, Miladinović Vladimir, Spaić Milan - SERBIA</td>
</tr>
<tr>
<td>Page</td>
<td>Title</td>
<td>Authors</td>
</tr>
<tr>
<td>------</td>
<td>--------------------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>613</td>
<td>Diagnostic value of preoperative systemic inflammatory markers in patients with intracranial meningiomas</td>
<td>Rahsan Kemerdere, Mehmet Yigit Akgun, Sureyya Toklu, Orkhan Alizada, Oguz Baran, Taner Tanriverdi</td>
</tr>
<tr>
<td>622</td>
<td>A Doughnut in the Brain: an overview of the pathophysiology and the current treatment options for intracranial doughnut-shape aneurysm</td>
<td>S.S. Hoz, L.R. Moscote-Salazar</td>
</tr>
<tr>
<td>632</td>
<td>A prospective observational study of clinical outcome of operated patients of intradural extramedullary spinal cord tumor in our tertiary care center</td>
<td>P.R. Singh, T.K. Pandey, F. Ahmad, D.K. Chhabra</td>
</tr>
<tr>
<td>641</td>
<td>Ruptured intracranial internal carotid artery aneurysm causing subarachnoid hemorrhage and ophthalmoplegia associated with metastatic carcinoma with unknown primary in sellar-parasellar region: True or Coincidental Association</td>
<td>G.D. Satyarthee, L.R. Moscote-Salazar, A. Agrawal</td>
</tr>
<tr>
<td>647</td>
<td>Isolated dorsal vertebral Chondroblastoma: a rare case with review of literature</td>
<td>S. Pandey, K. Kaushik, L.N. Gupta, R. Varshney, Prarthana Saxena</td>
</tr>
<tr>
<td>654</td>
<td>Therapeutic benefit of palmitoylethanolamide in the management of neuropathic pain</td>
<td>I.D. Chaurasia, Kunal Vinayak, Shashikant Tiwari, Prateek Malpani, Sheikh Behram, Mahim Koshariya</td>
</tr>
<tr>
<td>662</td>
<td>44th Congress of the Romanian Society of Neurosurgery Considerations</td>
<td></td>
</tr>
<tr>
<td>666</td>
<td>Short review of “Principiile chirurgiei neurologice”, 4th edition</td>
<td></td>
</tr>
<tr>
<td>669</td>
<td>Instructions for Authors on References (APA style)</td>
<td></td>
</tr>
</tbody>
</table>
Chronic subdural haematoma: a retrospective 232 cases review - a comparison of a single centre between a population aged under 75 and above 75 years old

S. Leuce², H.D. Bade¹, H. Pleș¹,²

¹“Victor Babeș” University of Medicine and Pharmacy Timișoara, ROMANIA
²Emergency Clinical County Hospital Timișoara, ROMANIA

Abstract: Chronic subdural haematoma represents a major problem in the neurosurgical field concerning population both under and above 75 years old. It is not only a matter of prevalence or pure statistics but it embodies true understanding of how the pathology affects older patients, their life expectancy and quality when reliable factors are implied such as comorbidities, relation with the moment of surgery, the existence of anticoagulation therapy, and many more. We target these challenges in a study on 232 cases of treated chronic subdural haematomas with impact on two major categories - those under and above 75 years old in the Neurosurgery Department, County Hospital “Pius Brânzeu” Timişoara, Romania.

Key words: antithrombotics, chronic subdural haematoma, midline shift, older population

Introduction

At the basis of chronic subdural haematoma (CSH) formation stands multiple aetiologies, such as trauma and acute subdural haematoma(aSH), spontaneous reasons including hydrocephalus, coagulopathies and chronic anticoagulation therapy, and iatrogenous causes such as a complication of a lumbar puncture (LP).

Among the risk factors involved are: predisposing of trauma, alcohol consumption, epilepsy, hemorrhage, and other predisposing factors such as coagulopathy, antithrombotics, high blood pressure, brain atrophy, hygroma [2,7,13,22,24] and others.

Clinical features include: motor deficiency, altering of consciousness, intracranial hypertension (ICH) syndrome, pseudotumoral, pseudodementia syndromes, headaches, and progressive speech impairment [11].

Differential diagnostics comprise of the following: stroke, dementia, encephalitis, cerebral abscess, tumor, and cerebral parasitosis as showed by standard imagistic
The treatment options for CSH are for symptomatic cases, midline shift (MLS) with a minimum of 5 mm, mass effect, etc., also, conservative treatment stands for neurologically intact elderly patients on antithrombotics - withdrawal of antithrombotic medication 7 days prior to the surgery - in the case of eligibility for an operation, perioperative antibiotic prophylaxis [5,14,16,17,19,21,33].

In respect of the well-established techniques used for CSH evacuation these include; single “burr-hole” or double “burr-hole” technique + drainage, craniotomy +/- cranioplasty + drainage, subdural evacuating port system (SEPS), twist drill craniotomy [23], and endoscopy [10,20,27,30,34].

In the matter of complications and prognostics, the surgical intervention may be grafted by complications such as; haematoma persistency, pressure pneumocephalus, subdural empyema, convulsions, intracerebral hemorrhage, and others [8,35].

Recurrence of CSH can be early - less than 3 months postoperative or late - more than 3 months postoperative [3].

Postoperative midline-shift over 5 mm, diabetes, preoperative convulsions, over 20 mm in size of the haematoma, intracranian (IC) hypotension, low Glasgow Coma Scale (GCS), mixed density of the haematoma on the CT-scan, antithrombotic therapy, cancer and male population are associated with a higher risk of recurrence [19,29,32].

**Aim of the study**

To assess the results of a retrospective comparative study of 232 aged-related subjects over and under 75 years old with CSH treated in the Neurosurgery Dep. Timisoara County Hospital between 1st of January 2013 and 30th of September 2017.

**Materials and methods**

A total of 232 enrolled patients diagnosed with CSH from which 181 were male and 51 were female. Age over 75 yrs.; 70 M and 25 F; under 75 yrs.; 111 M and 26 F. Age-related < 75 yrs. old: 0-10 yrs., 9; 11-20 yrs., 2; 21-30 yrs., 1; 31-40 yrs., 2; 41-50 yrs., 17; 51-60 yrs., 28 61-74 yrs., 78. Age-related >75 yrs. old: 75-80 yrs., 53; 81-85 yrs., 31; 86-90 yrs., 9; 91-95 yrs.:2, comprising a single-centre study of the Department of Neurosurgery County Hospital “Pius Branzeu” Timisoara, Romania.

Chi Square Test was utilized to predict a statistically significant importance of several findings in the study.
Regarding the data offered by the study, it shows that the incidence of CSH increases with lower ages in the population studied over 75 years old as follows: between 75-80 years old there were 53 patients included; between 81-85 years old, 31 patients; between 86-90 years old, 9 patients and from 91-95 years old, 2 patients.
Overall, fewer people in the segment considering the older than 75 years cohort spent between 1 and 3 weeks in hospital in comparison to the other studied cohort. Less than 1 week in hospital includes 26 patients vs. 34 in the same 2 groups; between 1-2 weeks it was 57 vs. 73 patients, and over 3 weeks in hospital there were 7 vs. 8 patients in total.

<table>
<thead>
<tr>
<th>Time of hospitalization</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 week</td>
<td>26</td>
<td>34</td>
</tr>
<tr>
<td>1-2 weeks</td>
<td>57</td>
<td>73</td>
</tr>
<tr>
<td>2-3 weeks</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Over 3 weeks</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

**Figure 4** - Cohorts in relation to hospitalization

In addition, they were 44 compared to 74 people with left-side CSH in the 2 groups, 37 vs. 40 people with right-side CSH and 14 vs. 23 having bilateral haematomas.

<table>
<thead>
<tr>
<th>Type of CSH</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left</td>
<td>44</td>
<td>74</td>
</tr>
<tr>
<td>Right</td>
<td>37</td>
<td>40</td>
</tr>
<tr>
<td>Bilateral</td>
<td>14</td>
<td>23</td>
</tr>
</tbody>
</table>

**Figure 5** - Cohorts in relation with localization of the CSH

Midline shift is another landmark of the study that shows the following: 61 vs. 83 patients did not have any midline shift; 6 vs.10 patients had 1-5 mm deviation; 15 patients in both groups had MLS between 6-10 mm; and 9 vs.18 had a deviation between 11-15 mm and 4 vs.11 patients had MLS over 15 mm.

<table>
<thead>
<tr>
<th>MLS (Midline-shift)</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 mm</td>
<td>61</td>
<td>83</td>
</tr>
<tr>
<td>1-5 mm</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>6-10 mm</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>11-15 mm</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>over 15 mm</td>
<td>4</td>
<td>11</td>
</tr>
</tbody>
</table>

**Figure 6** - Cohorts in relation with MLS
GCS at presentation was recorded for all the patients included in the study: GCS 3p was seen in 2 vs. 4 patients in the 2 groups studied; GCS 4p, 2 vs. 1 patient; GCS 5p, each group had 1 patient; GCS6p, none of the 2 groups; GCS 7p, 1 vs. 2; GCS 8p, 5 vs. 3; GCS 9p, 4 vs. 3; GCS 10p, 3 vs. 2; GCS 11p, 0 vs. 1; GCS 12p, 4 vs. 3; GCS 13p, 10 vs. 7; GCS 14p, 33 vs. 27; GCS 15p, 30 vs. 83 in the cohorts.

<table>
<thead>
<tr>
<th>GCS at presentation</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>30</td>
<td>83</td>
</tr>
<tr>
<td>14</td>
<td>33</td>
<td>27</td>
</tr>
<tr>
<td>13</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>12</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Figure 7 - Cohorts in correlation with GCS at presentation

Clinical features of the CSH were assessed as being part of the general findings in this study: One-side motor weakness in 61 vs. 73 cases; dysphasia in 31 vs. 37; headaches in 46 vs. 86; Convulsions in 6 vs. 15 patients; paraparesis in 1 vs. 4; tetraparesis 1 vs. 0; Unilateral Babinski signs in 22 vs. 23 and bilateral Babinski signs in 12 vs. 7 patients from the over/under 75 groups.
In the matter of imagistic data, we had 91 patients scanned with CT in the first group and 105 in the second one; 4 had taken an MRI scan in the first group vs. 16 in the second one, and both investigations were undergone by 16 of the patients in the second group.
The associated morbidity and mortality factors in the assessment of CSH are amongst other important elements in the evaluation of age-related evolution of the pathology, therefore CRF (Chronic renal failure) was seen in 2 vs. 4; Heart failure in 14 vs. 13; Stroke in 11 vs. 15; Respiratory failure in 12 vs. 9; Pneumonia in 7 vs. 9; Afib in 17 vs. 12; Ischemic cardiopathy in 27 vs. 18; Sepsis in equal parts 4:4; Cancer in 3 vs. 4; High blood pressure in 53 vs. 62; Type II diabetes in 14 vs. 24 and COPD in 1 vs. 5 cases.

<table>
<thead>
<tr>
<th>Associated co-morbidity</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic renal failure</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Heart failure</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>Stroke</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Afib</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Ischaemic cardiopathy</td>
<td>27</td>
<td>18</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Cancer</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>53</td>
<td>62</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>14</td>
<td>24</td>
</tr>
<tr>
<td>COPD</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

**Figure 11** - Associated co-morbidity factors in relation to the 2 populational groups

Regarding the use of antithrombotics, in the first group of patients we found 10 vs. 9 in the second one who were on antiplatelet therapy and 21 over 75 years old vs. 13 under 75 years old who took anticoagulants.

<table>
<thead>
<tr>
<th>Basic antithrombotic therapy</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelet</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>21</td>
<td>13</td>
</tr>
</tbody>
</table>

**Figure 12** - Use of antithrombotics in CSH regarding cohorts

<table>
<thead>
<tr>
<th>Median days of hospitalization from admission until surgery</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.30 days</td>
<td>2.99 days</td>
</tr>
</tbody>
</table>

**Figure 13** - Time of hospitalization between admission and surgery
**Figure 14** - Therapy options in respect of the 2 groups

<table>
<thead>
<tr>
<th>Therapy options</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>85</td>
<td>124</td>
</tr>
<tr>
<td>“Burr-hole” craniectomy</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Craniotomy</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Minimal craniectomy</td>
<td>83</td>
<td>119</td>
</tr>
<tr>
<td>CSH kit SEPS</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Conservative</td>
<td>10</td>
<td>13</td>
</tr>
</tbody>
</table>

**Figure 15** - 89 years old patient CT scan in axial plane showing left frontal-parietal CSH and a recent ischemic event localized left frontal-pole

**Figure 16** - Axial CT scan of a 67 years old patient with a 13 cm AP length and a 2.5 cm thick left CSH and right midline shift

**Figure 17** - A 61 years old patient, axial image showing fronto-parieto-temporal chronic subdural haematoma
Results

The study shows the mortality in patients older than 75 outnumber those under 75. The difference is statistically significant under the evaluation of the Chi Square Test (0.0001) thus the comatose patient number is higher in the cohort representing patients over 75 in comparison with the second group, this proved not to be statistically significant (Chi Square Score 0.125).

From the two groups, those over 75 were treated predominantly in a conservative fashion that meant 10.526% vs. 9.489%, also without importance in the study (value=0.725).

The number of those over 75 years old on antithrombotics is significantly higher than younger patients with the same treatment (Chi Square Test 0.007).

Bilateral chronic subdural haematomas (bCSH) were rarely observed in the over 75 years cohort vs. those under, (14.736% and 16.788%) but this also poses no statistical significance (Chi Square Test 0.943) evenly quoted by Song DH et al [28].

From the total number of patients, 54% from those under 75 years old, had left hemispheric CSH vs 29.1% showing right hemispheric involvement. In the second group regarding the patients over 75 years old, CSH was seen more frequently - 46.3% affecting the left side vs 38.9% in the right side.

In the matter of prevalence of the gender-dependent population, 81.1% of males and 18.9% females were under 75 years old in comparison to 73.6% of males and 26.3% females over 75 years also stated in between the values reported in the study by Oh J. et al.[24].

The improvement of deficits was more frequently found in the over 75 years old cohort (Chi Square Test 0.010).

The medium global hospitalization time was 10.48 days with a standard deviation of 7.233 days with a range from 1-49 days. In the over 75 year old group the study showed that a
total of 26 patients (25.86%) stayed under 1 week and 7 patients (6.47%) stayed for over 3 weeks. From that, those staying under 1 week comprised 27.37% and those staying over 3 weeks 7.37%, and in the cohort under 75 years old 24.82% under a week and 5.84% over 3 weeks.

The second group showed a medium hospitalization time of 10.36 days with a standard deviation of 6.803 days and in those over 75 years old 10.67 days with a 0.839 standard deviation.

Mortality was seen in 11.4% in the male population and 7.84% in the female population from the total of deaths. In our study, 33.3% were on antithrombotics either antiplatelet or anticoagulation treatment. 38.8% of the deaths registered in the over 75 years old cohort were on antithrombotics, but less than 16.6% was encountered in those under 75.

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Total</th>
<th>Patients over 75 yrs old</th>
<th>Patients under 75 yrs old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemiparesis</td>
<td>57,758%</td>
<td>64%</td>
<td>53,284%</td>
</tr>
<tr>
<td>Afazia</td>
<td>29%</td>
<td>32,631%</td>
<td>27,007%</td>
</tr>
<tr>
<td>Headaches</td>
<td>56,896%</td>
<td>48,421%</td>
<td>62,773%</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>9,051%</td>
<td>6,315%</td>
<td>10,948%</td>
</tr>
<tr>
<td>Babinsky sgn.</td>
<td>27,586%</td>
<td>35,789%</td>
<td>21,897%</td>
</tr>
<tr>
<td>Unilat.Babinsky</td>
<td>19,396%</td>
<td>23,157%</td>
<td>16,788%</td>
</tr>
<tr>
<td>Bilat.Babinsky</td>
<td>8,189%</td>
<td>12,631%</td>
<td>5,109%</td>
</tr>
</tbody>
</table>

**Figure 20** - Outcomes in respect to the clinical features

The average value of MLS was 4.32 mm with a standard deviation of 5.772 mm. For the first study-group the average MLS was 4.68 mm (standard deviation 6.043 mm) and for the second group the study showed a MLS of 3.74 mm with a standard deviation of 5.290 mm. A value of 4.45 mm was showed for the patients who overcame the pathology with a median standard deviation of 5.797 mm and in those who died the prevalence translates to a 3.21 mm MLS with a median deviation of 5.548 mm, thus there were no significant differences in the two median values concerning the 2 study-groups.
The average value for GCS was 13.34 with a standard deviation of 2.823. For those under 75 years old, the average GCS was 13.66 with a standard deviation of 2.648 and for those over 75 years old the study showed a value of 12.83 and a mean deviation of 3.027. There is a significant difference regarding the value of GCS between those who survived and those who died.

From the conservative-treated patients all of them had an initial GCS of 14 or 15 with 3 exceptions: one patient under 75 with a GCS of 12; one patient over 75 years with a GCS of 3 and one patient over 75 years with a score of 4. Overall, neurological improvement was seen in 60% over 75 years old and respectively in 84.61% under 75. Without any improvement there were 30% in the first group and 15.38% in the second one.

In matter of mortality-CSH topography relationship, our study showed statistically higher rates of mortality for the over 75 years group vs. younger ages not only for unilateral CSH but also bilateral (Chi Square Test 0.01).

The evolution of the disease according to age group can be summarized as follows:

<table>
<thead>
<tr>
<th>GCS</th>
<th>Total</th>
<th>Patients over 75</th>
<th>Patients under 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-15</td>
<td>5.263%</td>
<td>9.589%</td>
<td>2.564%</td>
</tr>
<tr>
<td>9-12</td>
<td>30%</td>
<td>45.454%</td>
<td>11.111%</td>
</tr>
<tr>
<td>GCS=8</td>
<td>38%</td>
<td>60%</td>
<td>0%</td>
</tr>
<tr>
<td>GCS=6-7</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>GCS=4-5</td>
<td>60%</td>
<td>66.666%</td>
<td>50%</td>
</tr>
<tr>
<td>GCS=3</td>
<td>33.333%</td>
<td>50%</td>
<td>25%</td>
</tr>
</tbody>
</table>

![Figure 21 - Outcomes according to GCS in cohorts](image)

Average time of hospitalization from admission to surgery was: 2.264 days in the 75-80 years old subgroup; 1.580 days in the 81-85 years old subgroup and 1.727 days for those over 85 years old evaluated.

The average time of hospitalization was 10.118 days (+/- 7.913) for the 75-80 years old subgroup; 11.709 days (+/- 8.327) for the 81-85 years old subgroup and 69.909 days (+/- 6.786) for those over 85 years old.

There are no significant differences between the 3 subgroups regarding the average time of hospitalization.

As for the topography of the CSH in relation with antithrombotics the study found that the prevalence of those over 75 was higher (19.35%) in the anticoagulated group vs. 12.50% in those who did not benefit from the treatment and the same in the under 75 years old group where 22.72% had antithrombotics vs 15.65% without treatment.

Regarding the prevalence of comorbidity in the study, high blood pressure with a total percentage of 49.568% and in those over 75 years old - 55.789% and below 75 years old- 45.255%; followed by ischemic cardiopathy
showing a total of 19.396%, atrial fibrillation comes third in line, followed by stroke, diabetes and others.

**Discussion**

The study found—that under several aspects—significant differences concerning the evolution of a chronic subdural haematoma in the population under and over 75 years old. The haematomas are frequently encountered in the male population evenly under and over the age of 75, thus the total number of deaths are often seen in those over 75 no matter of gender or topography affected by the pathology.

The state of coma was attributed more to those over 75. The administration of antithrombotics was a direct factor of correlation for the apparition and recurrence of the haematoma and presented higher incidence rates of bilateral CSH with respect to Edlmann E et al. [9] and De Bonis P. et al. [7]. The elder patients seemed to have a lower rate of favorable neurological outcomes after the treatment opposite those of younger ages. The mortality is greater in the male population, and the study shows the appearance of motor deficits and aphasia were frequently seen in those under 75 years old in contrast with convulsions and the Babinski signs that predominate in those over 75 years old. Midline shift as a contributory factor of mortality was on all of its deviations and levels predominantly seen in the over 75 years group and less in those younger, and also independently of the GCS at admission with reference to Kim HC et al. [17]. There were no differences in the matter of mortality for those who had bilateral haematomas in respect of the general CSH prevalence.

Those treated conservatively from the group over 75 years old had a lower improvement percentage, higher mortality and stationary neurological outcome than the younger ages [35].

In a 2015 study, Aristedis Rovlias, Spyridon Theodoropoulos and Dimitrios Papoutsaki[26] reported a direct correlation between the CSH prognostic and the neurology status at admission, an aspect that is strengthened by this study observing the increasing mortality in parallel with a lower GCS, therefore at a GCS between 13-15, mortality was 5.26%, at a GCS of 9-12 the mortality was 30%, at GCS 8 and 4-5 mortality was 37.5% and 60% respectively.

Masaaki Uno et al. [31] focused in an article over the less favorable outcome of the CSH in patients over 75 years old vs. those under 75, as did this study that showed a higher mortality among those over 75 (18.9%) than in those under 75 (4.3%), and lower favorable outcomes for elderly patients (75.7%) vs younger ages (86.8%).

Antithrombotic usage represents an independent rise factor for the appearance of the CSH and it can also influence the prognosis [32,33,27]. In this study, 32.6% of those in the over 75 years old group had antithrombotics in comparison with 16% of those in the younger group.

In a study made by Agawa et al. [1], he reported a more unfavorable outcome for those with bilateral CSH, a fact that this study also confirmed, that mortality from bilateral CSH was significantly higher in patients over 75.
Regarding the surgical treatment of the CSH, Masaaki et al. [31] presented a favorable outcome for those treated by surgery of between 70-90%, also demonstrated by this study in terms of neurological improvement (83.2%), even if the prognostic worsened for those over 80 than under, this aspect determined the making of age-related subgroups and showed that in those over 85 the mortality reduced by half.

In-hospital related mortality in this study stands at the limits somewhere at 10.3% in comparison to Masaaki with reported limits between 0.21%-27.5%.

In a 2012 study on 125 patients made by Danilo Otavio de Araujo Silva et al. [6] with CSH, headaches showed in 40% of patients and deficits at 44%. This study percentage is nearby those values with 56.8% for the first one and 57.7% for the deficit.

I. A. Iliescu [11,12], in an article, correlates the higher incidence of the CSH in the male population, also demonstrated by this study. From the total of 232 patients, 181 were male (78%) and only 51 were female (22%), and apparently the male gender is an independent negative factor for the CSH outcome, mortality being significative higher than in the female population (8.6% vs 1.7%). The same study reports a more right cerebral hemisphere dominance of the CSH (52%) and only 30% affecting the left side, therefore, in comparison this study found a more left-side prevalence of the CSH despite the 2 categories and last but not least between 2-19% of the patients had convulsions in the comparative study, in this study it was found that 9.05% of patients were affected which resemble the study of Battaglia et al. [4] who reports incidences of 10.6% and 14.9%.

Quiang-Ping Wang et al. [33] exemplified in a study that from their cohort of CSH-presenting patients, 20.5% had high blood pressure, 16.6% had heart failure and 13.9% had diabetes. In this study the findings were in the order 49.5%, 11.6% and 16.3% thus high blood pressure and heart failure were found more often in those over 75 years old.

Borger V. et al. [5] randomized patients in 3 age-related groups as follows: 65-74 years; 75-84 years and 85-94 years. They concluded that postoperative although all the groups had increased improvement scores, they synchronized with age. Our study has similar results, therefore in those treated under 75 the percentage was 86.8% and declining to 75.7% in those over 75.

In this study, 3.01% of patients showed a positive diagnosis for cancer, higher for those over 75 years old and it correlates with the study of Yuji Agawa et al. [1] that stated an unfavorable prognostic for those affected by a tumor.

Conclusions

There are significant differences between the CSH outcome in the two study populations, therefore we consider that those differences should be taken into consideration for the in-hospital care of patients in order to maximize the prognostic.

Patients over 75 years old are posing a higher mortality rate than the younger ages. Coma is a complication of the slower rates of improvement, convulsions and deficits in the
group over 75 do not contraindicate surgery when imposed.

Those on antithrombotics showed an increased risk of developing bilateral CSH at higher ages and a more unfavorable outcome, a fact that is also predicted by the value of the MLS or the associated comorbidities, making the approach more complex.

The aging process will eventually lead to a higher incidence and prevalence of CSH in the population and can also stimulate the necessity of permanent care and evaluation of these kinds of patients.

There is a need for supplementary studies and opinions in order to establish a common point of optimum treatment of this vulnerable category of patients.

Correspondence
Horia Pleș
“Victor Babeș” University of Medicine and Pharmacy, Timișoara
ples.horia@umft.ro

References


Primary intramedullary spinal cord non-Hodgkin lymphoma - case report and review of the literature

Aurelia Mihaela Sandu¹, M.A. Fürtös¹, G. Petrescu¹, Anamaria Gheorghiu¹, B.I. David¹, F.M. Brehar¹,², A. Giovani¹, M.R. Gorgan¹,²

¹“Bagdasar-Arseni” Department of Neurosurgery, Emergency Clinical Hospital, Bucharest, ROMANIA
²“Carol Davila” University of Medicine and Pharmacy, Bucharest, ROMANIA

Abstract: Introduction: Primary intramedullary spinal cord lymphomas are extremely rare, occurring mainly in immune compromised patients. Case report: We report a case of a 43 years old patient admitted with spinal cord compression. Spinal MRI revealed two thoracic intramedullary tumours. The patients underwent surgery and we performed resection of both primary intramedullary tumours, with favourable neurological outcome. The histopathologic exam was non-Hodgkin lymphoma. The patient underwent adjuvant radiotherapy. Two months later the patient presented thoracic and cerebellar drop metastases, confirmed histopathologically. Conclusions: The diagnosis of primary intramedullary spinal lymphoma must be kept in mind in patients with myelopathy. Surgery is needed to provide histopathological samples for positive diagnosis and spinal decompression. Primary intramedullary spinal lymphomas have a propensity to disseminate along the neuraxis.

Keywords: intramedullary lymphoma, non-Hodgkin lymphoma

Introduction

Spinal cord lymphomas are rare. Spinal lymphomas are usually extradural, occurring in vertebral bodies or in epidural tissue. Primary intramedullary spinal cord lymphomas are very rare and accounts for 1% of CNS lymphomas.¹,² The majority of intramedullary lymphomas are secondary drop metastases. Some studies found them most commonly located in cervical and thoracic spinal segments³, while other considered that conus medullaris and cauda equina are more affected⁴.

They usually occur in the fifth or the sixth decades of life.¹,³,⁴ Men are more commonly affected compared with women are white race is more affected.¹,⁴ Risk factors for occurrence of lymphomas are immune depression, such as: AIDS, congenital immune deficiency, cancer, organ transplant related immune
suppression, infection with Epstein-Barr virus, etc.

Intramedullary lymphomas usually appear as a solid, homogeneously enhancing mass, isointense in T1W and hyperintense in T2W. CSF cytology shows increased cellularity.

Treatment of spinal lymphomas usually consists of surgical biopsy to establish a positive diagnosis, followed by adjuvant radiotherapy. Chemotherapy is controversial.

Prognosis is poor, 2 years survival rate is 32-36%.

Case report

A 43 years old man was admitted in our department with spinal cord compression with neurological level T1, Frankel C severe right > left and loss of consciousness. The patient was immune competent and had no relevant medical history.

Neurologic exam showed paraparesis, right L2 ASIA 2, right L3 ASIA 2, right L4 ASIA 1+, right L5 ASIA 1+, right S1 ASIA 3-, left L2 ASIA 3-, left L3 ASIA 3-, left L4 ASIA 3-, left L5 ASIA 3- and left S1 ASIA 3. Total motor score on the right side was 34 and on the left was 40. We also found hypoesthesia with level T1, bilateral diminished osteotendinous reflexes, bilateral Babinski sign and urinary incontinence.

Spinal MRI revealed two solid intramedullary tumours hyperintense in T1W and isointense in T2W, contrast enhancing. The first intramedullary tumour was located right posterolateral at T1 level, had an important exophytic expansion sizing 27/13/12.5 mm, compressing and pushing the spinal cord to the left. It had an associated syringomyelia extending upwards to C4 and inferiorly to T7. The second tumour was also intramedullary exophytic, located left posterolateral at level T3 and measured 5/4 mm. (Figure 1)

Thoracic spine X-ray showed no radiological changes of vertebral bodies.

Cerebral MRI showed a right temporomesial infiltrative tumour.

Blood workout, EKG and pulmonary X-ray showed no relevant changes.

The patient underwent surgery. We performed a longitudinal midline skin incision, from C5 to T5 and bilateral subperiosteal skeletonization of paravertebral muscle from C7 to T4. We performed T1-T3 laminectomies and midline dural incision. We found two intramedullary infiltrative tumours with exophytic components, one located right paramedian at level T1, measuring 2.5/1.5 cm in diameter and another located left paramedian at level T3, measuring 0.5/0.5 cm. We performed total resection of T1 tumour and near total resection of T3 tumour. Haemostasis. Dural closure. Epidural external drainage. Wound closure.

Histopathological exam from both spinal tumours found malignant non-Hodgkin lymphoma. (Figure 2)

Postoperative outcome was favourable, without any additional neurological deficits.
He received dexamethasone 24 mg / d. He began rehabilitation the second day after surgery. He underwent adjuvant radiotherapy.

Two months later, the patient was readmitted with seizures, headache and diplopia. Neurological exam showed paraparesis, right L2 ASIA 3+, right L3 ASIA 3+, right L4 ASIA 3, right L5 ASIA 3, right S1 ASIA 4+, left L2 ASIA 4, left L3 ASIA 4, left L4 ASIA 4 and left L5 ASIA 4. Total motor score on the right side was 41 and on the left was 46. He also had pain and temperature hypoesthesia with level T3 and full sphincter control.

Spinal MRI showed dural contrast enhancement from C3 to T8 and numerous micronodular lesions from T2 to T10, suggestive for drop metastases. The largest lesion sizing 7/8 mm was located at T3 level. (Figure 3)

Thoracic spine X-ray showed T1-T3 laminectomies and no radiological changes of vertebral bodies.

Cerebral MRI showed bilateral cerebellar drop metastases, measuring 0.98 cm on the right and 0.92 cm on the left and right temporo-mesial tumour hypointense in T1W and hyperintense in T2W and FLAIR, without contrast enhancement. (Figure 4)

The patient underwent second surgery and we performed stereotactic biopsy of the right temporo-mesial tumour. Histopathological exam revealed diffuse infiltrative astrocytoma grade II WHO.

For the third surgery, performed under the same general anaesthesia, we performed a minimal left suboccipital craniectomy. Dural mater was cut in X. We found a cortical tumour located immediately inferior to the transverse sinus. We performed total resection of a tumour 1 cm in diameter. Haemostasis. Dural closure. Epidural drainage. Wound closure. Histopathological exam revealed malignant non-Hodgkin lymphoma.

Postoperative outcome was favourable; the patient presented no additional neurological deficits. Under antiepileptic therapy (carbamazepin 200 mg x 3 / d) the patient presented no seizures.

At 6 months follow-up the patients had paraparesis right L2 ASIA 4-, right L3 ASIA 4-, right L4 ASIA 4, right L5 ASIA 4, left L2 ASIA 4+, left L3 ASIA 4+ and left L4 ASIA 4+. 
Figure 1. Spinal MRI. Right posterolateral T1 intramedullary with exophytic mass; polar syringomyelia from C4 to T7; left posterolateral T3 intramedullary tumour with exophytic component

Figure 2. Histopathological exam. Malignant B-cell non-Hodgkin lymphoma. (HE stain, 20x)
Figure 3. Spinal MRI. Dural contrast enhancement from C3 to T8; micronodular drop metastases micronodular T2 to T10

Figure 4. Cerebral MRI. Right temporo-mesial non-enhancing tumour; cerebellar drop metastases
<table>
<thead>
<tr>
<th>No.</th>
<th>Author, year of publication</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bruni J et al., 1977</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Mitsumoto H et al., 1980</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Hautzer NW et al., 1983</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Itami J et al., 1986</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>Landan I et al., 1987</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>Slowik F et al., 1990</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>Wong Chung ME et al., 1991</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>McDonald AC et al., 1995</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>Urasaki E et al., 1996</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>Caruso PA et al., 1998</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>Bekar A et al., 2001</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>Nakamizo T et al, 2002</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>Peltier J et al., 2007</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>Machiya T et al., 2007</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>Matsuyama Y et al., 2009</td>
<td>3</td>
</tr>
<tr>
<td>16</td>
<td>Flanagan EP et al., 2011</td>
<td>14</td>
</tr>
<tr>
<td>17</td>
<td>Lin YY et al., 2012</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>Bhushanam TV et al., 2014</td>
<td>1</td>
</tr>
<tr>
<td>19</td>
<td>Sivi M et al., 2015</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>Guzzetta M et al., 2015</td>
<td>1</td>
</tr>
<tr>
<td>21</td>
<td>Yang W et al, 2017</td>
<td>346</td>
</tr>
<tr>
<td>22</td>
<td>Our case, 2018</td>
<td>1</td>
</tr>
</tbody>
</table>

TABLE I

Primary intramedullary lymphomas

Histopathologic diagnosis is made after surgery (tumour resection or biopsy) or at autopsy. According to WHO classification, the vast majority are B-cell non-Hodgkin lymphomas, with subgroups diffuse large B-cells and follicular being the most frequent. T-cell lymphomas are extremely rare, representing only 1.4% of primary intramedullary spinal lymphomas. Other histopathological types that can be found are small B-cell, Burkitt, precursor cells and unspecified. Primary intramedullary Hodgkin lymphoma is exceptionally rare.

Nowadays the diagnosis is made on MRI. Spinal lymphomas are hyperintense in T2W, in contrast with cranial lymphomas which are isointense. Multifocal lesions with contrast enhancement are pathognomonic for spinal lymphomas. CSF increased cellularity have no specific pattern. Even though MRI was suggestive for a subdural extramedullary tumour, intraoperative findings showed that the tumour was in fact intramedullary with massive exophytic component. The exophytic mass was contiguous with an intramedullary tumour and presented no other attachment to any structure.

Differential diagnosis is made with other intramedullary tumours: astrocytomas, ependymomas, epidermoid and dermoid tumours, metastases, hemangioblastomas, spinal embryonal tumours, multiple sclerosis.

Treatment consists from surgery, for establishing positive diagnosis and spinal cord decompression, concomitant high-dose corticosteroids, followed by adjuvant radiotherapy and chemotherapy.

Discussions

Primary intramedullary lymphomas are rare. So far, besides the two clinical studies reported by Yang et al. and Flanagan et al., only case reports have been described in the literature. (Table 1)

Being so rare, the diagnostic of patients without spinal cord compression syndrome is often delayed, so we must keep in mind this diagnosis to insure a prompt diagnosis and initiate appropriate therapy. Spinal lymphomas must be always suspected in immunocompromised patients.
Surgery is the first step in treatment of patients with spinal cord tumours. The goals of surgery are obtaining tissue for histopathological diagnosis, achievement of maximum tumour removal without inducing new neurological deficits and preservation of spinal stability. In lymphomas, if the tumour is small and does not cause spinal cord compression, there is no need to perform total resection, a biopsy being sufficient. If the tumour is large and compresses the spinal cord, surgical cytoreduction immediately reduces compression. Tumoral cytoreduction may also be beneficial for adjuvant therapy. Surgical decompression improves neurological outcome and survival.9

We performed a posterior approach, through T1, T2, T3 laminectomies. In this way we were able to gain access to both lesions. Although the patients had bipolar syringomyelia extending from C4 to T7, there is no need to address it, because it is secondary, and after tumour resection the syrinx will regress.

There are several ways to resect an intramedullary tumour. The most used surgical route is posterior midline myelotomy. This is a safe anatomic area. Keeping the midline does not induce neurological damage to surrounding structures. This approach is widely used in all intramedullary tumours, especially in those who have no expression on the cord surface. In some cases, when the tumour causes cord distortion keeping within the midline may be challenging. Tumours that come in contact with the cord surface and are not infiltrative display normal structures and can be approach through this safe zone. Exophytic tumours have an important part situated outside the cord. This part is resected first and then the approach can be done through the area where exophytic part of the tumour exited the cord. Intramedullary tumours can be either well-defined or infiltrative. In well-defined tumours the resection is made within the cleavage plane and complete resection is possible, in infiltrative lesions there is no such plane of demarcation and only subtotal or near-total resection is possible. We choose to resect the exophytic component and then enter the cord through this safe area and resect the intramedullary part from inside out. The larger the tumour, and more precisely the larger the area of effraction of the cord, the bigger is the surgical corridor, this is why the bigger tumour could be totally resected and the small one cannot. However, total resection is not needed in lymphomas and the tumour situated at T3 level was not causing compression on the spinal cord.

Intraoperative somatosensory and motor evoked potentials are very useful to monitor the effects on spinal cord induced by surgical gestures.

We did not consider necessary to perform osteosynthesis of the spinal column because the spinal thoracic column is stable and we performed only three laminectomies, with complete preservation of articular facets. Lymphomas have a high sensibility to corticosteroids and immediately after initiating the therapy neurological improvement occurs. Combined adjuvant oncologic therapy with radio and chemotherapy is more effective than either of
them used alone. Chemotherapy consists of cyclophosphamide, vincristine, doxorubicin, methotrexate, cytarabine, rituximab, vincristine.

Lymphomas of the CNS display a highly aggressive behaviour, are prone to disseminate and drop metastases can be found along the neuraxis, intracranial or spinal. Two months after surgery, our patient came with two drop metastases in the posterior fossa and numerous at the spinal level. Despite radiotherapy and chemotherapy, the prognosis is poor. Median survival rate is 6-9 months, and 2 years survival is 32-36%.1,4 Young age, early diagnosis, low stage, follicular histologic type are positive prognostic factors.1

Conclusions
The diagnosis of primary intramedullary spinal lymphoma must be kept in mind in patients with myelopathy. Surgery is needed to provide histopathological samples for positive diagnosis and spinal decompression. Rapid surgical decompression, corticosteroids and adjuvant radiotherapy improve neurological outcome. Primary intramedullary spinal lymphomas have a propensity to disseminate along the neuraxis.

References
Mid-term results in continuous intracranial pressure monitoring in severe traumatic brain injury in children - ERA-NET NEURON Grant

St.M. Iencean1,2, A. Tascu3,4, C.A. Apetrei2, C. Gheorghita5, Tsz-Yan Milly Lo6, Ian Piper7, A.St. Iencean2

1Neurosurgery, “Grigore T. Popa” University of Medicine and Pharmacy Iasi, ROMANIA
2Neurosurgery, “Prof. Dr. N. Oblu” Clinical Emergency Hospital Iasi, ROMANIA
3Neurosurgery, “Bagdasar-Arseni” Clinical Emergency Hospital Bucharest, ROMANIA
4Neurosurgery, “Carol Davila” University of Medicine and Pharmacy Bucharest, ROMANIA
5Neurosurgery, “Sf. Maria” Children Clinical Emergency Hospital Iasi, ROMANIA
6University of Edinburgh (Child Life & Health) / Royal Hospital for Sick Children (Paediatric Critical Care Medicine), UK
7BrainIT Group Coordinator, Principal Health Care Scientist, Neuro-Intensive Care Monitoring Research, UK

Abstract: This article presents the mid-term results of the multi-center grant “Paediatric Brain Monitoring with Information Technology (KidsBrainIT). Using IT Innovations to Improve Childhood Traumatic Brain Injury Intensive Care Management, Outcome, and Patient Safety”, acronym KidsBrainIT, of the Romanian team. Continuous real-time intracranial pressure monitoring is a standard in TBI intensive-care management and ICP-lowering therapy is recommended when ICP is elevated above 20 mmHg or more. Paediatric TBI patients requiring intensive care are recruited from more contributing centres in 4 different countries and the Romanian team includes doctors CA Apetrei, C Gheorghita and A Tascu as principal investigators. Children aged 2 to 16 years who require intensive care management after sustaining traumatic severe brain injury are included in this study in three neurosurgical hospital: "Prof. Dr. N. Oblu” Clinical Emergency Hospital Iasi, "Sf. Maria” Children Clinical Emergency Hospital Iasi and "Bagdasar-Arseni” Clinical Emergency Hospital Bucharest. Continuous ICP and mean arterial blood pressure (MAP) monitoring allow calculation of cerebral perfusion pressure (CPP) and establish of an optimal CPP. The aim of this study is to improve the treatments in severe traumatic brain injury in children.

Key words: cerebral perfusion pressure, children brain injury, intracranial pressure, paediatric brain monitoring
Introduction

Traumatic brain injuries in children represent an important cause of morbidity and the main cause of death in children older than one years of age. As it is presented in the scientific project proposal the “majority of children who survives a life threatening brain trauma have new disabilities that affect how they function throughout the rest of their lives. Currently the best option to improve survival and recovery of children with life threatening brain trauma is to improve their early hospital treatments including intensive care”. Also “the current best therapeutic option to improve severe traumatic brain injury in children outcome is to optimise physiological support in the intensive-care to minimise secondary physiological insults which are proven to negatively affect outcome. We urgently need clinically relevant and readily translatable research that optimises paediatric brain trauma treatment”.

Material and methods

Children aged 2 to 16 years who require intensive care management after sustaining accidental TBI are included in this study in three neurosurgical hospital: "Prof. Dr. N. Oblu" Clinical Emergency Hospital Iasi, "Sf. Maria" Children Clinical Emergency Hospital Iasi and "Bagdasar-Arseni" Clinical Emergency Hospital Bucharest.

This neurosurgical units have same treatment protocols, which include: defined raised ICP treatment guidelines using osmo-diuretics as a first line medical treatment; sedation and muscle relaxant protocol; mechanical ventilation to control PaCO2 to low normal values; using intravenous infusions of vasopressive drugs to drive mean arterial blood pressure to achieve a target CPP; actively controlling core body temperature to normothermia.

Patients’ anonymised clinical data are collected with the cause and nature of injury, age, Glasgow Coma Score (GCS) on admission and after acute non-surgical resuscitation, pupillary responses, initial radiological and computerized tomography (CT), operative and other treatment details. As planned in the scientific project CPPopt calculation and ICP dose-response visualisation analyses are performed and determine if TBI patients with favourable outcome have longer periods of measured CPP within the calculated CPPopt ranges and an enhanced tolerance of raised ICP. Figures 1, 2 and 3 show a case of a 2 years old children with severe TBI and continuous intracranial pressure monitoring intensive care unit.

Figure 1 - Case of 2 years old children with severe TBI and continuous intracranial pressure monitoring
Results

There were a total of 624 children with traumatic brain injury during 8 months in these three neurosurgical departments and 20 patients needed intensive care and 6 children have been ICP and blood pressure monitored, but only three patients were included in this scientific project. In two cases the values of ICP were high and very high and cerebral decompression was performed; unfortunately, the initial clinical condition was extremely severe and evolution was not favorable in these two cases. The third patient monitored showed elevated ICP values up to 28-30 mm Hg, which were medically treated and had a favorable evolution.
Discussion

The number of cases of pediatric TBI vary across clinical and epidemiological studies and our number of over 600 cases in 8 months should be interpreted by reference to only two neurosurgical centers: two hospitals in Iasi and one in Bucharest, so only for two areas from the country. The cases with ICP and CPP monitoring are few and a statistical analysis is not yet conclusive. With regard to cases that needed ICP monitoring, the gender distribution is predominantly male, and the most common cause was the road traffic accident.

Intracranial pressure monitoring is an invasive method but it assured an early detection of increased ICP in children with severe TBI. In our cases of monitored traumatic intracranial hypertension the performed maneuvers were decompressive craniectomy, drug therapy and CSF drainage in accordance with modern therapeutic guidelines.

The relationship between ICP elevation and CPP values is known in the adult, but in the pediatric TBI the studies are not conclusive; so “Chambers et al. proposed age-stratified critical levels of CPP: in the age groups 2–6, 7–10, and 11–16 years, CPP values of 43 mmHg, 54 mmHg and 58 mmHg, respectively, were associated with normal values of ICP and good outcomes”.

Treatment used sedatives, analgesics; hyperosmolar therapy as intravenous mannitol and hypertonic saline to control intracranial hypertension; mild hyperventilation; barbiturates, temperature control and prophylactic anticonvulsants. The routine steroid treatment in children with severe TBI is not conclusive; it has to be individualized and rather it is not indicated because the potential harm from infectious complications. Decompressive craniectomy was performed for controlling intracranial hypertension and it was effective at ICP reduction. Our study will continue with the inclusion of patients and ICP and CPP monitoring with the hope of obtaining conclusive and beneficial results for setting standards in care of severe traumatic brain injury in children.

Conclusion

The best care of severe traumatic brain injury in children requires a multidisciplinary approach in each phase of management. The initial evaluation with prompt diagnosis and multimodal monitoring must be followed by the management of intracranial hypertension (ICP and CPP) to minimize the pathophysiological damage to the brain.

Intracranial pressure monitoring assured an early detection of increased ICP in children with severe TBI.

The findings from our study are directly transferable to a wider clinical audience because no special equipment is required, beyond that is currently used for the routine minute-by-minute physiological bedside monitoring.

This study is within the grant: “Paediatric Brain Monitoring with Information Technology (KIdsBrainIT): Using IT Innovations to Improve Childhood Traumatic Brain Injury Intensive Care”
Management, Outcome, and Patient Safety”, grant: COFUND-NEURON III ERANET - KidBrainIT, funding no.2 / 01/06/2017.

Correspondence
A Tascu, “Carol Davila” University of Medicine and Pharmacy Bucharest, Romania
E-mail: tascu_alexandru@yahoo.com

References
Multidisciplinary approach to orbital fracture repair

V.V. Costan¹, M. Dabija²

¹"Grigore T. Popa” University of Medicine and Pharmacy Iasi, ROMANIA
²Faculty of Dental Medicine, Department of Surgery, Oral and Maxillofacial Surgery

Abstract: The orbit is a frequent location for fracture occurrence, often in association with other fractures of the facial skeleton. Due to the anatomical situation of the orbit at the crossroads of multiple specialties, including maxillofacial surgery, ophthalmology, neurosurgery and otolaryngology, this territory must be managed by multidisciplinary teams for an accurate diagnosis and treatment. This paper focuses on reviewing the main types of orbital fractures, the indication for surgical repair and the contribution of different specialties in the management of various orbital fracture patterns.

Key words: orbit, fracture, multidisciplinary, blow-out, blow-in

Introduction

Fractures of the orbit are often encountered in the context of facial trauma, either isolated or in association with other fractures of the facial skeleton. Over 40% of all facial fractures have an associated orbital involvement (1). The most frequent patterns of fractures including the orbit are orbitozygomatic fractures and naso-orbito-ethmoidal fractures. Isolated fractures of the orbital walls are reported in between 4-16% of facial fractures cases (2). With such a high occurrence and potential for important functional and morphologic impairment, it is important to accurately diagnose and treat orbital fractures.

The orbit pathology is situated at the intersection of multiple medical specialties due to the anatomical location, the neighboring anterior skull base and paranasal sinuses, but also due to its contents consisting of the globe and optic nerve. In a traumatic setting, all the named structures can be damaged to various degrees, necessitating a collaboration between the maxillofacial surgeon, the neurosurgeon, ophthalmologist and otolaryngologist for an accurate diagnosis, treatment and follow-up, aiming for minimal complications.

The anatomic characteristics of the orbital region explain the various fracture patterns and the frequent association of fractures involving multiple facial bones. The orbits and the anterior skull base form a guarding ensemble, in the biomechanical context of the naso-ethmoido-maxillo-fronto-orbital complex. The whole architecture of the nose, paranasal sinuses, the orbits and the anterior
The design of the orbit is well adapted to soften any traumatic impact on its fragile contents. The orbital rims are thickened bone structures forming horizontal and vertical buttresses of the facial skeleton absorbing and resisting the direct force of the impact (4). The orbital fat behaves like a cushion dissipating forces to protect the globe and optic nerve. The thin orbital walls allow for pressure to escape the orbit by fracturing in case of important traumatism, thus avoiding crushing of the intraorbital structures. Similarly, the orbital roof also serves as a pressure release for superior traumatisms, impacting the skull and brain. Its down-fracture dissipates the crushing force directed on the brain substance. In addition to these protective features, the surrounding paranasal sinuses act as air-bags consuming the strength of the traumatism (5, 6, 7). Their role is emphasized by the increased frequency of orbital blow-in fractures in children due to the absence of frontal sinus pneumatization (8).

In relation to the anatomical characteristics, the impact point, strength and direction, the fracture trajectory may interest to various degrees the orbital rims, the walls of the orbit, as well as the adjacent bones of the facial skeleton translating into the frequently encountered clinical forms: naso-ethmoido-maxillo-fronto-orbital complex (CNEMFO) fractures (3), more commonly named NOE complex (naso-orbito-ethmoidal) fractures, orbito-zygomatic fractures, isolated orbital walls fractures including blow-in and blow-out types, and combined orbital fractures comprising the orbital frame and walls (1). Less frequent, but with a high morbidity, is the association of orbital fractures with skull and skull base fractures in high-velocity traumatisms.

The complex shape of the orbit, as well as the anatomical situation in areas of high risk of injury to important structures, make the reconstruction of the orbital cavity a difficult task, often requiring multidisciplinary evaluation, diagnosis and management.

Multidisciplinary evaluation and management

A facial trauma patient is habitually evaluated by a multidisciplinary team in the emergency setting, including maxillofacial, neurosurgical, ophthalmological and otolaryngology consultations together with other necessary consultations for excluding serious injuries in other body parts. Common emergency procedures include maintenance of a patent airway, management of epistaxis and hemostasis for bleeding in soft tissue lacerations, drainage of retrobulbar hematoma, management of persistent oculo-cardiac reflex, and intracranial vascular lesions. The initial consultation is usually determined by the predominant emergency in each case. Diagnostic imaging is recommended in hemodynamically stable patients. Facial fracture repair is performed after the resolution of acute life-threatening injuries.
Clinical examination is often indicative of the type of fracture, but a thin slice CT (Computer Tomography) evaluation is cardinal for the assessment of orbital injuries (9, 10) that may otherwise be missed due to the presence of edema and masked clinical signs and symptoms. Even more so, CT is necessary due to the possible presence of skull base fractures, dura tears, posttraumatic intracranial lesions, possible occurrence of orbital apex syndrome, extraocular muscle incarceration, globe injuries. The three-dimensional reconstruction of the CT images aids the greater understanding of the fracture characteristics and assists in deciding the treatment plan (11, 12). Stereolithic models obtained by mirroring techniques and three-dimensional printing are useful for the choice and modelling of the reconstruction material, particularly in cases of comminuted fracture repair (13).

There is controversy on the indication for surgery and particularly regarding the most appropriate timing for performing surgical repair in orbital fracture cases. The indications for immediate surgery, performed within 24 hours, are less of a subject for debate. Consensus has been achieved regarding emergency interventions in cases of diplopia, incarcerated extraocular muscle and persistent oculo-cardiac reflex (syncope, bradycardia, heart block, nausea, vomiting), emergency intervention for “white-eyed” blowout fracture (patient under 18, minimal clinical signs, superior gaze restriction, muscle entrapment, trap-door mechanism), and also in cases with severe displacement of the globe, orbital apex syndrome, optic nerve compression and high risk of vision loss (14). The debate is ongoing regarding the indications for early (within two weeks) and late surgery (beyond two weeks). Consideration is given to the amount of fracture displacement, orbital volume changes, the comminution of the fracture, the degree of functional and esthetic impairment, the presence of priming neurosurgical lesions, and to the existence of important comorbidities as contraindications for surgery.

It is most difficult to determine the indication for the surgical repair or conservative management in minimally displaced fractures, in the absence of initial symptoms, since posttraumatic changes in the orbital soft tissues could progress with the apparition of late enophthalmos. Most authors agree that in the absence of contraindication, the best functional and cosmetic results are obtained by performing the primary repair of volume modifying orbital fractures, with primary grafting when necessary, or reconstruction using alloplastic materials (15, 16). This is true for the majority of inferior wall, medial and lateral wall orbital fractures. Orbital roof fractures, however, are commonly managed conservatively in almost 90% of cases comprising minimally displaced fractures (12). Possible complications include the onset of pulsatile exophthalmos and orbital encephalocele that has been reported to also occur late after the conservative management of minimally displaced fractures of the superior orbital wall (12). Blow- in fractures with severe displacement, as well as orbital roof fractures with a surface greater than 2 cm² must be closely monitored since there is a high risk of encephalocele development and orbital dystopia (8). For severely and moderately
displaced orbital roof fractures the surgery indication is maintained. The presence of an orbital encephalocele is a surgical indication for the removal of the herniated tissue with closure of the dura and orbital reconstruction (17). Surgery is also performed in the presence of superior orbital wall fractures in association with dural tears and cerebrospinal fluid (CSF) leaks (18). Other situations in which surgery is necessary encompass the presence of intraorbital foreign bodies, or impinging bone fragments causing the compression and lesion of the optic nerve, or of the extraocular muscles.

There is no agreement regarding the best reconstructive material, with some authors advocating for the use of autologous bone grafts (16), while others have obtained good outcomes by titanium mesh reconstruction and thus avoidance of donor site morbidity and associated complications (15, 19). In the absence of treatment due to late presentation, missed diagnosis or delayed surgery due to contraindication, the resulting orbital sequelae can be addressed in late correction procedures, performed after six months from the initial injury, for the maturation of the scar tissue (20, 21). Common orbital sequelae include the presence of enophthalmos, exophthalmos, orbital dystopia, hypoglobus, diplopia, orbital contour changes and facial asymmetry, eyelid malpositioning, epiphora, restriction of eye movements and soft tissue contraction. Following orbital roof fractures in the pediatric population that were managed non-operatively, and other skull and skull base fractures, there is concern for the development of “growing skull fractures” with enlargement of existing communications with the intracranial space, dural tears and brain herniation (22, 23). Timely diagnosis facilitates early intervention and prevention of complications.

Maxillofacial surgery contribution

Fractures of the inferior, medial and lateral orbital walls and rims, in the absence of associated skull and skull base fractures, in conjunction or not with other fractures of the facial skeleton, are managed by the maxillofacial surgeon, after the initial emergency multidisciplinary evaluation. Other fractures that comprise neurosurgical lesions, such as orbital roof fractures, or panfacial and skull fractures, are often managed in mixed surgical teams. Isolated blow-out fractures of the inferior orbital wall account for 22-47% of orbital injuries (24, 25, 26). Orbital floor fractures are often found in association with fractures of the medial orbital wall. Most remaining orbital fractures are found in the context of other facial fractures, mainly orbito-zygomatic fractures, or naso-orbito-ethmoid fractures (1, 3) (Fig. 1-6).

The recognition of emergency situations is key for preserving unaltered visual function. Retrobulbar hematomas in the context of orbital fractures is encountered in 0.45–0.6% of cases. The key to avoiding permanent injury to the optic nerve and posttraumatic blindness is the early recognition of the condition, with the help of the ophthalmologist and adequate imaging, followed by the drainage of the hematoma by lateral canthotomy. It is recommended to perform the drainage within one hour from onset, and under 24 hours, since studies showed that function preservation is better when the interval from...
onset to treatment is shorter (27). Careful monitoring for retrobulbar hematomas must also be performed in the postoperative period. Compression of the optic nerve by displaced bone fragments or intraorbital foreign bodies are also indications for emergency surgery, just like the un-resolving oculo-cardiac reflex. Other lesions indicating the need for immediate surgical treatment are related to the entrapment of the extraocular muscles and orbital fat (trap-door fracture) especially in children, when the thick periosteum causes more pressure on the entrapped tissues (14). The early and late treatment indications vary on the presence of clinical signs, the amount of fracture displacement and orbital volume change, the presence of comorbidities and associated traumatic lesions (19).

The maxillofacial surgeon is familiar with several types of access for repairing orbital fractures and complex midfacial fractures, such as the superior eyelid, inferior eyelid, transconjunctival, intraoral approaches, and the coronal flap offering exposure for the frontal skull, temporal regions, the superior, medial and lateral orbit (28, 4). The coronal flap is often used in mixed approaches for repairing skull fractures, frontal sinus fractures, superior orbital rim fractures, NOE fractures, and fractures of the orbital roof, particularly the blow-out type. The blow-in type of orbital roof fracture can be adequately accessed and repaired through an upper lid approach, in mixed surgical teams (29). Additionally, the closure of large CSF fistulas associated with tissue loss may be performed in mixed surgical teams, by using various types of pedicled or free flaps.
Orbital roof fractures are encountered in less than 9% of facial fractures in most studies (12, 18, 30). They are reported more often in children under the age of seven, because of the anatomical characteristics with incomplete frontal sinus development and a more prominent frontal region (18, 30, 31). In isolated superior orbital wall fractures, the direction of the impact force determines the type of fracture, with either a “blow-out” mechanism, which is more common and often determining orbital volume enlargement and
enophthalmos, or a “blow-in” mechanism seen in high velocity traumatisms, determining the diminution of the orbital volume and the onset of exophthalmos. As previously described, most orbital roof fractures are managed conservatively. Still, indications for surgery should be carefully revised and adequate monitoring of the patient must be implemented, for early diagnosis of possible complications. Surgical procedures for repairing orbital roof fractures often imply a collaboration between the neurosurgeon and maxillofacial surgeon for achieving adequate access. Simple blow-in orbital roof fractures can be surgically approached through an upper blepharoplasty palpebral incision, while blow-out fractures are more challenging, requiring a neurosurgical craniotomy approach via a coronal incision (29).

Severe neurosurgical lesions and ophthalmologic injuries may be encountered in conjunction with orbital roof fractures, consisting of brain injuries, pneumocephalus, dura tears, CSF leaks, pulsatile exophthalmos, orbital meningoencephalocele, entrapment of the extraocular muscles, globe rupture, optic neuropathies, retrobulbar hematoma (18). The morbidity is increased when there is association with other fractures of the orbital rims (Fig. 7-10), skull, skull base and facial skeleton. Orbital roof fractures, skull and skull base fractures in children require special neurosurgical surveillance, especially in cases where there is evidence of dural tears. This is due to the possibility of developing “growing skull fractures”, needing early diagnosis and management for prevention of complications and sequelae (22, 23).
Figure 9 - Coronal CT section demonstrating the displaced left intraorbital fractured fragment impinging on the left globe and the superior rectus muscle

Figure 10 - Sagittal CT section showing the presence of the displaced intraorbital fragment causing pressure on the globe and on the superior rectus muscle

Otolaringology contribution

Otolaryngology is often the first examination performed in the emergency setting for the management of epistaxis, frequently encountered in facial traumatisms, particularly in association with midface, lateral face and central face fractures.

Isolated naso-orbito-ethmoid fractures represent approximately 5% of facial fractures in adults, but they have a high incidence in the context of other facial fractures. More than half of all NOE fractures are associated to orbito-zygomatic fractures, while 20% are found in the context of panfacial fractures (32). The most challenging part in the treatment of central face fractures is management of the frontal sinus. Fractures located here often interest both the anterior and the posterior bone plates, with the possible occurrence of dura tears and brain herniation. Multidisciplinary management is important for minimizing the morbidity and achieving good functional and cosmetic outcomes. Complications of frontal sinus fractures include the formation of mucocele, sinusitis, osteomyelitis, meningitis, encephalocele, cerebrospinal fluid fistula, central face deformity (33). In the presence of small dural discontinuity and CSF leaks, conservative treatment may often lead to the spontaneous closure of the fistula, justifying the observation of these fractures for up to one week before considering surgery. Frontal sinus obliteration or cranialization is indicated in cases where the ventilation of the frontal sinus cannot be reestablished (33). The endoscopic management of central face fractures allows for a minimally invasive approach and accurate visualization (32). In skull base fractures with cerebrospinal fluid fistulas, local flaps from the nasal cavity can be utilized for the closure of CSF leaks using an endoscopic technique.

Fractures of the medial and inferior orbit can also be accessed endoscopically, or by a combined approach comprising a transconjunctival and an endoscopic trans-
nasal access (34, 35). There are some disadvantages to the entirely endoscopic approach consisting of difficult insertion of the reconstruction material, with the orbital contents being supported by the nasal packing, which predisposes to the onset of postoperative enophthalmos. Thus, a combined open and endoscopic approach would associate the superior endoscopic visualization of the posterior bone ledges, with the improved access for titanium mesh insertion (34, 35).

**Ophthalmology contribution**

Careful observation and interdisciplinary management are mandatory in orbital fractures, frequently requiring multiple ophthalmological examinations. One in four patients with orbital fractures has an associated ocular lesion (36). It is for this purpose that any periorbital trauma patient must be initially evaluated by an ophthalmologist. The eye examination involves determination of ocular lesions in the anterior or posterior segments, diagnosis of a globe rupturing or retrobulbar hematoma. Evaluation of eye mobility and the degree of exophthalmos and enophthalmos may not be accurate in the presence of posttraumatic edema and necessitates subsequent examinations. Studies have shown that the greatest risk for posttraumatic vision loss in orbital fracture patients is found in the ones presenting with penetrating orbital lesions, in patients with diagnosed fractures of the posterior orbit, involving the orbital apex, patients exhibiting a decrease in visual acuity, or an afferent pupillary defect (36, 37).

Ophthalmologic examinations are important in the perioperative period to rule out the occurrence of a retrobulbar hematoma, which represents an indication for emergency drainage surgery through lateral canthotomy. The finding of postoperative retrobulbar hematomas has decreased since the implementation of fenestration for reconstructive materials used in orbital surgery (38), but nevertheless the importance of periodic inquiry regarding visual acuity in the postoperative time remains crucial for the timely intervention in case of compressive hematoma development.

The ectropion-related ophthalmologic sequelae that are frequently linked to periorbital traumatisms may lead to a decrease in the life quality of the patient and often necessitate repeated correction procedures.

**Conclusion**

Maxillofacial surgeons, neurosurgeons, otolaryngologists and ophthalmologists handling the acute orbital trauma patient should be familiar with the possible complications, the indications for immediate, early and delayed surgery, or for the conservative management in different patterns of orbital fractures. Good collaboration between the different specialties increases the chances for early diagnosis, accurate operative or non-operative management with proper follow-up and minimal complications. The surgical approach often requires a multidisciplinary participation for achieving a good exposure, performing a proper anatomical repair, resulting in favorable functional and aesthetic outcomes.
References


Mirror, mirror on the wall, who’s the fairest of them all?
Atypical meningioma associated with multiple meningiomas

A.I. Cucu¹, Claudia Florida Costea¹,², Mihaela Dana Turluc¹,², Gabriela Florenta Dumitrescu¹, Anca Sava¹,², I. Poeata¹,²

¹“Prof. Dr. N. Oblu” Emergency Clinical Hospital, Iași, ROMANIA
²“Grigore T. Popa” University of Medicine and Pharmacy, Iași, ROMANIA

Abstract: The incidence of multiple meningiomas (MMs) without stigmata of neurofibromatosis or family history of meningiomatosis is rare. MMs with atypical histology are even rarer, since most of them have benign histology. The authors report three cases of MMs, of which the symptomatic meningioma removed was an atypical meningioma (AM). We also review their possible pathogenesis and histopathology. Although there has not been established any MMs management and therapy strategy so far, our recommendation is to treat symptomatic and accessible lesions or growing tumours and also to prefer a conservative approach consisting of the imaging follow-up of asymptomatic lesions.

Key words: atypical meningioma, multiple meningiomas, meningiomatosis, WHO grade II meningiomas

Introduction

The first description of a multiple intracranial meningiomas dates back to 1889 and was made by Anfimov and Blumenau, who had found one large and four small tumours on an autopsy that they performed (1). Later on, in 1938, Harvey Cushing and Louise Eisenhardt explained the pathology of this entity and used the term “multiple meningiomas” to refer to the case of a patient who had “more than one meningioma and less than a diffusion of them” (7).

Meningiomas represent about one third of all primary brain tumours in adults (8, 11), with an incidence that has increased in recent years (10, 35). Majority of meningiomas are solitary (33), and MMs are defined as the presence of ≥ 2 spatially separated metachronous or synchronous meningiomas and represents up to 10% of all meningiomas (18, 20). They may be sporadic, radiation induced or familial, when they occur as type 2 neurofibromatosis or familial meningiomatosis (33).

Nowadays, the term MMs is used to
describe a condition in which a patient has the simultaneous or sequential appearance of two or more independent meningiomas, whether the tumours have the same pathologic subtypes or not (13). Nonetheless, Borovich et al. considers that MMs might be truly multiple when tumours from the same patient have different histological subtypes and multicentric when tumours have the same histology (3).

The pathophysiologic mechanisms underlying the occurrence of MMs have not yet been fully understood and thus two different hypotheses have been suggested so far (16, 34, 37). According to the first theory, multiple lesions originate from multicentric neoplastic foci and grow independently under the stimulation of a supposed tumour-producing factor. The second theory argues that a signal transforming event occurs and an original clone of neoplastic meningothelial cells spreads throughout the meninges or along the cerebrospinal fluid, leading to the formation of multiple clonally tumours (13, 16, 34, 37). Nevertheless, the tumour histology and dynamics of histopathological changes undergone by these multiple lesions in time have not been fully understood.

MMs also give rise to special treatment problems, the most important of which are as follows: which lesion is symptomatic, which lesion needs to be treated and what is the best therapeutic approach, what is the best treatment option and how should incidental MMs be managed? Due to these aspects, and also to their relative rarity, unclear aetiology and issues related to management strategy (29), MMs have raised the specialists' interest and they should constitute a priority in meningiomas treatment.

**Methods**

We followed the 3 years evolution of three patients with MMs who underwent surgery in the "Profesor Dr. Nicolae Oblu" Emergency Clinical Hospital of Iasi in 2010, 2012 and 2013, respectively. The inclusion criteria were adult patients (>18 years) with diagnosis of ≥ 2 separate meningiomas on MRI examination, one of which removed by surgery and diagnosed with AM (WHO grade II). The exclusion criteria were patients with type 2 neurofibromatosis, history of radiotherapy or familial types.

**Results**

The 3 cases of MMs with AM are shown in Table 1.

**Case 1.** A 64-year-old male patient has had slowly progressing vision disorders for about 2 years, which were examined by several ophthalmologists. He had decreased visual acuity in both eyes. The MRI examination reveals three MMs: one diaphragm sellae meningioma with a right parietal meningioma and a left parietal meningioma (Figure 1). Through a left fronto-temporal approach the meningioma of the diaphragm sellae was completely resected with good optic chiasma and pituitary stalk decompression (Figure 1). Postoperative ophthalmologic exam revealed that visual acuity of right eye was 6/6 and left eye - 1/500 BCVA. Also, the fundus examination revealed normally coloured and regular edges of the optic disc, C/D ratio 0.3 for right eye and 0.4 for left eye.

**Case 2.** A 65-year-old female patient is hospitalized for intracranial hypertension syndrome with cerebellar syndrome. The MRI
scan reveals the presence of a left transverse sinus meningioma (Figure 2. A) with an associated left parasagittal meningioma (Figure 3). The left transverse sinus meningioma was resected through a paramedian suboccipital approach (Figure 2. B.). Total 0.9 Gy irradiation is also performed, both for the remaining tumour on the left transverse sinus and for the left frontal parasagittal meningioma.

Case 3. A 73-year-old female patient was admitted for gait disorders that have set in 2 years before and have progressively worsened and for 1-month-old intracranial hypertension syndrome. The MRI scan reveals superior sagittal sinus meningiomatosis. The surgical procedure, performed through a parieto-occipital approach, consists of intracapsular tumour resection and partial sinus and infiltrated falx cerebri resection (Figure 4).

In all three patients, both the meningiomas resected and the other meningiomas were followed by yearly MRI scan. The follow-up revealed that, 3 years later, the MMs had not increased in size. As concerns AM recurrence, a 0.1 cm increase of left transverse sinus meningioma was noted in case 2 after one year.

<table>
<thead>
<tr>
<th>Location (AM)</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>diaphragm sellae meningioma</td>
<td>left transverse sinus meningioma</td>
<td>parieto-occipital meningioma</td>
<td></td>
</tr>
<tr>
<td>Location of the other meningiomas</td>
<td>right parietal</td>
<td>left parasagittal</td>
<td>superior sagittal sinus meningiomatosis</td>
</tr>
<tr>
<td>Age, sex</td>
<td>M, 64 years</td>
<td>F, 65 years</td>
<td>F, 73 years</td>
</tr>
<tr>
<td>Symptoms</td>
<td>visual acuity decreased visual acuity in both eyes</td>
<td>intracranial hypertension syndrome, cerebellar syndrome</td>
<td>spastic paraparesis, intracranial hypertension syndrome</td>
</tr>
<tr>
<td>Ki - 67</td>
<td>4%</td>
<td>4.7%, with 7.59% on a field</td>
<td>6%</td>
</tr>
</tbody>
</table>

**Discussion**

Demography. As concerns the patients' demographic data, our findings are in accordance with other research shown in literature, which proves that the mean age of presentation with MMs is the 6th decade of life and it is the same as for patients with solitary meningioma (12, 13, 26, 27, 33).

MMs occur much more frequently in females than in males, and their predilection for the female gender is considerably higher than for the male gender, studies showing a significantly higher F: M ratio of 3.5:1 in MMs.
(12, 13, 27). However, it is still unclear why female preponderance is much higher in MMIs than in solitary meningiomas, yet according to a recent hypothesis, hormonal dependency may be higher, which may be accounted for by the stronger progesterone expression in these tumours compared with their solitary counterparts (13, 32, 33). Moreover, Tsermoulas et al. argue that genetic factors may enhance the potential for tumorigenesis in women (33). Our case series also exhibited a female predilection, as two of the three patients were women.

![Figure 1](image_url)

**Figure 1** - (Case 1) Preoperative (A) and postoperative (B) sagittal T1-weighted images with contrast. Multiple meningiomas with one right parietal meningioma (C) and one left parietal meningioma (E).
Figure 2 - (Case 2) Preoperative (A) and postoperative (B) axial T1-weighted images with contrast of a left transverse sinus meningioma.

Figure 3 - (Case 2) Axial T1-weighted images with contrast showing a left parasagittal meningioma. No increase in size of meningioma was observed at 3 years of follow-up.
Symptomatology

The frequency of symptoms in MMs was proportional to the size of the tumours, the largest meningiomas being more asymptomatic, which was to be expected, since the mode of presentation of meningiomas is due to their mass effect. Skull base and midline meningiomas are more symptomatic than convexity meningiomas (33), and the most common location for meningiomas in asymptomatic patients has proven to be the convexity (22). In our case series, the symptoms were due to the mass effect on optic
chiasm and optic nerves (case 1), cerebellum (case 2) and motor cortex (case 3).

MMs distribution in the intracranial space. According to the literature, in MMs most patients have a major meningioma accompanied by one or several smaller meningiomas (12, 13), which was also true for two of our patients: the two large skull base meningiomas (the diaphragm sellae meningioma and the transverse sinus meningioma) were accompanied by convexity meningiomas (Figure 1. C and E) and parasagittal meningiomas (Figure 3). As concerns this association, in a study that included 39 patients with MMs, Huang et al. noted that in MMs a major meningioma is often accompanied by one or more smaller meningiomas (13). This was also reported by Domenicucci et al. that found that 11 of the 14 cases of MMs were composed of small and large meningiomas (12). Thus, Huang et al. argue that several different-sized tumours in the same MMs case would be an indication of the fact that meningiomas may develop at different times and that it is possible that an original major meningioma may disseminate to form multiple foci through the subarachnoid or subdural space (13).

In the same study, they noted that the main location of MMs is the cerebral convexity (12, 13). Huang et al. think that this predilection may be accounted for by the assumption that MMs develop from the major meningioma through the subarachnoid space, since disseminated meningioma cell tend to grow at the cerebral convexity by the circulation of the cerebrospinal fluid (13). This theory is also supported by the location of most of the MMs in the hemicranial space in some studies (4, 34).

Histopathology. In MMs, most meningiomas are benign (WHO grade I) and have uniform histology, the atypical or anaplastic subtypes being rare (15). Nevertheless, most meningiomas are benign on presentation. Thus, Turgot et al. removed 28 meningiomas from 8 patients, of which 14 were meningothelial (50%) (34). The predominance of the meningothelial subtype is also supported by Domenicucci et al.’s patient series (12). Other authors also reported predominantly benign histologies, yet different, like the fibrous and transitional subtypes (21) or the psammomatous type (27).

As concerns meningioma histology in the same patient, some studies have shown that the same patient may have meningiomas of different grade and different histological features (13, 19, 21). In a study that they recently published in 2017, Tsermoulas et al. also found that among patients who had more than 2 meningiomas removed, about 1 in 5 had tumours of different grades and most of them had different histological subtypes. From this point of view, some authors argue that these findings are evidence of the different origins of tumours from multiple foci and that their multiplicity is not the consequence of cell migration through the subarachnoid space (4, 19, 21). On the other hand, other authors have supported the theory of clonal spread from a single tumour (13, 16, 17, 24, 27, 30, 37). Some authors are of the opinion that both theories may apply in different cases and that further research on the genetics of MMs would clarify
the controversial standpoints on the histology and pathogenesis of these lesions (33).

Atypical meningiomas. As we have said before, most of the published series concluded that the vast majority of MMs cases described in literature have benign histology (27, 34), the atypical or anaplastic subtypes being rare (15). As far as the simultaneous occurrence of benign and atypical histological grades in sporadic MMs is concerned, Mocker et al. consider that this is extremely rare (19), as literature contains only few reports of benign histological types mixed with atypical types (4, 19, 23, 31).

Tumour recurrence is one of the main problems that have to be dealt with in AM management (8). Thus, Huang et al. found that four meningiomas in three patients were AM and all of these three patients had recurrence after the operation (13). In our three-patient series, only one AM exhibited tumour recurrence after 2 years (case 2). As concerns the other meningiomas, on which no surgery was performed, they did not grow in size during our 3 year follow-up (Figures 1 and 3). Our findings are in line with Wong et al., who did not note the tumour growth rates in patients with MMs to be higher than the growth rates of incidentally found solitary meningiomas (36).

Genetics of meningiomas. The most significant genetic abnormality in sporadic solitary meningiomas is the loss of heterozygosity on chromosome 22, which occurs in about 50% of patients. An early event of tumorigenesis in one third of these cases was found to be the somatic mutation of the NF2 gene (22q12.2) (5). On the other hand, familial MMs do not show mutation or loss of NF2 (28).

Some authors have described genetic alterations associated with meningioma progression and initiation, yet it is not yet possible to predict the rate of tumour growth or the probability of tumour recurrence (6). Thus, the genetics of tumour nodules for the appearance of MMs not yet fully known (19).

Management. Not all patients with MMs require treatment, and a challenge in the management of MMs may be the identification of the responsible tumour. In this algorithm, surgical removal remains the main form of treatment. Since the neurological deficits are usually caused by major tumours and peritumoral oedema, the size of the meningioma is an important factor in determining which of the meningiomas need to be removed (9, 13).

Radiosurgery seems to be an attractive and interesting option for MMs up to 3 cm in diameter or residual tumours, but further research is required to establish its effectiveness and determine whether it is safe or not (33). Therefore, the authors’ opinions are controversial: some of them support the treatment of asymptomatic meningiomas with prophylactic radiosurgery, even without documented growth (14, 25), whereas others are more reserved on that point and they report a complication rate of radiosurgery of 10% (26). As far as MMs prognosis is concerned, it depends on the grade of the tumour, on the histological types and on the resection degree of the tumour (2, 8).
Conclusions

There has not been established any MMs management and therapy strategy so far. Our recommendation is to treat the symptomatic or the potentially symptomatic tumours and to avoid useless procedures and complications. The form of treatment is surgical removal, but radiotherapy may also be considered and may also play an important role, especially for AM. Nevertheless, even in MMs only some of the lesions require treatment, since most of them are small and asymptomatic and they only require clinical and imaging follow-up. Our philosophy is to treat symptomatic and accessible lesions or growing tumours and to apply the conservative approach, consisting of imaging follow-up for the asymptomatic lesions.

Correspondence
Claudia Florida Costea
"Prof. Dr. N. Oblu" Emergency Clinical Hospital,
Iasi, Romania
E-mail: costea10@yahoo.com

References
Thoraco-lumbar spine injuries – a retrospective study on 651 cases

Ioana Viorela Jitaru, Al. Stan, Antonia Nita, C.E. Popescu

Emergency Clinical Hospital "Prof. Dr. N. Oblu", Neurosurgery, Iasi, ROMANIA

Abstract: Introduction: Thoracolumbar spine fractures are common injuries that can result in significant disability, deformity and neurological deficit. There are standard classification systems that have been described based on fracture morphology, injury mechanism, neurological deficit and injury to posterior ligamentous complex. The thoracolumbar junction (T10-L2) is uniquely positioned in between the rigid thoracic spine and the mobile lumbar spine. This transition from the less mobile thoracic spine with its associated ribs and sternum to the more dynamic lumbar spine subjects the thoracolumbar region to significant biomechanical stress. Hence, fractures of the thoracolumbar region are the most common injuries of the vertebral column. Material and Methods: This retrospective study was conducted on 651 cases with thoracolumbar spine fractures admitted in Emergency Clinical Hospital “Prof. Dr. N. Oblu”, Neurosurgery, Iasi, Romania between Ian 2014- Dec 2017. Conclusions: Trauma to the thoraco-lumbar spine and spinal cord is potentially devastating injury an it can be accompanied by significant neurologic damage , including paraplegia . Patients with incomplete neurologic deficits may regain a large amount of useful function with early or rapid surgical treatment. Imaging studies are essential to confirm the exact location of lesion, to assess the stability of the spine. Key words: Thoracolumbar spine fractures

Introduction

The thoracolumbar junction (T10-L2) is a biomechanical transition zone prone to injury because of an inherent susceptibility to the kinetic energy transfer from the stiff, rostral thoracic spine to the relatively more flexible, caudal lumbar spine(1). The most common mechanisms of injury are those of a high-velocity pattern; these include motor vehicle collisions, falls, occupational injuries, and sport injuries.(2) High-velocity bony injuries carry an additional 25% risk for accompanying spinal cord injury (SCI) and 30% risk for intra-abdominal injury. Further complicating this problem is the estimated rate of 50% of concomitant neurological injury that is associated with these fractures.(3) Estimates of the North American incidence of
thoracolumbar traumatic injury ranges from 12 to 50 million patients annually, mostly occurring in the adolescent to young adult population aged 15 to 29 years. With the aforementioned 50% rate of neurological injury, 6 to 25 million new cases of neurological injury per year can be expected in a demographic whose subsequent lifelong disability results in a huge societal cost from an injury that occurred during their chief productive years.(1-5)

**Classification of thoraco-lumbar spinal injuries**

With the variety of fracture morphologies that can be seen at the thoracolumbar junction, multidisciplinary teams caring for the trauma population have sought for a simplified classification scheme for determining spinal stability and recommended management. The initial classification schemes have focused on fracture types. Because of the highly controversial status of the preferred management of thoracolumbar burst fractures, classifying thoracic and lumbar injuries has been a modern topic of research interest. One reason for the lack of consensus among health care providers is the presence of level I evidence supporting the management of stable thoracolumbar burst pattern fractures in patients without neurological deficit with the use of an orthosis. In this study, equivalent outcomes were found between bracing and arthrodesis. With the considerable number of fracture morphologies, a simplified algorithm for evaluating and organizing fractures gave birth to early thoracolumbar classification systems (1). Modern classification systems not only evaluate the fracture pattern but also have evolved with our understanding of the likelihood of a patient’s need for surgery through our knowledge of factors that contribute to spinal instability. The extent of canal compromise and morphology of the thoracolumbar fracture type, presence of a neurological deficit, and radiographic findings that constitute a stable thoracolumbar spine are three major areas of confusion that play a major role in the newest classification system in use, the thoracolumbar injury classification and severity score (TLICS), a classification system put forward by the Spinal Trauma Study Group (STSG).(1, 3, 6, 7, 8)

**AOSpine Thoracolumbar Spine Injury Classification System**

In 2013, the TLICS was further expanded and developed into a newer AOSpine thoracolumbar spine injury classification system. This classification system was developed by an international panel of members evaluating three basic parameters: morphologic classification of the fracture, neurological status, and clinical modifiers. The morphologic classification is based on three main injury patterns: type A compression (including wedge impaction, split pincer, incomplete burst, or complete burst, type B tension band disruption (divided between osseous and osseoligamentous disruptions), and type C displacement-translation (hyperextension, translation, or separation) injuries. Eight subtypes were proposed (five in the A group, three in the B group, and one in the C group). Additionally, clinical modifiers were incorporated to address indeterminate injuries and patient-specific comorbidities such as ankylosing spondylitis and diffuse idiopathic skeletal hyperostosis. Unlike the TLICS, the updated AOSpine classification is based on CT scan, an imaging tool widely
available at trauma centers worldwide. This classification adds clinical aspects that can better guide fracture management when combined with a severity score in the future. However, clinical validation requires large prospective observational studies.

**Thoracolumbar Injury Classification and Severity Score**

Proposed by the STSG, the TLICS set out to standardize the decision-making process for operative versus nonoperative management of thoracolumbar spine fractures. For this classification, the STSG evaluates the integrity of the PLC, the injury mechanism, and the presence of a neurological deficit. Disruption of the PLC is given special attention, creating conditions of near instability as detected by MRI. Hence, PLC injury provides enough points alone to warrant surgical correction. (6)
Material and Methods

This retrospective study was conducted on 651 cases with thoracolumbar spine fractures admitted in Emergency Clinical Hospital “Prof. Dr. N. Oblu”, Neurosurgery, Iasi, Romania between 2014-2017.
Inclusion criteria: patients diagnosed with T-L injuries, recent injuries (<30 days) regarding the neurological status.
Exclusion criteria: minor injuries, pathological fractures.

**Sex distribution**
In all 3 studies we can see that the majority of the patients were males (60%).

**Age distribution**
The average age was 52.26, between 8 and 86 years old with 2 peaks between 41-50 in men and 61-70 in women.

**Mechanism**
Regarding the mechanism the most frequent are falls from a height (41%), followed by car accidents (14%). Other mechanism implicated are falls from the same level (9%), from cart (6%), aggressions (7%) and unknown (23%).
Treatment options

There are 2 options for treatment: conservative and surgical. We used a conservative treatment in 65% cases (stable lesions A-type). Indication for surgery: patients with neurological deficit, unstable lesions, TLICS >5. Regarding surgical treatment we use a posterior approach with a short or long instrumentation, an anterior approach or in selected cases a combined one (9).
Results

Overall the results for surgical treatment have a good outcome for patients with A3, B1, B2 fractures because in this cases we use short instrumentation, one level above and one level below the lesion. For patients with A4 fractures the results were less satisfying with short instrumentation due to the degree of comminution (Load-sharing >6 points). In this cases we recommend anterior reconstruction and posterior fixation. Postop patients were clinical evaluated at 45 days, 3, 6, 12 months. For the evaluation of pain we used the Visual Analog Scale (VAS) (fig 1), ODI, kyphosis angle (KA) and vertebral body height (VBH).
### Table: Moment of evaluation

<table>
<thead>
<tr>
<th>Moment of evaluation</th>
<th>Conservative treatment</th>
<th>Surgical treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>9,1 (8 – 10)</td>
<td>9,2 (8 – 10)</td>
</tr>
<tr>
<td>At 3 months</td>
<td>5,3 (4 – 7)</td>
<td>4,1 (3 – 6)</td>
</tr>
<tr>
<td>At 6 months</td>
<td>4,4 (3 – 6)</td>
<td>2,4 (1 – 3)</td>
</tr>
<tr>
<td>At 12 months</td>
<td>3,4 (2 – 4)</td>
<td>1,8 (1 – 3)</td>
</tr>
</tbody>
</table>

It is seen an important decreasing pain at 3 months after the injury regardless of the type of treatment. Though patients who underwent surgery had less pain at 12 months.

KA and the reduction of the VBH in the anterior segment of the vertebral body for the patients treated conservatively are represented in the next table:

### Table: KA and VBH

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>At 6 months</th>
<th>At 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>KA</td>
<td>13,80</td>
<td>16,53</td>
<td>17,42</td>
</tr>
<tr>
<td>VBH %</td>
<td>73,8</td>
<td>65,4</td>
<td>63,7</td>
</tr>
</tbody>
</table>

For this patients we can see an increase in local kyphosis with approx 4 degrees and a reduction of VBH with 10% at 1 year after the injury.

### Surgical treatment

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>At 6 months</th>
<th>At 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>KA</td>
<td>14,22</td>
<td>11,2</td>
<td>13,8</td>
</tr>
<tr>
<td>VBH %</td>
<td>67,4</td>
<td>63,5</td>
<td>62,7</td>
</tr>
</tbody>
</table>

For the patients treated surgically the local kyphosis decreased with 0,4 degrees and the VBH decreased with 5% at 1 year after surgery. Statistically the KA decreased significant in the group of patients treated surgically (p<0,01).

### ODI

<table>
<thead>
<tr>
<th>Evaluation moment</th>
<th>ODI conservative</th>
<th>ODI surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>82,5 (73 – 88)</td>
<td>84,3 (69 – 92)</td>
</tr>
<tr>
<td>At 3 months</td>
<td>48,4 (33 – 53)</td>
<td>39 (28 – 47)</td>
</tr>
<tr>
<td>At 6 months</td>
<td>30 (21 – 38)</td>
<td>21 (16 – 28)</td>
</tr>
<tr>
<td>At 12 months</td>
<td>23 (17 – 32)</td>
<td>18 (9 – 28)</td>
</tr>
</tbody>
</table>

We can see an important decrease with 50% of the disability at 3 months after the treatment but at the final evaluation we can't see any significant difference between this 2 groups.

### Discussion

In spine surgery, there is an ongoing effort to increase the knowledge of spinal surgery with the generation of well-designed, prospective, randomized trials. Wood and colleagues, in a randomized prospective trial comparing operative and nonoperative treatment of thoracolumbar burst fractures, found no clinically significant advantage of surgery. In the surgical arm, the choice of an anterior, posterior, or combined approach was left to the discretion of the surgeon (3,10). Siebenga and associates in a multicenter prospective randomized study of operative versus nonoperative treatment of thoracolumbar burst fractures, concluded that surgery resulted in fewer deformities at the mean 4-year follow-up but in superior functional and pain outcome scores (11). Gnanenthiran and colleagues in a meta-analysis comparing operative and
nonoperative outcomes for thoracolumbar burst fractures, found four prospective studies, only two of which were randomized. They concluded that patients who underwent surgery tended to have lower rates of kyphosis, but these patients did not statistically differ in terms of functional and pain outcomes at 4 years. However, because thoracolumbar burst fractures are not all the same with regard to their likelihood of developing kyphosis or instability, future prospective studies should incorporate the TLICS system into the inclusion and exclusion criteria.(12)

Operative planning is a multifactorial decision-making process. Arguably, the most important factor for determining anterior or posterior approach is the location of the pathology. The most common pathologies at the thoracolumbar junction are anterior and middle column (axial compression mechanisms, e.g., compression or burst). One other pitfall in prospective studies is the heterogeneity of treatment plans with regard to combining anterior, posterior, or combined approaches. However, modern techniques allow for all three columns to be addressed by the posterior approach (14). Also, less invasive techniques such as percutaneous pedicle screw instrumentation and lateral interbody placement allow for stabilization as needed, with minimal disruption. For specific pathology, such as retropulsed fragments into the canal, some authors argue that an anterior, retroperitoneal approach allows for the greatest ease of neural decompression. However, many advocate for the benefits of a posterolateral approach in the ability to access all three columns, decompress retropulsed anterior pathology, and provide three-column stabilization through an anteriorly placed graft as well as a pedicle screw-rod construct. Lin and colleagues compared anteroposterior with posterolateral decompression and instrumented fusion, finding no statistically significant difference between the two groups with respect to all functional and radiographic outcomes scores.(13)

One systematic review of posterior versus anteroposterior decompression and fusion for thoracolumbar burst fractures found a greater degree of restoration of the sagittal anatomic alignment at the higher cost of blood loss, extended hospital stay, longer intraoperative durations, higher morbidity, and higher monetary costs for anterior – posterior approach.

In our cases we had less satisfying results in patients with A4 fractures who had a short fixation due to the degree of comminution in comparison with the other spine units.

Conclusion

The management of thoracolumbar junction pathology remains controversial. The TLICS represents the latest advancement in classification, providing a standardized guide for possible surgical management of thoracolumbar junction fractures. Using both AO spine revised classification and TLICS score we can establish more accurately the surgical indication.

The conservative treatment is a reliable solution for patients with simple stable fractures and no neurological deficit. Surgical treatment is the best solution for patients with
unstable fractures, complex fractures and neurological deficit.

Trauma to the thoraco-lumbar spine and spinal cord is potentially devastating injury and it can be accompanied by significant neurologic damage. Patients with incomplete neurologic deficits may regain a large amount of useful function with early or rapid surgical treatment.

Correspondence
Alexandru Stan – alexandrustan21@yahoo.com

References
Thrombectomy for ischaemic stroke in a young patient.

Case presentation

A. Chiriac, Georgiana Ion1, N. Dobrin1, Z. Faiyad1, I. Poeata

"Grigore T. Popa” University of Medicine and Pharmacy, Iasi, ROMANIA
1“Prof. Dr. N. Oblu” Clinic Emergency Hospital, Iasi, ROMANIA

Abstract: Acute Ischemic stroke in young patients has been increasingly diagnosed with the development of neuroimaging technique. Early endovascular treatment can lead to significant improved functional outcome. We present a case of 19-years old boy with acute ischemic stroke by distal middle cerebral artery occlusion. A selective thrombus aspiration with Penumbra system was performed. Satisfactory recanalization was achieved with significant recovery of the patient.

Key words: thrombectomy, ischemic stroke, young

Introduction

Ischemic stroke is a devastating disease that affects young adults with incidence ranges from 3.4 to 11.3/100,000 people per year in primarily white population. Endovascular thrombectomy for an acute ischemic stroke in young patients is a lifesaving treatment that also leads to eloquent functional outcome. Wide spectrum of etiologies, risk factors and management strategies for ischemic stroke in young patients were described, in correlation with factors such as genetic differences, environmental influences, and the development and accessibility of health services. Better surviving chances have been reported in stroke to young group of patients than older ones. However, the ability of prediction and early diagnosis would be of maximum importance in this patient population category[2,7,8].

In this report, we present our experience with a case of young patient with acute ischemic stroke, which was successfully treated with mechanical thrombectomy, by using Penumbra's aspiration system.

Case presentation

The patient was a 19-years-old, right-handed boy, with no significant past medical history, developed sudden onset of dysarthria, left-sided weakness at 9:30 I the morning. He was taken to a primary emergency center one and a half hour later, where cerebral CT demonstrated a fresh thrombus in the M2 segment of right middle cerebral artery (MCA), suggestive for an intracranial arterial thrombosis. The patient was transferred to our
clinic approximately 9 hours after the onset of
the symptomatology. The patient was
transferred to our clinic approximately 9 hours
after the onset of the symptomatology. Given
his age and time interval from onset of
symptomatology, a decision was made to
avoid intravenous administration of tissue
plasminogen activator (iv t-PA). National
Institutes of Health Stroke Scale (NIHSS)
score at the time of arrival to our hospital was
estimated to 20. Repeated brain CT showed
effacement of right basal ganglia and loss of
gray-white differentiation in the right superior
temporal lobe. The cerebral CT angiography
has highlighted the extension of intimal
thrombus from right M2 temporal segment to
M1 segment of right MCA. The patient was
immediately transferred to
neurointerventional suite. The cerebral digital
subtraction angiogram demonstrated an
abrupt proximal occlusion of the right M1 and
distal A4 segment partial occlusion. The
distal right MCA territory was good supplied
through well retrograde compensation from
right anterior cerebral artery and right
posterior cerebral artery. In order to avoid an
aggressive manipulation of an unknown
vascular territory (possible vascular
dissection) we decided to initially use the
Penumbra aspiration system rather than a clot
retrieval device (figure 1).
Figure 1 - A, B – right M2 thrombus; C – right M2, M1 thrombus; D – angio-CT aspect of M1 thrombus occlusion; E – postoperative CT control; F – 24 h CT control; G – 3 days CT control; H – 5 days CT control; I – 15 days CT control
Technique procedure

The patient was intubated and a 6 French shuttle sheath was placed to the right femoral artery. A 6 French guiding catheter (Guider Softip XF, Boston Scientific) was positioned at the petrous segment of the right internal cerebral artery on hydrophilic coated guide wire 0.035 (Radiofocus, Terumo). A 0.032 Penumbra System was easy advanced initially to M1 segment over a 0.014 microguidewire (Transcend EX, Boston Scientific). After three aspiration session, partial recanalization of MCA territory was achieved. The temporal branch of inferior M2 segment was still occluded on control angiography. After selective micro-catheterization of this vascular branch a new aspiration session was initiated. Finally a good recanalization right MCA was achieved. The last angiography control showed a good right hemisphere blood supply. Intravenous heparin or atiplatelet agents were not administrated during the procedure to avoid massive reperfusion intracranial hemorrhage (figure 2).
Outcome and follow-up

The patient was extubated at 2 hours postinterventional and accommodated for 10 days to intensive care unit. Severe headache and confusion was maintained still 5 days from admission. The patient was discharged after 17 days to a recovery department with left predominantly brachial hemiparesis.

Control cerebral CT scan were performed postoperatively, fallowed at one, 3 and 15 days. Postoperatively the CT scan demonstrates intense contrast accumulation in basal ganglia, caudat nucleus and with diffuse aspect right superior temporal lobe. At 24 h postinterventional a diffuse hiperintense aspects residual to basal ganglia were detected. Foci of infarction were well detected at two weeks in right basal ganglia, mesial and superior right temporal lobe.

Discussion

Ischemic stroke is not a common situation in young patient, and should be considered as the differential diagnosis. Most of the authors included young adults in the 16 – 40 years age group. The etiology of stroke in young adults is different from that in older patients, and has an influence on diagnostic evaluation and treatment. Numerous studies have showed a large spectrum of stroke aetiologies and risk factors for young patients such as Moya-Moya syndrome, vascular dissections, haematological causes, vasculitis and drugs consumption (table 1). There was a general agreement that young patients have a better chance of surviving and outcome than older group (50 -80 years)[1,3,4].

The option of therapeutic strategy is decisive for successful treatment of ischemic stroke. Recent meta-analysis reported that intravenous administration of tissue plasminogen activator (iv aTPA) is safe and efficient for use in young patients. Nevertheless, its effects are limited due to limited time window and inadequate recanalization rate for large arterial occlusion. Ineffectiveness of iv aTPA in patients who already exhibited early ischemic changes has been demonstrated in numerous studies. Also, proximal middle cerebral artery occlusion was proved to be correlated with higher rates of symptomatic intracerebral hemorrhage after iv aTPA[6,7,9,10].

Endovascular mechanical thromectomy have also been advocated for the treatment of stroke in young patients, especially for those who are ineligible for iv aTPA or in which iv aTPA has failed. It was already proved that the upper time limit for endovascular thrombectomy of large anterior vessel occlusions in selected cases was extended up to 16 hours. The recent DEFUSE-3 and DAWN trials extended the role of delayed thrombectomy to selected patients up to 16
and respectively 24 h after symptom onset. While the main goal of thrombectomy is to save penumbral brain tissue, the possible risk of symptomatic intracranial hemorrhage transformation is continuously present. The remarkable clinical recovery after acute ischemic stroke in young patients is largely due to the good pial collateral flow[3,4].

References

Penetrating brain injury with 2 nails as an attempt of suicide

Ancuţa Negru, M. Angelescu

Department of Neurosurgery Emergency County Hospital, Timişoara, ROMANIA

Abstract: We report the case of a 47-year-old man that was admitted to our hospital secondary to a penetrating brain injury with 2 nails as an attempt of suicide. Emergency head CT scan revealed the presence of 2 nails intracranially. The patient underwent surgical removal of the nails by minimal craniectomy. The particularity of the case is the minimal invasiveness of the approach completed by specific follow-up imagistic studies to maximise the outcome.

History

We present the case of a 47 years old man with no medical or psychiatric history who tried to commit suicide by shooting a nail gun in his temple. Patient was referred to the closest hospital where the CT scan of the brain revealed the presence of 2 nails intracranially. He was then transferred to our facility for definitive neurosurgical management.

Examination

At presentation, it was noted that the patient was in remarkably good condition with a Glasgow Coma Scale score of 14 (motor 6, verbal 5, Eye 3). A close examination of the scalp revealed 2 small (approx. 5mm) penetrating wounds over right temporal fossae. No portion of any of the nails was visible on the external examination of the head as the wounds where sutured at the previous hospital. The neurological examination demonstrated an incomplete abducens palsy of the right eye, trochlear palsy of the right eye, with diplopia and a slight right-sided hemiparesis. Admission laboratory results were within reference limits. The psychiatric evaluation confirmed acute predominantly delusional psychotic disorder. The thorough examination of the CT scan of the brain revealed 2 linear radiopacities with a linear thickness of 0,4 cm and a length of 6,2 cm in the form of nails with a right temporal bone point of entry with comminuted fracture and slight depression at this level. They pass the right temporal lobe and pass beyond the median line, the tip of one being located at the petrous part of the left temporal bone and the other's tip next the fourth ventricle (figure 1). The foreign bodies produce artefacts at the level of the brain, which does not allow the visualization of possible brain damage in their vicinity (figure 2).
Preoperative management

Brain CT angiography was performed preoperatively to assess the circulation and demonstrated no evidence of arterial trauma (figure 3).

Operation

Under general anesthesia, minimal right temporal craniectomy was performed (figure 4) by the means of carefully raising the comminuted bone fragments right adjacent to the nails with the help of Kerrison Rongeurs. Both nails were extracted by gentle traction and the musculocutaneous incision was rapidly sutured.

Postoperative course

Following the neurosurgical procedure, the patient directly underwent brain CT scan for assessing the cerebral parenchyma lesions (figure 5).

Antibiotics (Meropenem and Vancomycin) and anticonvulsants were prophylactically administered.
Infection control was done by the aid of Contrast-Enhanced CT scan of the brain 6 days postoperatively and a brain magnetic resonance 10 days after surgery, both ruling out any signs of infection. Furthermore, a cerebral angiography DSA revealed intact anterior and posterior circulation on both sides without any vascular abnormalities.

Clinically, without fever, biologically, laboratory results within reference limits and neurologically, GCS 15p with a slight improvement of palsies.

Given the patient's possible admission that all injuries were self-inflicted, he was transferred to a psychiatric service.

Figure 3

Figure 4

Figure 5 - No abnormal findings except a low-density lesion along the path of the nail and small pneumocephalus
Discussions and literature review

In 40% of cases, penetrating skull injuries are fatal because of damage to critical structures, vascular disruption, concussion blast injury, or meningitis. (1, 2, 3, 4, 5, 6, 7). Regarding the operation technique there are 2 main options: either by emergency craniotomy under general anesthesia or in an awaked fashion with only local agents (8, 9). The decision is ultimately the choice of the neurosurgeon. As for the infection control there are several measurements to consider: as large as possible debridement of the surrounding tissue, drain catheters inserted in the remaining cavity, and of course broad-spectrum antibiotics. In our case we choose to be as minimally invasive as possible.

Conclusions

Preoperative cerebral angiography and CT scan are highly recommended to precisely evaluate the brain tissue and vascular damage. We don’t find it mandatory for a wide surgical exposure, but brain CT scans should be repeated as soon as possible. Careful neurological examination of the patient as well as late contrast-enhanced images are essential to reveal any potential complications.

Correspondence

Ancuțiă Negru
Department of Neurosurgery, Emergency County Hospital, Timișoara, Romania, Bld. Iosif Buluca no. 10, tel: +40 356 433 422. E-mail address: ancuta.negru@hosptm.ro

References

Stent assisted coiling technique for anterior communicating artery aneurysms treatment

A. Chiriac, Giorgiana Ion¹, N. Dobrin¹, I. Poeata

"Grigore T. Popa” University of Medicine and Pharmacy, Iasi, ROMANIA
¹“Prof. Dr. N. Oblu” Clinic Emergency Hospital, Iasi, ROMANIA

Abstract: The anterior communicating artery was reported as the most common location for intracranial aneurysm by most clinical trials in literature. The use of intracranial stent detachment at the anterior communicating artery complex for treatment of wide-neck aneurysms with this location is increasingly reported. In this article we present the various management strategies for stent assisted coiling treatment of the anterior communicating artery aneurysms, their limits and complication.

Key words: anterior communicating artery, wide-neck aneurysm, stent-assisted technique

Introduction

The anterior communicating artery aneurysm was described in literature as the most common location for intracranial aneurysms responsible for up to 40% of the subarachnoid haemorrhages in adults. Microsurgical clipping or endovascular coiling are both techniques alternatives for the treatment of intracranial aneurysm with this location. The inconveniences due to deep lesion location, unfavorable projections or anatomical complexity of anterior communicating artery complex region have made the endovascular treatment the first choice. With the introduction of the stent-assisted embolization technique for resolving wide-neck aneurysms, this was also considered for the treatment of complex aneurysms of the anterior communicating artery. The development of new types of intracranial stents allowed the successful use of single or double stent techniques for coil embolization of anterior communicating artery aneurysms.

Endovascular treatment techniques

The low invasiveness, high feasibility and effectiveness of endovascular embolization of anterior communicating aneurysms made this treatment the prime method in most of the neurosurgical centres. The primary technique for endovascular occlusion of ACoA is represented by the coil embolization. However, the high rate of small and complex aneurysm for this location and adjacent anomalies of the ACoA segment made this
first option technique more difficult to be applied. It is well known the difficulty of coil embolization of wide-neck aneurysm. For these challenging situations a variety of adjuvant techniques and devices were developed. The remodelling techniques with balloon or microguidewire, and stent assisted technique are the most widespread. Detachment of coils in the aneurysmal sac under the protection of a temporarily inflated balloon over the aneurysmal neck has been shown to be associated with lower rate of progression of occlusion and higher rate of retreatment and procedural complication for ACoA location.

The stent assisted technique consists in deployment of a self-expandable stent in the parent artery over the aneurysm neck. The stent serves as a scaffold to prevent the coil protrusion into the parent artery or the thromboembolic event due to an earlier coil migration into the parent vessel. Also, the stents contributes to an earlier thrombosis of the aneurysmal sac by its hemodynamic effects of blood flow redirection and neointimal overgrowth stimulation by its biological properties.

There were described various intervention strategies regarding the time of stent deployment in relation with coiling. Thus, the stents can be detached before or after the microcatheter is placed into the aneurysm sac. In so called “jailing” technique the microcatheter is introduced into the aneurysm before the stent deployment. By this method, the microcatheter is placed between the vascular wall and the stent, which gives it a good stabilization during coiling. In the “trans-cell” technique, the microcatheter is placed into the aneurysm sac through the mesh of stent [1,2,4,7,8].

In particular cases of aneurysm incorporating both A2 and ACoA or in acute angles configuration between the parent and distal arteries, the “waffle-cone” technique is the best alternative. This method consists in deployment of the distal end of the stent into the aneurysm lumen and the proximal end in the afferent vessel. The major advantage of this method is the preservation of the parent artery patency.

Complex wide-necked ACoA aneurysm may also be endovascular treated by the “dual stent” technique. In this method 2 stents are deployed in X or Y configuration at the anterior communicating artery (ACoA) complex. The dual stent X-configuration is an optimal method in cases of large neck aneurysm involving both A1-A2 junctions, with ACoA partially incorporated within the sac and both A2s originating from the aneurysm. In such arrangement the first stent is deployed from the contralateral A2 to the ipsilateral A1 segment, crossing through the ACoA and the second stent is crossed from the other side. Usually, the side with the smaller angle between the A1-ACoA and contralateral A2 is stented first. The dual stent X-configuration could also be applied in two techniques: - the “kissing” technique with the stent deployed in a parallel fashion; - the “crossing” technique with the second stent is passed through the first stent interstices [1,2,4,7,8,9].
“jailing” technique
“trans-cell” technique
“waffle-cone” technique
If the X configuration technique is indicated in patients with both normal caliber A1, the dual stent Y-configuration is reserved for patients with hypoplasia/aplasia A1 on one side, and the aneurysm neck involving the ipsilateral A2 and ACoA. In this technique stents are deployed through the large-sized A1 in the bilateral A2 artery [8,9].

**Stent assisted coil Procedure**

The procedure is performed with the patient under general anesthesia. The double anti-platelet medication is mandatory initiated before the procedure. The loading dose varies depending on the treatment of a ruptured or unruptured aneurysm. 75 mg of acetylsaliclyic acid and additional 75 mg clopidogrel were administrated daily for 7 to 10 days before endovascular procedure in patients harbouring unruptured aneurysm. In case of patients presenting subarachnoid haemorrhage a “shock dose” of 300 mg acetylsaliclyic acid administrated 30 minutes before starting the procedure followed by 5000UI heparin after the introducer sheath placement are performed. Both conventional and rotational intra-arterial digital subtraction angiography is performed for 3D reconstruction. The planning procedures imply complete evaluation of aneurysmal dome, neck size and anterior communicating complex configuration.

A 6F introducer sheath is placed usually into right femoral artery. A 6F Impulse guiding catheter (Boston Scientific) is then navigated into the internal carotid artery to obtain a stable position. The right or left side is chosen depending on the dominant A1 segment, calibre of the anterior communicating artery and predominant side of aneurysm injection. Then, a Excelsior SL-10
A microcatheter (Stryker Neurovascular) with support of Transend 0.014 microguidewire (Boston Scientific) is introduced distally in the ipsilateral or contralateral A2 segment. The microguidewire is retired and a Neuroform Atlas stent (Stryker Neurovascular) is advanced into microcatheter and deployed when the precisely targeted location is confirmed. The deployment microcatheter is easy advanced over the stent delivery wire until it reached the neck aneurysm level. At this moment the stent delivery wire is retired and the 0.014 microguidewire is introduced into the microcatheter and navigated until the aneurysm dome. The aneurysm is catheterised via stent mesh and subsequently coiled with GDC-10 coils (Stryker Neurovascular). At the end control angiography images are performed to confirm the complete aneurysm occlusion. The microcatheter is then carefully retired followed by the guiding catheter and introducer sheath.

During the procedure heparinised saline is continuously administrated via a venous line. The patient is transferred to intensive care unit for clinical monitoring. The dual antiplatelet treatment is continued postoperatively for at least 2 month followed my mono- antiplatelet therapy.

**Case report**

A 52-year-old woman presented with sudden onset of worst headache of his life followed by single grand mall seizure. On admission to our emergency room the patient was confuse, agitated and vomiting. There were no focal deficits during neurological examination. Initial computed tomography (CT) scan showed thin subarachnoid hemorrhage into the base of the interhemispheric cistern. Three-dimensional (3D) CT angiography revealed an ACoA aneurysm with a bleb. Emergency endovascular coil embolization was decided to be performed. The diagnostic 3D digital subtracted angiography (DSA) showed ACoA aneurysm of which maximum diameter was 3.0 mm with broad-neck and a fragile bled on top. The initial coil embolization, was conceive to occlude the ruptured point of the aneurysm, was performed by the simple technique utilizing 1.5/2 mm nano platinum coils. After safety coil deployment the microcatheter is retracted from aneurysmal sac and guided to proximal part of left A2 segment. A 3/2.4 mm Neuroform Atlas stent was deployed from left A2 over the aneurysm neck and distal part of left A1 segment. Using a trans-cell technique the microcatheter is inserted again to aneurysmal sac. The aneurysm was completely angiographic occluded by deployment of two more coils. There were no peri-procedural complications or postoperative sever vasospasm. Follow-up CT scan was performed on postoperative day 14, revealing no ischemic or hydrocephaly signs.
Figure 2 - A – Diagnosis CT scan showing SAH; B – 3D reconstruction of CTA; C – Diagnosis DSA; D – DSA control after first coil deployment; E – Fluoroscopy for stent complete deployment control; F – Control DSA after complete aneurysm coil occlusion; G – Postoperative CT scan control
Techniques complications

The thromboembolic events are the most common cause of morbidity and mortality associated to stent-assisted coiling technique. The literature studies reported values of rates of thromboembolic complications related to stent-assisted coiling technique ranging from 4.2% to 17.1% [2,8,9]. Usually, these events are minor complications clinically silent or causing transient neurological symptoms. They may be diagnosed on later MRI investigation as a high-signal intensity lesion on diffusion-weighted image (DWI). However, the correct and careful use of double antiplatelet therapy significantly reduces intra and post procedural thromboembolic risks. The debates are still existing concerning this therapy in patients with subarachnoid haemorrhage and unprotected aneurysm in which an accidental intraprocedural rupture occurs.

Delayed in-stent stenosis is a rare event that can be clinically silent which may require sometime additional treatment. The rate of in-stent stenosis was reported between 2.5% (Biondi et al) and 29.7% (Wingspan) and a percutan transluminal angioplasty was performed in majority of cases[6,8].

Stent dislodgement is another complication reported during treatment. This technical problem may be caused by aneurysm catheterization through the stent struts and by retrieving the coiling catheter jailed between the stent and vessel wall. In most of the reported cases the stent still covered the aneurysm neck and procedure was completed successfully. In case of exposure of a portion of aneurysm neck with the possible risk of coil herniation into the parent artery, a secondary stent was deployed across the aneurysm neck.[8]

The intraprocedural aneurysm perforation is another important complication reported for stent-assisted coiling technique. Disastrous clinical outcome were reported by the most studies in this situation. The coil protrusion between the stent and the parent artery wall with a reduction of distal outflow was also reported as technical complication of this procedure.

The long-term aneurysm recanalization was reported by literature studies but with lower rate (13.1%) suggesting that this technique is an effective and durable treatment for complex AcoA aneurysms. In this regard, most authors argued that stenting in aneurysms confer a protective effect, stopping especially minor recanalization and thus avoiding the need for additional treatment.[2,10,11]

Discussions

Complex anterior communicating artery aneurysms are still challenging lesion for both surgical or endovascular approaches. Because most of the studies of anterior circulation aneurysms show for anterior communicating artery aneurysm the higher incidence of postoperative morbidity, the endovascular approaches became the main treatment option. Unlike other intracranial aneurysms, the embolization of anterior communicating artery aneurysms are more challenging due to increased incidence of small and complex aneurysm configuration and common anatomical vascular variants. In these
situations, the endovascular treatment requires application of adjuvant technique like stent-assisted coil embolization. First described by Higashida in 1997, as treatment option for wide-necked aneurysm was also applied for complex anterior communicating artery aneurysms[2,8,9].

Besides the role of mechanical support for the colis arrangement into aneurysm, hemodynamic and biologic favourable effects of intracranial stenting were highlighted in the literature.

The jailing technique and the trans-cell technique are the two type of stent-assisted coiling intervention used by the interventionists. Numerous studies have shown the efficiency of using both techniques with the limits and benefits of each [3,4,5].

Most of the literature reports showed that stent-assisted coil embolization of intracranial aneurysms lead to a lower rate of immediate complete aneurysm occlusion compared with simple coiling technique. The main cause associated with these results was the more limited manoeuvrability of the coil microcatheter after the stent deployment due to its fixation between the wall stent and arterial lumen, or passing through the stent struts.

The anatomy of the anterior communicating artery complex plays an important role in stent assisted treatment of anterior cerebral circulation aneurysms. The presence of hypoplastic A1 segment, small AcoA and difficult angles between A1, AcoA and A2 are important factors for stent placement.

The double stent placement has been described in some series for the treatment of complex and wide-neck aneurysms. The two stent may be used in X or Y configuration. X and Y stent-assisted coiling of AcoA aneurysms is an effective technique, leading to long-term stability of aneurysm occlusion. Nevertheless, a higher rate of technical failures and clinical complications were reported compared with those of other endovascular techniques, such as single stent–assisted coiling or balloon-assisted coiling[9].

References
Combined treatment of a giant anterior skull base meningioma

Georgiana Ion, Z. Faiyad¹, I. Poeata, A. Chiriac

“Grigore T. Popa” University of Medicine and Pharmacy, Iasi, ROMANIA
¹“Prof. Dr. N. Oblu” Clinic Emergency Hospital, Iasi, ROMANIA

Introduction

Meningiomas are tumors developed from arachnoid cells, and represent 20% of all intracranial tumors, from which 6% are located at the anterior skull base. Incidence is higher in female population, with an age peak in the fifth and sixth decade. Regarding anterior skull base meningiomas, 3.6% have the dural attachment at the level of tuberculum sellae and 3% at the olfactory groove. These tumors may invade the surrounding structures, such as dura mater and bone. These tumors are vascularized by ethmoidal arteries and rarely by frontopolar branches.

Case presentation

A 65 years old female, having cardiovascular pathology associated was admitted to our department for memory disorders (in particular short-term memory), urinary incontinence and bilateral anosmia with 1 year onset. For this reason, the patient was initially diagnosed with dementia. For the last 3 months, the condition of the patient is deteriorating, with behavioral changes, headache and visual symptoms (decreased visual acuity, lack of campimetry).

Non contrast CT scan revealed a well circumscribed low density formation without calcifications located in the frontal cranial fossa that invades the right ethmoidal air cells. The MRI with contrast scan, highlighted an anterior skull base meningioma, well vascularized with very little brain edema and erosion of the cribriform plate. Tumor insertion is located at the olfactory groove with extension in the planum sphenoidale and tuberculum sellae.

Figure 1 - non-contrast CT scan - giant tumor with right ethmoidal cells infiltration

Figure 2 - MRI T1 with contrast 7/7,83/7,49cm size tumor
For better understanding of the tumoral vascular supply, an angiographic exploration has been achieved. Right internal carotid artery contrast injection pointed out a significant posterior shift of the anterior cerebral artery and few small branches from ophthalmic artery that supply the tumor.

Left carotid artery showed the same anterior cerebral artery displacement, and a major tumoral pedicle from ethmoidal branches of the ophthalmic artery, with important tumoral blush. From the external carotid artery, there were no arterial intake.

We decided that the major arterial contribution from ethmoidal artery should be closed with liquid agents (glue n-butyl-2-cyanoacrylate). After embolization patient declared decreased visual acuity until only light perception on the left eye, important headache and confusional periods. Comparative CT scan pre and post embolization showed no semnificative modifications.
Figure 6 - left ICA DSA; CRA-central retinal artery ophthalmic artery anatomy; pedicular contrast injection

Figure 7 - glue injection

Figure 8 - pre/post glue occlusion of the ethmoidal artery

Period between embolization and surgical resection was of 6 days.

Tumor resection has been achieved through a bifrontal approach. Intraoperative, the right side of the tumor was relatively well vascularized, while the left side it was almost no bloody, clearly delimited, white colored. Subtotal resection of the tumor was achieved with CUSA (intraethmoidal part was left in place), with coagulation of the dural insertion at the cribiform plate, wax coating and anterior base reconstruction with vascularized pericranial flap.
Postoperatively, patient develop an involution of the cognitive function (decrease of the Mini Mental State Examination with 5 points) with a good recovery during hospitalization without other complications. Postoperative CT scans (immediate and at 7 days) showed a discreet increase in size of the ventricular system.

Definitive anatomic-pathology result was of atipic meningioma (WHO grade II)

Discussions

Embolization of ethmoidal branches from the ophthalmic artery represents a real challenge for the neurointerventional surgeon because of the high risk of ophthalmic artery occlusion and blindness. That’s why a superselective catheterization of the distal branches is necessary. The highest risk with liquid agents, is that of reflux into the central retinal artery. A most reliable agent in this situation would be onyx injection because of the low precipitation rate. Complications of glue agent use are: hemorrhage, local reflux and distal delivery of emboli.

There are not many studies to report mortality rates and complications of Internal Carotid artery feeding vessels embolization, but the study of Rosen et al.demonstrates an overall complication rate of 21% in this cases.

In giant meningioma reducing blood supply it’s necessary by facilitating tumor resection (Simpson I and II). In skull base meningiomas, control and access of the vascular pedicles are difficult and are accessible only after at least a subtotal resection has been achieved. Complications which could appear during or after embolization are: intratumoral hemorrhage (due to intratumoral necrosis or rupture of fragile vessels), retinal artery occlusion or tumor swelling.
In general, the indications for embolization of the tumors are: very vascularized tumors, deep and hardly accessible arterial intake, eloquent area location, tumor with the diameter over 3-4 cm.

Regarding the optimal period of time necessary for safe resection of the tumor after embolization, studies vary, with a mean period of 7 days.

Conclusions

Giant anterior skull base meningiomas represent a challenge for every neurosurgeon, starting from choosing the most advantageous approach, total tumor resection with minimal complications and a long term lower recurrence rate. Preoperative embolization decreases surgical mortality and morbidity and increase the probability of total tumor resection.

Correspondence

Prof. Dr. Ion Poeata - ipoeata@gmail.com

References

5. Embolization of Skull Base Meningiomas and Feeding Vessels Arising From the Internal Carotid Circulation; James S. Waldron, MD*, Michael E. Sughrue, MD†, Steven W. Hetts, MD†, Sean P. Wilson, BA, Steven A. Mills, BFA*, Michael W. McDermott, MD*, Christopher F. Dowd, MD†, Andrew T. Parsa, MD, PhD*; Neurosurgery 68:162–169, 2011
Familial cerebral cavernous malformation syndrome in Serbian family

Aleksić Vuk1, Mandarić Aleksandar2, Mihajlović Miljan1, Aleksić Nemanja3, Rapaić Marko1, Jovančević Miroljub5, Stanić Milenko1, Samardžić Marko1, Popović Igor1, Miladinović Vladimir1, Spaić Milan1

1Department of Neurosurgery, Clinical Hospital Center Zemun, Belgrade, SERBIA
2Department of Radiology, Clinical Hospital Center Zemun, Belgrade, SERBIA
3Clinic for Cardiac Surgery, Clinical Center of Serbia, Belgrade, SERBIA
4Faculty for Special Education and Rehabilitation, University of Belgrade, SERBIA
5Department of Radiology, “Euromedik” Hospital, Belgrade, SERBIA

Abstract: Cavernomas are benign vascular malformations, and about 50% of all cases are multiple. The hereditary form of brain cavernomas is uncommon, and it is certainly under diagnosed. Another entity is familial cerebral cavernous malformation syndrome. It is defined as the occurrence of multiple cavernomas or the occurrence of cavernomas in at least two members of a family or the presence of a mutation in one of the three genes causing familial cerebral cavernous malformation syndrome. We present a Serbian family in which three consecutive members of family had brain cavernoma. According to our knowledge, this is second case of hereditary cavernoma described in Serbian population.

Key words: Cavernoma; Familial cerebral cavernous malformation syndrome; multiple cavernomas

Introduction

Cavernomas are a benign vascular malformations (e.g. hamartomas), and about 50% of all cases are multiple (1). They are located in the brain or rarely in the spinal cord. The size of cavernomas ranges from a few millimeters to several centimeters. Cavernomas increase or decrease in diameter and increase in number over time. The majority of cavernomas become apparent between the second and fifth decades with presentation such as focal neurological deficit, headache, seizure, or cerebral hemorrhage (2). The hereditary form of cavernomas is relatively rare, and this, usually autosomal dominant pathology generally presents with focal neurological symptoms and seizures, however, many patients remain
asymptomatic, although, acute hemorrhages sometimes appear over time (3).

We present a Serbian family in which three consecutive members of family had brain cavernoma. According to our knowledge, this is second case of hereditary cavernoma described in Serbian population.

**Case presentation**

The first patient is a 35 years old female who presented to our emergency department with headache, right sided paresthesia, and persistent singultus (hiccup). She rated the pain as 8 out of 10. A head CT was performed and brain stem bleeding was suspected. The cranial MRI revealed a cavernoma with signs of hemorrhage in the region of medulla oblongata and medulla spinalis junction (Figure 1).

**Figure 1.** Cranial MRI showing a cavernoma with signs of hemorrhage in the region of medulla oblongata and medulla spinalis junction. (A) SWI sequence. (B) T2 sequence

Corticosteroid therapy was started, and symptoms disappeared. However, she had occasional attacks of right sided body numbness. One year after first onset of symptoms, control MRI showed enlargement of cavernoma with signs of hemosiderin deposits, after which she was accepted for stereotactic radio-surgery treatment in another hospital, which was performed about 2 years after the first onset of symptoms. Also, she was treated with a total of 1200cGy to 85% isodense line to the cavernoma lesion, using 6D skull IGRT system. She didn’t suffer from any side effects, and control MRI showed signs of cavernoma regression, without signs of de novo hemorrhage (Figure 2).

**Figure 2.** Control MRI with signs of cavernoma regression

Her neurological finding was normal, and she was without complaints. Control MRI after two years showed state after radiation therapy, and cavernoma dimensions were unchanged. However, SWI MRI sequence was performed and multiple brain cavernomas without signs of hemorrhage were found, and further neuro-radiological follow ups were advised. Control MRI was performed in another hospital, and we couldn’t obtainen the images, but only radiological description. Also, since multiple cavernomas were found on the last MRI, familial form of cerebral cavernous malformation was suspected. MRI was performed in patient’s father at the age of 73, and multiple brain cavernomas, without signs of hemorrhage were found (Figure 3).
Patient had normal neurological finding, and also only follow ups were recommended. In further investigation, we performed brain MRI in patient’s 15-year old son, and single caveroma located in pons was found (Figure 4).

Figure 3. Brain MRI showing multiple cavernomas

Figure 4. Brain MRI showing caveroma located in pons. (A) SWI sequence. (B) DWI sequence

This young patient had normal neurological status, and since he is symptom free, only regular brain MRI controls are recommended. No other members of family undergo radiological investigations.

Discussion

Brain cavernous malformations or cavernous angiomas are vascular malformations in the brain or sometimes in spinal cord. In one third of patients, these cavernous malformations are multiple. The hereditary form of brain cavernomas is uncommon, and it is certainly under diagnosed (3). We present a Serbian family in which three consecutive members of family had brain cavernoma, of which in 2 members,
cavernomas were multiple, and one member had solitary lesion.

Another entity is familial cerebral cavernous malformation syndrome. It is defined as the occurrence of multiple cavernomas (usually 5 or more) or the occurrence of cavernomas in at least two members of a family or the presence of a mutation in one of the three genes causing familial cerebral cavernous malformation syndrome. Three genes are known to cause mutations in familial cerebral cavernous malformation syndrome: KRIT-1 (CCM-1), CCM-2, and PDCD-10 (CCM-3) (Table 1) (3-6).

<table>
<thead>
<tr>
<th>TABLE I</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnostic criteria's for familial cerebral cavernous malformation syndrome (at least 1 of the following criteria)</strong></td>
</tr>
<tr>
<td>The presence of multiple brain or spinal cord cavernomas (typically 5 or more)</td>
</tr>
<tr>
<td>The occurrence of brain or spinal cord cavernomas in at least 2 members of a family</td>
</tr>
<tr>
<td>The presence of a mutation in one of the three genes causing familial cerebral cavernous malformation syndrome</td>
</tr>
</tbody>
</table>

According to presented criteria’s, this is almost typical familial cerebral cavernous malformation syndrome, and to our knowledge, this is second case of hereditary cavernoma described in Serbian population, first being described by Mitić et al. (7).

The disease frequently presents with focal neurological deficit (35-50%), and epileptic seizures (38-55%) (8). A headache, spontaneous paraplegia, or signs of cerebral hemorrhage are less frequently encountered symptoms and signs. Also, one quarter to one half of patients with cavernomas remain symptom free during life (9). In presented family, one patient had two frequent symptoms: headache, and focal neurological deficit-parestheis. However, this patient also had prolonged hiccups (singultus), which is defined as singultus lasting more than 2 days. Eisenacher and Spiske presented a similar case in which patient had persistent hiccups as the presenting symptom of medullary cavernoma. Conducting literature review we found two more similar cases of persistent cavernoma due to presence of medullary cavernoma (10). According to described cases, as well as study of Musumeci et al, conducted on animals, the region of the medulla oblongata lateral of the obex is probably responsible for the singultus reflex (11). Overall, singultus is rarely described in the context of a tumor or vascular malformation (e.g. cavernoma) in the region of the medulla oblongata, but persistent singultus, lasting more than 48 hours should arouse suspicion on this rare cause or some other rare neurological disorder.

Genetic testing may confirm suspicion on familial cerebral cavernous malformation syndrome. Three genes mutations are found in this hereditary syndrome: KRIT-1 (CCM-1), CCM-2, and PDCD-10 (CCM-3) (6). Also, this is an autosomal dominant disease, and
each child of a person with familial cerebral cavernous malformation syndrome has a 50% chance of inheriting the mutation. A higher incidence of this disease is found in Hispanic-American individuals of Mexican descent, probably due to a common ancestor with a mutation in the KRIT-1 gene (12). In presented family, we didn’t perform genetic testing, since family wasn’t motivated.

In majority of cases, MRI shows multiple focal regions of susceptibility induced signal loss of different size, well seen on gradient-echo sequences, or better on susceptibility-weighted imaging (SWI sequence). Lesion can be multiple (about 30% of patients), and in familiar form, the number of cavernomas is higher, in majority of cases more than 5. Number of lesions is increasing with age. However, young patients may already have numerous cavernomas (13). In our case, MRI features of all patients were typical, with SWI sequence being most valuable. In two out of 3 patients from presented family, cavernomas were multiple, while the youngest patient had only one cavernoma. One patient received stereotactic radio-surgery treatment, after which neuroradiological follow ups were advised. For other two patients only regular follow ups were indicated.

Microsurgical removal of cavernoma is may be reasonable if patient has epileptic seizures, or focal deficit due to mass effect or recurrent bleeding. Stereotactic radiosurgery is a safe therapy for cavernomas located in deep or eloquent sites (3, 14). It is important to find structural and the functional abnormalities with data from EEG, MRI, and SPECT so the spatial relationships may be demonstrated, which can help in the decision making for right therapy approach. In presented family, one patient had to be subjected to stereotactic radiosurgery, since she had cavernoma presented with focal neurological deficit, and radiological signs of repeated bleeding, while other two patients were asymptomatic, and only neuroradiological follow ups were advised.

References
Diagnostic value of preoperative systemic inflammatory markers in patients with intracranial meningiomas

Rahsan Kemerdere¹, Mehmet Yigit Akgun¹, Sureyya Toklu¹, Orkhan Alizada¹, Oguz Baran², Taner Tanriverdi¹

¹Department of Neurosurgery, Medical Faculty, Istanbul University-Cerrahpasa, Istanbul, TURKEY
²Neurosurgery Clinic, Istanbul Research and Training Hospital, Istanbul, TURKEY

Abstract: Introduction: The role of inflammation in cancer has been defined, and now, inflammation is accepted as one of the hallmarks of cancer development. The aim of this study was to evaluate the difference regarding preoperative neutrophil to lymphocyte (NLR) and platelet to lymphocyte ratios (PLR) in patients with meningioma between patients and healthy controls and between grade-I and grade-II meningiomas. Methods: Retrospective analysis of preoperative neutrophil, lymphocyte, monocyte, and platelet counts and NLR, and PLR were evaluated in 61 patients underwent meningioma surgery. Results: Neutrophil count was significantly increased while lymphocyte count significantly decreased patients compared to controls. Similar findings were obtained in grade-II meningiomas compared with grade-I meningiomas. NLR were significantly higher in both grade-I and grade-II meningiomas than controls. Conclusion: We for the first time provided that higher NLR may be associated with grading of meningioma and be a predictive factor for progression of meningiomas. The use of medication against neutrophil-related inflammation may be helpful for patients with higher grade of meningioma decreasing peritumoral edema before and after surgery.

Key words: Inflammation; Meningioma; Neutrophil-lymphocyte ratio; Platelet-lymphocyte ratio

Introduction

Meningiomas are the most commonly seen intracranial extra-axial tumors, accounting for 25% of all intracranial space-occupying lesions. Females are affected more predominantly than males due to estrogen functions (1). Although meningiomas are accepted as generally benign in nature, the recurrence rate in some cases is extremely high, even after the total surgical removal of the lesion. Thus, in 2007, the World Health Organization classified meningiomas into three grades. Grade I is more commonly encountered when compared to grades II and III, and the recurrence rate for grade I tumors
is very low. However, in grade II or III tumors, a high recurrent rate is common, and radiotherapy is required after surgery (2). Meningiomas originate in the arachnoid cap cells, but the exact nature of the development of these common tumors remains unknown.

The role of inflammation in cancer has been defined, and now, inflammation is accepted as one of the hallmarks of cancer development (3). With regard to inflammation in brain tumors, meningiomas have been focused on less when compared to gliomas. However, recent evidence has suggested that inflammation plays a pivotal role in the development and progression of brain tumors, including gliomas (4, 5). Finding a useful biomarker to predict the progression of brain tumors would be exciting for neurosurgeons because there has been no such marker used in brain tumors, as opposed to certain other solid tumors such as breast cancer (6). Recent studies have shown that the preoperative blood inflammatory markers, such as the neutrophil to lymphocyte ratio (NLR) or platelet to lymphocyte ratio (PLR), can be used as indices of glioma progression. For example, it has been reported that a high NLR (increase in the neutrophil count and decrease in the lymphocyte count) has a diagnostic value, and it correlates with the glioma grade (4, 5, 7-10). Those studies emphasized the fact that local inflammation around the tumor microenvironment can be reflected systemically, and that the inflammation severity can be tested by using peripheral blood tests that are cheap, reproducible, and effective.

Surprisingly, there have been no reports focusing on the preoperative blood markers in intracranial meningiomas. Therefore, in this retrospective analysis, we wanted to show how the preoperative NLR and PLR levels change when compared to the controls. We hypothesized that the NLR and PLR would be higher in meningioma cases (compared to controls), and that the levels would correlate with the meningioma grade, given that the same inflammatory processes take place in both glioma and meningioma cases.

**Materials and Methods**

**Patients**

The patient group included here underwent surgeries for intracranial-supratentorial meningiomas by a single surgeon between 2010 and 2017. A total of 100 cases were retrieved from the medical records, but only 61 patients were included, according to the following criteria: 1) the meningioma grade was verified by a histopathological study, 2) no chemotherapy, radiotherapy, and steroids were taken before the surgery, 3) no co-morbidities or extracranial tumors were seen, 4) there was no previous surgery due to any intracranial pathology; 5) there was a complete blood count (CBC) before surgery; and 6) an informed consent form was completed.

**Data collection**

The demographic, clinical, radiological and histopathological data were retrieved from each patient’s medical records. After hospitalization, blood samples were taken for a CBC and other tests, including hepatic function, serology and the electrolyte level, as a standard preoperative work-up. The neutrophil (103/mm3), lymphocyte...
(103/mm³), and platelet (103/mm³) counts were recorded. Additionally, the preoperative NLR (quotient of the absolute number of the neutrophil count to the lymphocyte count) and PLR (quotient of the absolute number of the platelet count to the lymphocyte count) were calculated.

All of the patients underwent cranial magnetic resonance imaging (MRI) with contrast enhancement. The anterior-posterior diameter (cm) was measured by using T1-weighted contrast-enhanced axial images, and the presence of peritumoral edema was noted by using T2-weighted and fluid-attenuated inversion recovery (FLAIR) images.

Controls
The control group in this study was composed of 35 subjects who were admitted to our clinic and underwent CBC testing for some other reason, such as a headache. None of the subjects exhibited any abnormalities in their cranial MRI scans and no other organ system illnesses were detected. The blood samples were obtained during their admission to our outpatient clinic.

Statistical Analysis
The statistical analysis was performed by using IBM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA). The results were reported here as the mean ± standard deviation. An independent samples t-test and chi-squared test were used in the appropriate comparisons and the correlation analysis was judged using Pearson’s correlation coefficient. The area under the curve (AUC) for the NLR and PLR with a receiver operating characteristics (ROC) curve analysis was used for the diagnostic performance. A probability value (p value) < 0.05 was considered to be statistically significant.

Results

Demographic characteristics
The patient group included 26 males (42.6 %) and 35 females (57.4 %) with a mean age of 51.91 ± 13.01 years old (range = 23 to 76 years). The control group had 19 males (54.3 %) and 16 females (45.7 %) with a mean age of 32.08 ± 10.09 years old (range = 10 to 51 years). Based on the cranial MRI scans, there were 26 (42.6 %) and 35 (57.4 %) right and left-sided meningiomas, respectively. Peritumoral edema was noted in 37 patients (60.7 %). The histopathological diagnoses revealed grade I meningiomas in 48 patients (78.7 %) and grade II in 13 patients (21.3 %). All of the patients with grade II meningiomas had peritumoral edema. The mean of the anterior-posterior diameters of the tumors was 36.73 ± 13.6 cm.

Inflammatory markers: patients versus controls
Table I shows a summary of the comparisons between the patients and the controls with regard to the preoperative inflammatory markers studied here. The mean of the neutrophil count levels was significantly higher in the patients when compared to controls (p = 0.001). The lymphocyte and platelet counts were lower in the patients; however, the differences were not significant. As expected, the NLR was significantly higher in the patient group (p = 0.001). Moreover, the mean PLR level was higher in the patients than the controls, but the difference was not significant. However, there was a trend toward
significance in the PLR levels of the patients ($p = 0.05$).

**Inflammatory markers: meningioma grade and edema versus controls**

Given that inflammation has been shown to play an important role in upgrading of tumors and the presence of peritumoral edema, we compared how the preoperative inflammatory marker levels change. Table II shows that the neutrophil count increases, whereas the lymphocyte and platelet counts decrease in grade II when compared to grade-I meningiomas.

**TABLE I**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Patients (n = 61)</th>
<th>Controls (n = 35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>5.42 ± 2.63</td>
<td>4.20 ± 0.81</td>
<td>0.001*</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>2.11 ± 1.09</td>
<td>2.39 ± 0.54</td>
<td>0.15</td>
</tr>
<tr>
<td>Platelets</td>
<td>252.54 ± 76.18</td>
<td>271.57 ± 57.66</td>
<td>0.20</td>
</tr>
<tr>
<td>NLR</td>
<td>3.42 ± 3.62</td>
<td>1.83 ± 0.49</td>
<td>0.001*</td>
</tr>
<tr>
<td>PLR</td>
<td>136.46 ± 57.27</td>
<td>118.51 ± 34.24</td>
<td>0.05</td>
</tr>
</tbody>
</table>

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio.
*Denotes statistically significant difference.

**TABLE II**

<table>
<thead>
<tr>
<th>Marker</th>
<th>Neutrophils</th>
<th>Lymphocytes</th>
<th>Platelets</th>
<th>NLR</th>
<th>PLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade-I</td>
<td>5.14 ± 2.54</td>
<td>2.21 ± 1.13</td>
<td>255.46 ± 61.29</td>
<td>2.75 ± 2.17</td>
<td>128.78 ± 48</td>
</tr>
<tr>
<td>Grade-II</td>
<td>6.45 ± 2.81</td>
<td>1.71 ± 0.82</td>
<td>241.73 ± 118.9</td>
<td>5.90 ± 6.28</td>
<td>164.83 ± 79.15</td>
</tr>
<tr>
<td>Controls</td>
<td>4.20 ± 0.81</td>
<td>2.39 ± 0.54</td>
<td>271.57 ± 67.66</td>
<td>1.83 ± 0.49</td>
<td>118.51 ± 34.24</td>
</tr>
<tr>
<td>Edema+</td>
<td>5.84 ± 2.96</td>
<td>2.03 ± 0.87</td>
<td>252.82 ± 85.73</td>
<td>4.0 ± 4.47</td>
<td>141.18 ± 66.95</td>
</tr>
<tr>
<td>Edema-</td>
<td>4.77 ± 1.91</td>
<td>2.22 ± 1.37</td>
<td>252.10 ± 60.28</td>
<td>2.52 ± 1.39</td>
<td>129.19 ± 30.07</td>
</tr>
</tbody>
</table>

| Grade-I versus Grade-II | P value | 0.11 | 0.14 | 0.69 | 0.09 | 0.13 |
| Grade-I versus Controls | P value | 0.02* | 0.4 | 0.22 | 0.006* | 0.28 |
| Grade-II versus Controls | P value | 0.01* | 0.002* | 0.4 | 0.03* | 0.06 |
As expected, the NLR and PLR were increased in the grade II meningiomas but no significant differences were found between these two grades. However, there was a trend toward significance with regard to the NLR. When the grade I meningiomas and the controls were compared, we found that the neutrophil count and NLR increased, while the lymphocyte count, platelet count, and PLR decreased in the grade I cases. However, the difference reached significance only regarding the neutrophil count and NLR. Findings supporting the role of inflammation in the upgrading of a meningioma were found when a comparison between the grade II meningiomas and the controls was performed. The neutrophil count, platelet count, NLR, and PLR were higher and the lymphocyte count and platelet count were lower in the grade II cases than in the controls. The presence and/or absence of peritumoral edema caused differences in the inflammatory marker levels, but none reached a significant level. Here, we must emphasize the fact that the neutrophil and lymphocyte counts increased and decreased, respectively, suggesting that inflammation may play a role in the development of peritumoral edema. Although we did not find significant differences between the presence and absence of peritumoral edema with respect to the NLR and PLR, both showed elevations in the presence of peritumoral edema.

**Correlations**

The strong positive correlations were as follows: neutrophil count and NLR ($r = 0.65$, $p = 0.00001$), neutrophil count and PLR ($r = 0.28$, $p = 0.005$), lymphocyte count and platelet count ($r = 0.32$, $p = 0.001$), platelet count and PLR ($r = 0.21$, $p = 0.03$), and NLR and PLR ($r = 0.61$, $p = 0.00001$). Contrarily, the strong negative correlations were as follows: lymphocyte count and NLR ($r = -0.47$, $p = 0.00001$), lymphocyte count and PLR ($r = -0.63$, $p = 0.00001$), and platelet count and NLR ($r = -0.26$, $p = 0.008$).

**Diagnostic efficacy**

When the patients with meningiomas were tested against the controls (Figure 1), the AUCs were 0.70 [95 % confidence interval (CI) 0.59-0.80, $p = 0.001$] for the NLR and 0.57 (95 % CI = 0.45-0.69, $p = 0.22$) for the PLR.

However, when grade I meningiomas were tested against the grade II meningiomas (Figure 2), the AUCs were 0.70 (95 % CI = 0.53-0.86) for the NLR and 0.64 (95 % CI = 0.45-0.83, $p = 0.1$) for the PLR. The findings showed that the NLR exhibited the best
accuracy for a meningioma diagnosis and predicting the meningioma grade.

![Figure 1 - ROC curve analysis showing diagnostic efficacy when patients with meningioma were tested against healthy subjects](image)

**Discussion**

The role of chronic inflammation in both the development and progression of cancer has been identified, and it has been strongly suggested that inflammation-related neutrophils and lymphocytes, as well as platelets, participate in angiogenesis and the proliferation of tumor cells (11, 12). Meningiomas, especially grade I lesions are slow-growing tumors, and obviously, chronic inflammation may take place in their development and progression. However, the exact mechanism(s) behind the neutrophilia and lymphopenia that are commonly found in cancer is poorly understood. Some researchers have suggested that the cytokines and chemokines secreted by tumor cells can cause neutrophil infiltration, thus causing an elevation in their counts in both the tumor microenvironment and the peripheral blood (13, 14). The increased neutrophil levels subsequently inhibit the white blood cells, including lymphocyte activity, and this leads to lymphocyte apoptosis.

The studies reported during the last decade showed that higher neutrophil and lower lymphocyte counts are associated with poor prognoses in various cancers, including glial tumors of the brain (4, 5, 7-10, 15, 16). Unfortunately, there have been a limited number of studies focusing on brain tumors with regard to the preoperative inflammatory markers, when compared to the other organ system tumors, and there have been no reports focusing on meningiomas. A few studies have reported the preoperative inflammatory markers, such as the NLR, PLR, and lymphocyte to monocyte ratio (LMR), in some extra-axial tumors, such as vestibular schwannomas and craniopharyngiomas (15, 16). For example, Kontorinis, et al. (15) demonstrated that a very high NLR is a reliable marker for vestibular schwannoma growth.
and that it can predict grooving schwannomas. Chen, et al. (16) found that the levels of white blood cells, neutrophils, NLR, and PLR were higher in craniopharyngiomas when compared to other sellar tumors, and they emphasized the fact that these markers can be used to differentiate craniopharyngiomas. Moreover, Zheng et al. (5) provided the first evidence that patients with gliomas have higher NLR levels than patients with non-lesional epilepsy, vestibular schwannomas, meningiomas, and healthy controls.

Because there have been no previous reports studying preoperative inflammatory markers in meningioma cases, we could not compare our results with those from the current literature. However, we did discuss our results with regard to previous reports including gliomas. First, we would like to emphasize the fact that our results were strongly in line with those of other studies including patients with gliomas (4, 5, 7-10). A significantly higher neutrophil count and NLR were found in our patient group when compared to the healthy controls. Although we did not find a statistically significant difference regarding the PLR, there was a trend toward significance. The lymphocyte count was also lower in the meningioma patients, but the difference was not significant. These results mentioned above support the previous glioma studies in which a higher neutrophil count, lower lymphocyte count, higher NLR, and, in some studies, a higher PLR were found to be strongly associated with the prognosis (5, 8). More importantly, the glioma grade was associated with a higher NLR, and it was stated that the NLR can be used as an index for glioma progression, with an NLR ≥ 4 showing a poor prognosis (5, 8).

It is clear that as tumor grade increases, the inflammatory reaction increases and the levels of the inflammatory markers, such as the neutrophil count, NLR, and PLR, increase. For the first time, we demonstrated preoperative inflammatory marker levels in different meningioma grades (grade I and II). We obtained very supportive findings that malignancy increases, the inflammation-related markers increase. The grade II patients showed higher and lower levels of neutrophils and lymphocytes, respectively, when compared to the grade I patients, but more importantly, the NLR and PLR were higher in the grade II patients although the differences were not significant. This may be due to the fact that the number of grade II patients (n = 13) was smaller than that of the grade I patients (n = 48). We believe that if we were able to include an equal number of patients in each grade, the differences would be significant. The neutrophil counts and NLR were also clearly higher in each grade when compared to the healthy subjects but the biggest differences were found when comparing the grade II and the healthy subjects, suggesting that inflammation may play a role in tumor progression, as in the current literature on glioma patients (4, 5, 7-10).

From a clinical standpoint, we know that as the tumor malignancy increases, the peritumoral edema, which can sometimes cause life-threatening conditions, increases. Recent studies have shown that inflammatory cells play roles in the formation of peritumoral edema, and they have been found in
edematous tissues (17). We hypothesized that because peritumoral edema is associated with inflammation, the levels of the inflammatory markers studied here, would increase in those patients who exhibited peritumoral edema on their cranial MRI scans. We note the fact that peritumoral edema was observed in all 13 of the patients who were diagnosed with grade II meningiomas. The neutrophil count and lymphocyte count were increased and decreased, respectively, in the patients with peritumoral edema when compared to those who had no peritumoral edema, and there were higher NLR and PLR levels in those patients with peritumoral edema. These finding supported our hypothesis that inflammation may play an important role in the development of peritumoral edema, and an anti-edematous treatment including a medication inhibiting neutrophil action in addition to steroids would be beneficial.

As in the few studies including extra-axial tumors, such as vestibular schwannomas and craniopharyngiomas (15, 16), and the studies including gliomas (4, 5, 7-10), the NLR compared to the PLR exhibited the highest diagnostic value in predicting meningiomas. This can differentiate grade I meningiomas from grade II meningiomas, and it could be used as an index for possible tumor progression after surgery.

Limitations
The authors contributed to this study are aware that there are a few limitations. First, this is a retrospective study that may cause selection bias although we had strict selection criteria. Second, our patient sample consisted of a relatively small number of patients with meningioma, in particular, limited number of grade I meningiomas thus the literature needs prospective studies with larger cohort of meningioma patients. Third, higher levels of neutrophil count, NLR, and PLR can be a reflection of non-specific inflammatory response due to meningioma thus we have a risk of having false-positive results. We underline that until we have enough number of studies including larger cohort of patients, the results obtained from the current literature and from the present study should be evaluated carefully.

Conclusion
Apart from the limitations mentioned above, we for the first time provided that higher NLR may be associated with grading of meningioma and a predictive factor for progression of meningiomas. The use of medication against neutrophil-related inflammation may be helpful for patients with higher grade of meningioma for decreasing peritumoral edema before and after surgery. We were not able to compare our results with the current literature due to absence of studies included same type of tumor. Thus, further studies are needed.

Correspondence
Oguz Baran, M.D.
Istanbul Research and Training Hospital, Neurosurgery Clinic, Istanbul, Turkey.
E-mail: oguzbaran@gmail.com
Telephone Number: +905325990034 Fax : +90 (212) 459 62 30
Mailing Address: Istanbul Egitim ve Arastirma Hastanesi, Beyin ve Sinir Cerrahisi Klinigi, Kasap
References
A Doughnut in the Brain: an overview of the pathophysiology and the current treatment options for intracranial doughnut-shape aneurysm

S.S. Hoz¹, L.R. Moscote-Salazar²

¹Department of Neurosurgery, Neurosurgery teaching Hospital-Baghdad, IRAQ
²Department of Neurosurgery, Latin-American Neurotrauma and neurocritical care (Red Latino), Bogota, COLOMBIA

Key words: Doughnut aneurysm, giant aneurysm, outflow occlusion, partially thrombosed aneurysm

Giant aneurysms, those larger than 25 mm in diameter, are relatively uncommon and are often accompanied by thrombosis (1). Doughnut-shaped aneurysms are giant round-shaped aneurysms composed of an intraluminal thrombus and marginal parent arteries (2). Doughnut-shaped aneurysms are rare subtype of partially thrombosed giant aneurysms and account for ≤1% of large/giant aneurysms (2,3).

Pathophysiology:

The Doughnut-shaped aneurysms formed when the aneurysm geometry and flow conditions result in circular laminar flow (4). This type of aneurysm constitutes of 3 parts: the inflow artery, outflow artery and a central thrombosed part which is already excluded from circulation.

Disruption of flow (slow flow) within the aneurysm results in progressive thrombosis and exclusion from the intracranial circulation (5). Horowitz et al. described a mathematical model showing the intraluminal pressure changes that might be expected following outflow occlusion (6). They reported that the resulting variations in pressure should be less than those induced by normal daily activities and concluded that outflow occlusion would not be expected to increase the risk of an aneurysm rupture (1).

On imaging, Rooij et al describe the ‘donut sign’ on angiography, with the central filling defect which is the doughnut hole represent the intraluminal thrombus and is responsible for the donut-shaped appearance seen at angiography (4).

Treatment options:

Optimal management of giant doughnut-shaped aneurysms has not yet been established. In contrast to the usual saccular aneurysm, giant doughnut-shaped aneurysms have separate inflow and outflow vessels; therefore, clipping the aneurysmal neck is
unsuitable (1). Given its rarity and unusual appearance, the best treatment approach for this type of aneurysm has not been well established (5).


Although complete obliteration of the aneurysm lumen with or without resection is an ideal treatment for such complex aneurysms, for some cases, it is difficult to achieve trapping and distal revascularization during surgery (7).

Outflow occlusion with distal revascularization could be an effective surgical option for such a unique aneurysm. For some cases, trapping of the involved segment with or without distal bypass is recommended (1,6). Bypass surgery to treat distal ACA aneurysms can be categorized as intracranial–intracranial (IC–IC) and extracranial–intracranial (EC–IC) types. IC–IC bypasses include in situ bypass, reanastomosis, reimplantation, and bypass with graft placement. IC–IC bypass has several advantages. IC–IC bypass could provide enough hemodynamics to the target region without additional blood flow (1).

Furthermore, IC–IC bypass do not require secondary incision and graft harvest. However, IC–IC bypass also has disadvantages. This maneuver is technically challenging in the narrow and deep working space in the interhemispheric fissure. In addition, if a bypass fails and occludes, both distal arterial territories could develop serious ischemia (1).

Proximal occlusion is also considered to be suitable for cases with surgical difficulty of trapping because proximal occlusion for aneurysms is believed to reduce the hemodynamic burden of the aneurysm, promote complete thrombosis in the aneurysm sac, and reduce the size of the aneurysm (8). Recently, endovascular treatment has shown good results for large and giant aneurysms. However, the usefulness of coil embolization for partially thrombosed giant aneurysms remains controversial because of coil compaction and/or migration into the thrombus (1).

Endovascular coil embolization is typical for some cases but the technical difficulty limits its application in most of the circumstances (5).

Endovascular flow diversion has been shown to be an effective alternative to coil embolization of intracranial aneurysms (5). However, while effective in treating intracranial aneurysms, flow diverter stents are associated with procedure-related complications (9).

Partially thrombosed aneurysms in particular have a high recurrence rate of up to 75%, with larger aneurysms having a worse prognosis (10). Limited published experience with donut aneurysms suggests they are also prone to recurrence (4).

Conclusion

The treatment of partially thrombosed giant (doughnut) aneurysm is critical and should be individualized case by case putting in mind the above surgical and endovascular options.
References


Giant facial schwannoma with intracranial extension: a case report

Gokhan Canaz¹, Izzet Durmusalioglu¹, Mustafa Ali Akcetin², Nur Topyalin³, Cemile Ozdemir⁴, Ali Osman Akdemir²

¹Bakirkoy Research and Training Hospital for Neurology, Neurosurgery and Psychiatry, Department of Neurosurgery, Istanbul, TURKEY
²Haseki Training and Research Hospital, Department of Neurosurgery, Istanbul, TURKEY
³Van Yuzuncu Yil University, Department of Neurosurgery, Van, TURKEY
⁴Haseki Training and Research Hospital, Department of Pathology, Istanbul, TURKEY

Abstract: Introduction: Facial nerve schwannoma is a rare benign tumor which may originate from any segment of the facial nerve. We present a case of a giant cystic facial nerve schwannoma that showed extension to the middle cerebral fossa, together with its clinical and radiological characteristics, and a short review of the related literature.

Case Report: A 52-year old female patient attended with complaints of numbness in the right half of her face, and mild hearing loss. Examinations revealed House-Brackmann Grade 3 peripheral facial paralysis, sensorineural hearing loss of 30% in her right ear. She described three episodes of facial paralysis in the last six years. Cranial MRI and CT scan revealed a round cystic lesion of about 40x44x38 mm, located centrally and medially in the right temporal area. The surgical operation was performed and the lesion was totally extracted. The histopathological investigation reported the lesion as a schwannoma.

Conclusion: Facial nerve schwannoma is a rare, benign tumor that occurs in different localizations. It may commonly be mistaken in prediagnosis and may be confused with other clinical states due to its clinical characteristics. It has to be kept in mind in the prediagnosis of patients with facial paresis and hearing loss.

Key words: Schwannoma, Facial Palsy, Tinnitus, Hearing Impairment

Introduction

Facial nerve schwannoma (FNS) is a benign tumor that is rarely seen, and is generally difficult to diagnose before surgery. It may originate from any segment of the facial nerve through its extension from its origin in the cerebellopontine angle, to the parotid gland. Schwannomas account for 8% of all intracranial tumors. Of these, FNSs account for about 1.9%. FNSs that extend to the middle cerebral fossa are rare, as they commonly
originate from the geniculate fossa (9, 10). Here, we present a case of a giant cystic facial nerve schwannoma that showed extension to the middle cerebral fossa, together with its clinical and radiological characteristics, and a review of the related literature.

Case

A 52-year old female patient attended with complaints of numbness in the right half of her face, and mild hearing loss. Her physical examination revealed House-Brackmann Grade 3 peripheral facial paralysis, and hearing loss. The audiometric evaluation revealed a sensorineural hearing loss of 30% in her right ear. In her anamnesis, the patient described three episodes of facial paralysis: the first one occurred six years previously, the second four years, and the most recent one 15 days previously; a radiological investigation had not been performed. Cranial contrast enhanced magnetic resonance imaging (MRI), revealed a round cystic lesion of about 40x44x38 mm with regular margin, and with a peripheral capsule of about 8 mm maximal thickness, located centrally and medially in the right temporal area (Figure 1). In the computerized tomography (CT), we observed erosion of the petrous bone and widening in the facial hiatus on the right side (Figure 2). The patient was operated with a pre-diagnosis of meningioma, metastasis or schwannoma. The tumor was accessed using a right pterional craniotomy and sylvian dissection. The tumor was grey-yellow colored and it has hemorrhages in some areas. The tumor was easily dissected from the surrounding tissue. A tissue specimen was transferred for frozen section investigation. The pathological examination excluded malignancy. The mass was totally extracted following internal decompression. The optic nerve, carotid cisterns, and anterior communicating artery and its segments were intact. It was established that the petrous bone and dura were eroded in the area where the mass was adjacent to the temporal bone; therefore the dura was repaired in this region using a galeal graft, and the operation was completed. The histopathological investigation reported a schwannoma from the palisading pattern with S-100 protein positive, glial fibrillary acidic protein (GFAP) and epithelial membrane antigen (EMA) negative (Figures 3A,B).

A post-operative physical examination of the patient revealed progression of right facial paralysis to House Brackmann Grade 4 level; her hearing loss was also determined to progress. An investigation of the facial nerve electromyography (EMG) revealed severe axonal damage in the facial nerve. A control EMG was recommended one month later. Almost complete hearing loss was determined on the right side in her audiometric evaluation. In the post-operative contrast enhanced cranial MRI, it was determined that the mass has been totally excised (Figure 4). The patient was discharged from hospital on the post-operative 14th day. The second control EMG was administered about two months later, and the result was compatible with a lesion causing complete axonal damage to the right facial nerve segments that branches off from the orbicularis oculi and frontal muscles, and severe axonal damage in the segment that branches off from the orbicularis oris muscle.
**Figure 1** - Contrast enhanced cranial MRI: A round cystic lesion of 40x44x38 mm in size with a regular margin, and with a peripheral capsule of 8 mm in maximal thickness, located centrally and medially in the right temporal lobe. A: Axial section. B: Coronal section

**Figure 2** - A: Widening and erosion in the facial hiatus in axial section, in the temporal CT. B: Erosion in the right temporal bone petrous segment, in the coronal section
Figure 3 - A: Bundles of fusiform cells by hematoxylin staining, magnified 100 times. B: Diffuse positive reaction by S-100 immunohistochemical staining

Figure 4 - Postoperative changes in the postoperative contrast enhanced cranial MRI
Schwannomas are simply benign tumors that originate from the Schwann sheaths of the peripheral neural cells (cranial and spinal). Giant size described as > 4.0 cm in maximal extrameatal diameter by Samii et al. (7). They arise from sensory nerves, and are also known as neuromas. Schwannomas that originate from cranial nerves account for 8% of intracranial tumors, and they occur at a relatively high frequency. FNS accounts for 1.9% of all intracranial tumors. A FNS generally extends intracranially to the cerebellopontine angle, and to a lesser extent, to the middle cerebral fossa (11). Its rare occurrence in middle cerebral fossa, and the presence of more frequently seen lesions in this area that have similar appearances radiologically, make the differential diagnosis and accurate pre-diagnosis difficult.

FNS occurs clinically as a facial nerve paresis or paralysis with a long-lasting, fluctuating and progressive course. It has to be kept in mind that hearing loss (sensorineural or conductive type) occurs as frequently as facial paralysis. It has found to occur even more frequently in some studies, including large case series (4). This clinical feature often leads to false pre-diagnosis of vestibular schwannoma. Symptoms are often found to be associated within the region of the facial nerve in which the lesion is located. The symptoms are generally characterized with various distributions of the facial, otologic, and mass effect signs; however this is not a clinically pathognomonic sign for the diagnosis of FNS. A high correlation has been detected between the degree of facial nerve dysfunction and intratemporal location; otologic complaints like sensorineural hearing loss, tinnitus, and vertigo have been reported most frequently in patients with intracranial tumors (2). Because the differential diagnosis of acoustic neuroma and FNS is difficult, diagnosis of FNS is almost always ascertained perioperatively or postoperatively.

There are different studies and classifications related to the localization and frequency of FNSs on the facial nerve. In many studies, it has been reported that FNS most frequently occurs in the geniculate ganglion along the course of the facial nerve (4). In a study comprising 24 patients with a histopathological diagnosis of FNS, the facial nerve has been investigated in eight separated segments, as follows: cerebellopontine angle, internal acoustic canal, labyrinth, geniculate fossa, nervus petrosus major, tympanic, mastoid, and intracranial. In this study, the geniculate fossa was established to be the most frequent location (83%); of these tumors located in the geniculate fossa, 60% occurred with extension to the labyrinth, and 30% were with petrosal nerve involvement. Only two cases were determined with intracranial extension (8.3%), and both of these originated from the geniculate fossa. Facial neuropathy was identified in these two cases with intracranial extension, and one case with sensorineural hearing loss (11). In a study, the location of FNS was classified as intratemporal, extratemporal and intracranial, and the most frequent location was in the intratemporal region (61%); tumors with extratemporal (parotid area) and intracranial
(cerebellopontine angle) locations, were reported in equal frequencies. In this study, extension to the middle cerebral fossa was not included in the intracranial location, and one tumor was reported with intracranial extension occurred in the intratemporal location (2).

High-resolution enhanced CT and MRI, are the most important visualization methods in the radiological diagnosis of FNS. CT may not be considered absolutely essential; however it is important in the visualization of the changes in the temporal bone, to determine the origin of the tumor, and when planning surgery. Erosion of the petrous bone, internal acoustic canal and a widened facial hiatus can easily be visualized using CT, which also helps in the preoperative differential diagnosis (8). An contrast enhanced MRI is the preferential diagnosis for FNS, independent of the size and location of the tumor. These tumors classically occur in MR imaging as hypo-hyperintense in the T1 weighted sequences, hyperintense in the T2 weighted sequences, and with contrast enhancement (3). Large tumors commonly show cystic differentiation, and peripheral contrast enhancement.

FNSs with extension to the middle cerebral fossa, are benign tumors, and they frequently cause mass effect; the first choice of treatment is therefore surgery. Different studies make different recommendations regarding the surgical indication and approach; however the most common suggestion for tumors beyond House-Brackmann stage 3, is surgery (4). FNSs are tumors that grow very slowly (0.02 cm3 /year); however surgery must not be delayed when there is involvement of the middle fossa (6). Taking into consideration the sense of hearing, and location of the tumor in the facial nerve segment, suboccipital, infratemporal, frontotemporal, transpetrosal, and retrosigmoid approaches may be undertaken by neurosurgeons, with the participation of nose-ear-throat specialists, if needed. FNSs are tumors of the nerve sheath, and it is theoretically possible to extract them without damaging the nerve; however following middle fossa surgery, this segment of the facial nerve is almost always extracted together with the tumor. This results in permanent facial paralysis. There are studies in the literature using different methods of reconstruction; however nerve function better than that of House-Brackmann stage 3 cannot be maintained (2, 5). The general methods applied include the interposition of the nervus auricularis major, and hypoglossal nerve anastomosis by grafts from the sural nerve or vestibular nerve. Additional techniques including sutures and fibrin tissue adhesives without sutures are also used. Facial nerve conduction can be maintained in some of these studies; however clinical improvement does not occur, due to atrophy developing in the muscles that it innervates. In cases with unimpaired hearing occurring with tumors extending to the middle cerebral fossa, transmastoid- middle fossa combined surgery is recommended. Hearing may be maintained to some extent following surgery, in small or moderate tumors (3-15 mm); in large tumors (>18 mm), but it has also been reported that it’s not possible to protect the sense of hearing (1).
Conclusion

Facial nerve schwannoma is a rare, benign tumor that occurs in different localizations. It may commonly be mistaken in prediagnosis, and may be confused with other clinical states due to its clinical characteristics. It is possible to protect the sense of hearing, and the facial nerve functions in cases diagnosed at an early stage; therefore it has to be kept in mind in the differential diagnosis of patients with facial paresis and hearing loss.

Correspondence
Gokhan Canaz, Bakirkoy Research and Training Hospital for Neurology, Neurosurgery and Psychiatry, Department of Neurosurgery, Bakirkoy / Istanbul, Turkey.
Phone: +90 212 409 15 15
Mail:gokhancanaz@gmail.com

References
A prospective observational study of clinical outcome of operated patients of intradural extramedullary spinal cord tumor in our tertiary care center

P.R. Singh¹, T.K. Pandey², F. Ahmad³, D.K. Chhabra⁴

Department of Neurosurgery, Vivekananda Polyclinic and Institute of Medical sciences, Lucknow, INDIA

Abstract: Aim: This prospective observational study aimed at finding out the efficient clinical and functional factors which affect the surgical outcome on the basis of location of the intradural extramedullary spinal cord tumors (IESCTs) and in follow up period of 1 year post surgery, treated at a single tertiary institution (Vivekananda Polyclinic and Institute of Medical Sciences, Lucknow). Material and Methods: We prospectively analyzed 44 consecutive cases of IESCTs diagnosed on radiology and operated at our center from 2014 to 2016. The demographic data, clinical presentation, tumor radiological parameters (axial and sagittal location and tumor occupancy ratio), treatment modality, and follow up outcome of these patients are reviewed. We have excluded patients with Neurofibromatosis, recurrent tumors and intradural cauda equina and conus lesions. Result: A clinical series of 44 patients with IESCTs, underwent surgery (standard laminectomy) and excision of tumor have been followed for 1 year. The most commonly involved spinal level was dorsal (65.91%) followed by cervical (20.45%) and lumbar (18.18%) spine. The axial location of tumor was dorsal/posterior (6.82%), ventral/anterior (13.64%) while most common axial location of tumor was lateral (79.55%). We have found that the gait disability score and frankel score shows significant improvement within 1 week after surgery and after 1 year of follow up, 90.91 % patients have gait disability score of > 2 while frankel scale has shown, 81.82 % were ambulatory and only 18.18 % were non-ambulatory. Conclusion: Analysis of the MRI findings should be undertaken in a routine, standardized fashion to insure the accurate evaluation of the location of the tumor for planning the surgical interventions. As a surgeon we should be more cautious while operating on the purely ventrally located tumors through the posterior approach and we may prefer anterior approach in them. Similarly in sagittal location, we should be cautious to operate the thoracic locating tumors to prevent the post-op complications.

Key words: Intradural extramedullary tumors, meningioma, schwannoma, neurofibroma
Introduction

Intradural extramedullary spinal cord tumor (IESCTs) constitute approximately two third of these tumors. The most common primary IESCTs are derived from sheath cells covering the spinal nerve roots (schwannoma and neurofibroma) or meningeal cells located along the spinal cord surface (meningioma). Spinal nerve sheath tumors account for approximately 40% of all spinal tumors (0.3-0.4 cases annually per 100,000 people) while spinal meningioma accounts for about 30% of the IESCTs. Most of the Indian studies have shown male preponderance in IESCTs except in meningioma which has more female preponderance. The female preponderance is thought to arise from the sex hormone or other type receptor common in women.

More than 50 % of the IESCTs are located in the thoracic spine, and they occur in the cervical and lumbosacral spine at a similar rate, 22 % and 18 %, respectively. Most nerve sheath tumors are frequently observed in thoracic spine (39%), lumbar spine (32%), and cervical spine (23 %). Spinal schwannoma arise from dorsal root (hence posterior, lateral or posterolateral in position ) and < 5% originating at the anterior (ventral) root, however as much as 23 % of the cervical nerve sheath tumor have an anterolateral component consistent with ventral root origin. Spinal meningioma is nearly 80 % found in thoracic region, in cervical region it is about 14-27 % and of lumbar is about 2-14 % while sacral meningioma are very rare.

Surgical approach is determined primarily depending on the location of tumors in spinal canal. However tumor consistency and pathology should also be considered. Standard posterior approach through bilateral or unilateral laminectomy provides adequate exposure to safely remove the vast majority of these lesions, without the need for potentially destabilizing facet or pedicle resection. Now, modified approaches are used which are minimally invasive and may be routinely used to remove IESCTs. Posterior exposures with varying degree of lateral bone resection, dentate ligament division, and gentle cord rotation may also provide adequate exposure for safe removal of non midline ventro-lateral superficial pial presenting spinal cord lesions. Solid ventral midline schwannoma are optimally managed by anterior and anterolateral approaches, although soft consistency tumors can be approached from postero-lateral approach with satisfactory outcome. Radiosurgery in intradural spinal tumors is evolving and seems to be an effective tool for the patients, who are not suitable for open surgery, as well as with multiple lesions, recurrences or tumor remnants after microsurgery.

Patients and Methods

A prospective review was performed between June, 2014 and June, 2016 of all the consecutive 44 operated patients of IESCTs at our institutions. The study was approved by the ethical committee of the hospital and all the patients involved in this study signed the informed consent. A detailed clinical history elucidated, followed by careful clinical examination, which was recorded as per the performa. Clinical disability was assessed by
the Gait disability scale and Frankel scale in both pre-op, at the time of discharge, 3 months and 12 months follow up.

Diagnostic evaluations included MRI (spine) with or without contrast with an axial slice demonstrating the tumor and the respective spinal column (Sagittal and axial) location of the lesion. The axial location of the tumor were categorized as anterior, posterior, or lateral with respect to the spinal cord and were described to correlate with a clock face. The tumors that were predominately between “10 and 2 o’clock” were considered anterior while if tumor predominately occupied “4 to 8 o’clock” then they were considered posterior and those that were either “2 to 4 o’clock” of “8 to 10 o’clock” were considered “lateral”. Tumor occupancy ratio was also studied in axial MRI (spine).

Surgery was done in all cases as standard posterior laminectomies and unilateral medial facetectomy was done in anteriorly located tumor. Dura was opened in median or paramedian manner and in few ventrally located tumors or with extra dural extension; we opened dura in T shaped manner and may require for cutting the dentate ligament to retract the cord for removal of the tumor. After dural opening, a plane was developed between arachnoid membrane and tumor surface. The tumor was removed en bloc or piecemeal. The involved nerve roots were coagulated and cut in case of schwannoma while in case of meningioma dural origin coagulated using bipolar cautery in most of cases (Simpson grade II). Gross total excision of tumor done in all cases.

In immediate post-op, complications were noted and neurological status was again assessed at the time of discharge by Gait disability score and Frankel score and then patient was followed up in next 3 months and after 1 year.

**Results**

The age of all patients ranged from 16-75 yrs with mean (±SD): 42.6 (±17.25) yrs. Most of the patients were in 40-60 yrs age group (31.2%) followed by 20-30 yrs (27.27%), > 60 yrs (15.91%) and <20 yrs the least (11.36%). Most patients were male (70.45%) while only (29.55%) were female. The mean age of presentation in male was 38.5 yrs while in female; it was 46.83 yrs. Mean duration of illness was 11 months (male 12.08±12.18, female 9.91±10.60) and it showed no significant difference between the genders.

Around 38.64% patients were of ≤ 5 months duration while only 18.18% were of > 20 months duration. Further, All (100%) patients had back pain, 97.73 % had sensory complaints while 68.18% had myelopathy, 56.85% had motor deficit and 50% had sphincter dysfunction while only 25% had radiculopathy.

The most commonly involved spinal level was Dorsal (65.91%) followed by Cervical (20.45%) and Lumbar (18.18%) spine. It has been found that most common location of tumor was D5-D9 in Meningioma (56.25%) and in Schwannoma most common location is Lower dorsal-lumbar group (39.29%). I have also divided the axial location of tumor into Dorsal (6.82%), Ventral (13.64%) while most common axial location of tumor was Lateral.
(79.55%) which is approximately similar in both the tumor types.

We have analyzed the sagittal location of the tumor with the clinical outcome in all the clinical outcome groups (on discharge/3 months/12 months) and found that patient with thoracic location has more improvement (> 2 grades) in clinical outcome than with other tumor location while least change in disability score was noticed in lumbar group.

The tumor occupancy ratio was divided into 3 groups (70-80, 80-90 and > 90) and found that only 6.81 % have tumor occupancy > 90 % while 70-80 and 80-90 % tumor occupancy was approximately equally divided in 2 groups. I have also analyzed the tumor occupancy ratio with the disability score and found that once the tumor occupancy increased, the disability also increased (r= 0.66, p< .001).

According to Gait disability score, most of the patients at Pre-op were at Grade 4 (38.64%), followed by Grade 2 (25%), Grade 5 (18.18%), Grade 1 (15.91 %) and Grade 3 only 2.27%. The χ2 test revealed significant improvement in Grade of patients in immediate post-op (7 days after surgery) and then over the periods (12 months) of follow up after surgery. Frankel scale also has shown similar results as most of patients at Pre-op were at Grade D (45.45%), Grade C (34.09%), Grade E (13.64%) and Grade B in only 6.82%. Similarly the χ2 test revealed significant improvement in Frankel score in immediate post op and then over the periods of follow up after surgery.
At final evaluation (i.e. after 12 months), the outcome was that patient was that 90.91% patients have Gait disability score >2 while in Frankel Scale it was shown that after 12 months follow up 81.82 % were ambulatory while only 18.18% were non-ambulatory.

**Discussion**

Most patients were male (70.45%) while only (29.55%) were female and no significant difference was found between the clinical presentation and duration of illness between the genders. The literature shows the female preponderance in western countries while Asian studies favors male preponderance although our study reflects more male ratio which may be because of social stigma or delayed follow up of female patients in eastern U.P of Indian population. The female preponderance of meningioma is a well-known entity and our study supports it. We found that meningioma favors the elderly female population while schwannoma are more in young male population similar to the previous literature. The mean age of presentation in our study was 38 years in male and 46 years in female which is same as compared to that of western world along with other asian studies as Arora et al, 2015, Mondle et al, 2016, Govind M et al, 2016, Iacob G, 2014.

The mean duration of illness was 12 months in male patients and 9 months in female patients in our study. It was found that meningioma groups have more myelopathy in upper thoracic spine as reviewed on other studies. Early presentation of the patients are more in upper thoracic spine group which is
explained by the higher cord-to-canal ratio, as well as the tenuous vascular supply to that region of the spinal cord. The lesser mean duration of illness in female may be found due to higher incidence of thoracic locating tumor in female.

No association between the axial location (dorsal- dorsolateral/ventral- ventrolateral) and the clinical outcome was found in our study (p < 0.26) supported by Mehta et al, 201320, Riad et al, 201323, Rinaldo et al, 201624. The extradural component was noted in 6 (14%) of our all patients of nerve sheath tumors which is similar to other studies22 in literature which is 10%.

Our study gives the similar results to Mehta et al 20 as the ventrally located tumors trended toward development of neurological deficit as occurred in our 2 patients, although trend not significant (p= 0.45). This can also be explained by the difficult approach to purely ventral locating tumor. Mehta et al, 2013 had done the first systemic study to assess the association between axial/saggital tumor location and outcomes and post-operative complication19. However, a saggital spinal column level was significantly associated with the development of a neurological deficit, as patients with IESCTs tumors located in upper thoracic spine were more likely to have a post-operative neurological deficit.

I have also analyzed the tumor occupancy ratio with the disability score and found that once the tumor occupancy increased, the disability also increased (r= 0.66, p< .001). Song et al, 200927 and Haq el at, 201510 has included this tumor occupancy ratio in their study but has not shown any co relation with the clinical outcome similar to our study. In our study, only 6 (18.18%) has 2 level of column of tumor while majority of the patients 38 (81.1%) has only 1 level of involvement. Stawicki et al, 200728 has considered level of tumor as a prognostic factor but our study did not support it.

In case of meningioma we had done gross total excision of tumor with Simpson grade II resection in all of the cases and found no recurrence in the follow-up period as favored by other studies also which consider Simpson grade I and grade II equally effective in complete surgical resection.30 however our follow up was of very short duration to comment on the recurrence. We have done coagulation and cutting of involved rootlet in nerve sheath tumor similar to many of the studies20 and found no functional neurological deficit even in ventrally located tumors except sensory deficits in few cases in the involved region.

In post-op we have seen that within 7 days after surgery approx 60 % of the patient walking either with minimal support or independently (Grade 4 and 5) within 7 days after surgery similar to Frankel score. Majority (90%) of clinical improvement noted within 3 months of the operative intervention.24,2 At final evaluation (i.e. after 12 months), the outcome was that patient was that 90.91% patients have Gait disability score >2 while in Frankel Scale it was shown that after 12 months follow up 81.82 % were ambulatory while only 18.18% were non-ambulatory.
Conclusion

Location of the tumor was important to understand the nature and course of the disease in these tumors. We have found deterioration in 2 ventrally located tumors hence we should be careful in operating purely ventral located tumors through posterior/posterolateral approach and we may prefer anterior approach for purely ventral tumors. In thoracic locating tumors due to higher cord-to-canal ratio, we should always be more cautious and purely ventral and thoracic tumor has higher chances of post-op complication.

MRI findings should be undertaken in a routine, standardized fashion to insure that important details are not missed for more accurate evaluation of location of the tumor along with the measurement of tumor occupancy ratio in all the patients. Radiological finding as tumor occupancy ratio has an impact on the early presentation of the symptoms and thereby defining the role of location of the tumor.

Tumor type on the basis of pathology has also not shown any significant association with the clinical outcome in our study. We have found that disability score (Gait disability score and Frankel score) both are good clinical outcome predictors in these patients.

We have found that approx 60% of the patient walking either with minimal support or independently within 7 days after surgery while majority (90%) of clinical improvement noted within 3 months of the operative intervention. At final evaluation (i.e. after 12 months), the outcome was that patient was that 90.91% patients have Gait disability score >2 while in Frankel Scale it was shown that after 12 months follow up 81.82% were ambulatory while only 18.18% were non-ambulatory. Thus we should consider that early excision of the tumor for better outcome and recovery.

I have not commented on the recurrence of the tumor because of the limited duration of the study as we know the usual period of recurrence is 3 years and follow up radiology should be done after 5 years after surgery.

Finally the skill of an individual surgeon always be a factor affecting our results and hence can never be ruled out.

Correspondence

Dr. P.R Singh, Senior Resident, Department of Neurosurgery, Vivekananda Polyclinic and Institute of Medical sciences, Nirala nagar, Lucknow. Email: prashantsingh2010@yahoo.com

References

Ruptured intracranial internal carotid artery aneurysm causing subarachnoid hemorrhage and opthalmoplegia associated with metastatic carcinoma with unknown primary in sellar-parasellar region: True or Coincidental Association

G.D. Satyarthee¹, L.R. Moscote-Salazar², A. Agrawal³

¹Department of Neurosurgery, Neurosciences Centre, AIIMS New Delhi, INDIA
²Red Latino. Latin American Trauma & Intensive Neuro-Care Organization, Bogota, COLOMBIA
³Neurosurgery Department, Narayana Medical College Hospital, Chinthareddypalem, Nellore, Andhra Pradesh, INDIA

Abstract: Unruptured intracranial aneurysm can be picked up incidentally on cranial angiography screening for other cause. However, with increasing use of neuroimaging led to increasing rate of pickup and many such incidentally detected cases are treated with endovascular treatment, or craniotomy and clipping of aneurysm or uncommonly a very small aneurysm unsuitable for retreatment by currently available modality may be observed as wait and watch policy. Extremely uncommonly a patient undergoing investigation for suspected subarachnoid hemorrhage following aneurismal rupture, computed tomography scan revealed presence of subarachnoid hemorrhage associated with sellar mass. Such association was previously unreported. In extensive Pubmed search by authors could find a case reported by Yang et al., a case of known surgically resected gastric carcinoma developing secondary in sella, CT angiography of the intracranial artery revealed an aneurysm of ICA located at the inner edge of the siphon segment. Authors report an interesting case of 65 - year -old male presented with aneurysmal subarachnoid hemorrhage with secondary in sella with unknown primary, CT Scan showed presence of sellar mass, underwent digital subtraction angiography at our centre, revealed presence of right supracliniod internal carotid bifurcation aneurysm, underwent craniotomy and successful surgical clipping of aneurysm with gross total decompression of sellar and suprasellar mass. To the best knowledge of authors, current case represents first case in western literature, who presenting first time
with aneurysmal subarachnoid hemorrhage and coincidentally associated with incidental sellar mass of metastatic origin Pertinent literature is discussed briefly. **Key words:** Adenocarcinoma, aneurysm, secondary in sella surgical management, primary lesion, association

**Introduction**

Intracranial aneurysm can be detected after rupture or rarely picked up incidentally. The ruptured intracranial aneurysm present with sudden severe headache may be associated with focal neurological deficit. [1][2][3] Imaging study may show presence of subarachnoid hemorrhage, intracerebral hematoma, intraventricular hemorrhage, obstructing hydrocephalus, or in late stage may show developing infarct due to vasospasm. However ruptured intracranial aneurysm associated with parasellar mass is uncommon, although cases of incidental aneurysm with intracranial tumor like pituitary adenoma, meningioma, are reported. However, ruptured internal carotid artery aneurysm with metastatic mass lesion is extremely uncommon. Pre-operative knowledge of aneurysms coexisting with sellar mass may help in planning special strategy to deal both lesions simultaneously.

**Case Illustration**

A 65-year old man was admitted to Department of neurosurgery at neuroscience centre of All India Institute of Medical sciences. He experienced sudden onset very severe headache in left frontal and temporal region associated with vomiting. Next morning, he noticed diminution of vision involving left eye along with drooping of left eyelid. However, he had persistent headache but intensity has markedly reduced with progressive worsening of drooping of left upper eyelids along with painful progressive ophthalmoplegia. On admission, his supine BP was 130/70. Positive neurological findings included with left eye, he was able to count finger at three feet, while, and on right side was 6/6. Fundi revealed normal retinal arteries and normal appearance of fundi. His extraocular movement of the left eye-ball was completely absent. Routine hemogram and serum biochemistry was normal. Endocrine study revealed serum cortisol (8 am) level 0.8 μ g / dl (N 5 -18 ) TSH- 1.8 μ IU /dl (N0.4- 4.6 ), T3 1.3 pg / ml (N 1.6-3.4), T4 – 6.4 ng /dl (N 0.7-1.8). As serum cortisol level was low, so corticosteroid replacement was started.

X-ray chest and electrocardiography were normal. An X-ray skull revealed sellar enlargement with erosion of anterior clinoid process. CT scan of cranium revealed sellar, suprasellar lesion with left parasellar extension, showing enhancement with contrast agent. A 4-vessel digital subtraction angiographic study was done for evaluation, which revealed left internal carotid artery aneurysm which was directed superiorly.

Through a left pterional osteoplastic flap craniotomy after eighth day of ictus. There was mass filling up left parasellar and suprasellar region, gross decompression was also done, with intra-operative diagnosis of pituitary adenoma was made. In the postoperative
period, he made good recovery. Just prior to discharge from hospital, a repeat angiography was carried out, revealed well clipped aneurysm to look for completeness of aneurysm clipping. He was discharged from hospital on sixth post-operative day. However, the histopathology turns out to be poorly differentiated metastatic adenocarcinoma.

Discussion

The metastatic mass lesion accounts for only 1% of the tumors located in the sellar-parasellar regions, for cases, who underwent transsphenoidal surgery [1]. Breast and lung cancer are among the most common sites of primary malignant tumors to sellar regions [3] other includes gastrointestinal tract, prostate, kidney, thyroid, and pancreas. The important routes of metastasis to the pituitary gland include hematogenous or direct invasion through the skull base. The hematogenous route is the principal pathway of metastasis and lymphatic system is absent in the brain. The most commonly involved part of the pituitary gland in the order of decreasing frequency is posterior lobe, anterior hypophysis, both the anterior and posterior hypophysis, and the stalk [4]

Intracranial aneurysms commonly occur in the region of Circle of Willis, are often saccular or arteriosclerotic in origin. Although saccular aneurysms can occur in peripheral branches of the circle of Willis, but it is very rare. Aetiology of aneurysms occurring in the peripheral branches includes, in the decreasing order of frequency are mycotic, post-traumatic or secondary to tumour and Moya-Mmoya diseases. Usually the occurrence of intracranial aneurysm association with intracranial brain tumours or secondary’s are extremely uncommon [1][2][3][4][5][6][7][8]

Very rarely incidental aneurysm can be picked up while investigation of sellar mass and few cases of intracranial aneurysm with associated with pituitary adenoma is reported. Such association of intracranial aneurysm with tumor significantly increases the risk of inadvertent rupture during the intraoperative phase; surgery is attempted utilizing either trans-sphenoidal decompression or endoscopic approach.

The commonest presenting symptom in patients with sellar metastases is central diabetes insipidus, followed by anterior hypopituitarism, visual loss, [9][10]

However, diagnose of sellar metastasis is difficult because symptoms are mostly nonspecific and the radiological differences from primary tumors are nonspecific . [12][13][14][15] Imaging study play an important role in the diagnosis of sellar parasellar region, besides clinical examination and hormonal assessment. CT scan head can show presence of subarachnoid hemorrhage, intracerebral hematoma, intraventricular hemorrhage, obstructing hydrocephalus, obstructing hydrocephalus, or in late stage may show developing infarct due to vasospasm. However ruptured intracranial aneurysm associated with parasellar mass further MRI better delineates soft tissues and common lesion in sellar region needs exclusions are meningioma, pituitary adenoma and vascular mass. MRI shows presence of sellar suprasellar mass, showing
contrast enhancement, may be associated with areas of hemorrhage or necrosis representing previous pituitary apoplexy. Meningiomas are solid, with occasional cyst on the edge or associated with peritumoral arachnoid cap, usually show uniform contrast enhancement. In the coronal section images can show a compressed normal pituitary gland can be seen separately from tumour in cases of meningioma at the bottom of the sella turcica and epicenter of mass lies above the sella.

A diagnostic MRI sign of flow voids is 100% specific for aneurysms as described by Teng et al. with the sensitivity of 88%, on T1-weighted and T2-weighted imaging sequences[10] however Olsen et al. reported only 80% giant aneurysms shows sign of blood flow in the aneurysm sac. So MRI may fail to detect aneurysm if size of aneurysm being smaller[11].

In MRI scan, T1W image may show evidence of hypointense signal representing flow void caused by as rapidly flow blood in a carotid aneurysm. Cases of thrombosed aneurysm, DSA study can be very helpful in arriving at diagnosis, delineating shape, size, direction of fundus, vessel originating from aneurysm, relation with adjoining branches of artery, presence of teat.

Regarding management of such co-existing aneurysm with secondary is debated is debated and controversial and depends on size of aneurysm, location on anterior or posterior circulation, proximity to sella or, size of sellar mass adenoma, status of adenoma, volume of adenoma, associated neurological manifestation, visual symptom, extension into multiple cranial fossa or multi-compartmental and general status of cases. [16][17] [18][19] Although differentiating whether a lesion of interest is primary or secondary is very vital in planning treatment modality for such cases and diagnosis mainly rest on histopathological and immunohistochemistry. If a tumor in the pituitary gland is confirmed to be metastatic, local tumor control is planned to relieve symptoms, and the overall prognosis depends on the site of the primary malignancy[9][10].

Yang et al reported a case of known surgically resected gastric carcinoma in a 57-year-old woman with internal carotid aneurysm developing secondary in the sella. [2] She presented with oculomotor paralysis, postorbital pain, and hypopituitarism as onset symptoms. She had a history of the surgical removal of gastric cancer CT angiography of the intracranial artery revealed an ICA of at the inner edge of the siphon segment. Magnetic resonance imaging and single-photon emission study revealed recurrent sellar mass with intracranial and multiple metastases of bone. He underwent subtotal removal followed by chemotherapy and radiotherapy. [2]

With increasing usage of endovascular approach, aneurysm can be coiled and sellar mass can be resected using microsurgical or endoscopic approach separately, however if aneurysm lying in close proximity to mass can be managed in a single setting with clipping of aneurysm and adenoma resection.[20][21][22] However, approach should be individualized and tailor made after analyzing imaging study. However, high degree of suspicion of associated aneurysm is
must be made, if MRI shows some atypical features and DSA must be carried out.

**Conclusion**

In cases of suspected subarachnoid hemorrhage following aneurysmal rupture, and imaging study showing sellar mass possibility of primary as well as metastatic lesion must be considered. Ruptured aneurysm co-existing with metastatic sellar mass with unknown primary is previously unreported and constitute a rare but difficult to manage association, which has not received proper attention in the literature. As awareness about coexisting aneurysm can aid in proper planning to deal both associated pathology in safest way, if surgery is attempted. However, precise knowledge can avoid injury, if strategy can be planned to deal both lesion in a single operative session.

**Correspondence**

G.D. Satyarthee  
Department of Neurosurgery  
Room No. 714  
Neurosciences Centre, AIIMS New Delhi  
E-mail: dgrguruduttaaiims@gmail.com

**References**

Isolated dorsal vertebral Chondroblastoma: a rare case with review of literature

S. Pandey, K. Kaushik, L.N. Gupta, R. Varshney, Prarthana Saxena
Department of Neuro Surgery, P.G.I.M.E.R. DR Ram Manohar Lohia Hospital, New Delhi, INDIA

Abstract: Accounting for approximately 1-2% of all bone tumors, chondroblastoma is a benign bone tumor that is locally aggressive too typically affects the epiphyses or apophyses of long bones. Less commonly affected sites include the talus and calcaneus of the foot and flat bones. Vertebral involvement by chondroblastoma is very rare, with advance Pubmed search we could find only 30 cases, reported in literature of vertebral chondroblastoma. We are presenting one such rare case with review of available literature to evaluate clinical radiological and pathological characteristics of vertebral chondroblastoma.

Key words: Chondroblastoma, bone tumor, Vertebral involvement

Introduction

Accounting for approximately 1-2% of all bone tumors, chondroblastoma is a benign bone tumor that is locally aggressive too typically affects the epiphyses or apophyses of long bones. It arises from an outgrowth of immature cartilage cells (chondroblasts) from secondary ossification centers, originating from the epiphyseal plate or some remnant of it.1 This tumor is known to be prevalent in children and young adults in the second decade of life14 with predilection towards the male sex (male to female ratio 2:1). It commonly involves the femur, followed by the humerus and tibia with talus and calcaneus of the foot and flat bones being the less affected.1

However, its vertebral involvement is very rare and with advanced Pubmed search we could find only 30 cases of vertebral chondroblastoma, which have been so far reported in literature.

One such rare case with review of available literature to evaluate clinical radiological and pathological characteristics of vertebral chondroblastoma is discussed below.

Case report

History & clinical examination

A 30 year male patient was admitted with chief complaints of backache for two months which was gradually progressive and was
radiating to left subcostal region intermittently with aggravation of pain during walking or lifting any weight by forward bending. Patient also developed insidious onset rapidly progressive ascending type of weakness of both lower limbs for last two weeks. However he had no bowel or bladder complaints. There was no history of trauma, recent fever or tuberculosis.

On neurological examination: Tone of bilateral lower limbs was increased (modified Ashworth Grade 2). Power at hip and knee joints was 4/5 and ankle and below was 3/5 (as per MRC grading). There was decreased sensation, vibration & proprioception below 8th thoracic vertebra. The deep tendon reflexes of the lower limbs was exaggerated and Babinski sign was present bilaterally.

**Radiological examination**

Plain X-ray shows osteolytic lesion involving right side of D7 vertebrae. M.R.I. thoracic spine revealed bony expansile lesion involving D7 vertebra with involvement of right transverse process, spinous process and right posterior body with involvement of adjacent paraspinal soft tissue, causing compression of spinal cord and signal change in the cord. Patient was worked up for unknown primary and on lines of plasmocytoma which was negative.

**Surgery**

By a posterior approach, he underwent D7 laminectomy and a thorough intralesional excision involving the posterior elements and the vertebral body, with complete decompression of spinal cord. D7 spinous process and right sided lamina and posterior part of body were eroded out by tumor, which was greyish yellow and moderately vascular. It was located in epidural space and there was no breach in dura. After tumor debulking spinal cord returned to normal position and began to pulsate. Near total excision of tumor was achieved. A spinal stabilization was performed with a posterior fusion from D6 to D8 with pedicle screws and titanium rods.

**Post-operative course**

Postoperatively patient was given thoracolumbar brace and gradually mobilized. There was gradual improvement in lower limb power and patient regained his normal power. There was no postoperative complication.

**Histopathology**

Showed multiple fragments of tumour composed of mononuclear oval to spindle cells arranged in sheets with collagenised stroma. The cells show mild pleomorphism with nuclear groove and indentation intervening many thick and thin walled blood vessels, with chicken wire calcification and focal cartilaginous differentiation. Scattered osteoclast type of giant cells were also seen. These histopathological findings were consistent with chondroblastoma (Figure 1).

**Discussion**

The term Chondroblastoma was described by Ernest Armory Codman, in 1931 as an epiphyseal chondromatous giant cell tumor of the proximal humerus, hence the term Codman Tumor. This tumor was described to be benign in nature by Henry L. Jaffe and Louis Lichtenstein in 1942.
Although chondroblastoma occur most often in the epiphysis of the major tubular bones, this tumor can appear in any secondary ossification center, such as greater trochanter. One of the rare locations of this tumor is vertebrae due to presence of a secondary ossification center. First case of Chondroblastoma of the mobile and nonmobile spine was reported in 19575. The incidence of vertebral chondroblastoma is 1.4% of all chondroblastomas, and 30 cases have been reported in the English (28 cases)4 and Korean literature (two cases)5,6 (Table 1). The most common location in spine is cervical followed by thoracic spine2.

The most common presenting complaint is localised pain. The clinical findings are somewhat nonspecific and vary depending on the tumor extent and level of involvement. This tumor has a typical radiological finding of an eccentric osteolytic lesion, frequently accompanied by a thin sclerotic rim. Vertebral chondroblastomas may sometimes appear malignant radiologically due to bony destruction and/or soft tissue extension, as compared to chondroblastomas of the extremities, which are usually well demarcated from surrounding bony tissue2,4,7,12,13. However, these findings are nonspecific in vertebral chondroblastomas thus not of much diagnostic help. Spinal cord compression and/or neurological deficit occasionally accompany the lesion2,4,14. Therefore, the possibility of vertebral chondroblastoma should be kept in mind if vertebral mass imaging findings are reminiscent of a malignancy such as a destructive bony lesion with large soft mass formation or spinal invasion.

The differential diagnosis includes both benign and malignant lesions, including tuberculous spondylitis, eosinophilic granuloma, aneurismal bone cyst (ABC), giant cell tumor, chondromyxoid fibroma, osteoid osteoma, osteoblastoma, chondrosarcoma, and metastasis. The final diagnosis should be confirmed by histological examination. As far as size is concerned these tumors range from 2.3 cm to 8.2 cm (diameter). With respect to histological findings vertebral chondroblastoma are not different from chondroblastomas at other usual sites. This tumor is defined to be cellular with sheets of uniform round- to polygonal mononuclear cells with well-defined cytoplasmic borders which have clear to slightly eosinophilic cytoplasm with occasional nuclear grooves admixed with scattered giant cells5. Importantly, chondroid differentiation and characteristic chicken-wire calcification are needed to confirm the diagnosis admixed with scattered giant cells. Approximately 35-50% of chondroblastomas show matrix calcification4,14 and more than one-third of chondroblastomas contain secondary ABC-like changes3,10.
<table>
<thead>
<tr>
<th>Author et al Year</th>
<th>No. of cases</th>
<th>Sex/age</th>
<th>Neurological deficit</th>
<th>location</th>
<th>Extent</th>
<th>Operation</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wisniewski et al (1973) [4]</td>
<td>1</td>
<td>M/17</td>
<td>No</td>
<td>C1, C2</td>
<td>STE</td>
<td>Curettage</td>
<td>NS</td>
</tr>
<tr>
<td>Hoeffel et al 1987 [6]</td>
<td>1</td>
<td>M/9</td>
<td>Yes</td>
<td>C7</td>
<td>STE</td>
<td>Repeated surgery</td>
<td>72 months Recurrence and death from tetraplegia</td>
</tr>
<tr>
<td>Leung et al (2001) [10]</td>
<td>1</td>
<td>F/54</td>
<td>Yes lower limb weakness</td>
<td>L5</td>
<td>SCE and STE</td>
<td>Intracapsular tumor excision, L5 vertebrectomy</td>
<td>Two recurrences then lost to follow-up</td>
</tr>
<tr>
<td>Nishida et al (2001) [11]</td>
<td>1</td>
<td>M/19</td>
<td>Yes tetrapresis</td>
<td>C5, C6, C7</td>
<td>SCE and STE</td>
<td>Thorough curettage, combined anterior and</td>
<td>2 years and 3 months NED Neurologic deficit fully recovered NED</td>
</tr>
<tr>
<td>Study</td>
<td>Sex</td>
<td>Age</td>
<td>Presence</td>
<td>Lesion</td>
<td>Approach</td>
<td>Treatment Details</td>
<td>Outcome</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-----</td>
<td>-------</td>
<td>----------</td>
<td>--------</td>
<td>----------</td>
<td>----------------------------------------------------------------------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>Attar et al (2001) [12]</td>
<td>1M</td>
<td>48</td>
<td>No</td>
<td>T2</td>
<td>SCE</td>
<td>Thorough curettage. combined anterior and posterior approaches</td>
<td>NS</td>
</tr>
<tr>
<td>Ilaslan et al (2003) [14]</td>
<td>9M&amp;F</td>
<td>28</td>
<td>NS</td>
<td>C2,T5, L1, S1</td>
<td>SCE in 6 cases &amp; STE in all cases</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Vialle et al (2005) [15]</td>
<td>2F</td>
<td>55, 23</td>
<td>No</td>
<td>L4/L3</td>
<td>NS</td>
<td>Vertebrectomy in two cases</td>
<td>6 years NED 3 years NED</td>
</tr>
<tr>
<td>Lee YH et al (2005) [16]</td>
<td>1M</td>
<td>40</td>
<td>Yes lower extremity weakness</td>
<td>T7</td>
<td>SCE and STE</td>
<td>Combined anterior and posterior surgery, T7 vertebrectomy</td>
<td>NS</td>
</tr>
<tr>
<td>Mohamed et al (2011) [18]</td>
<td>1M</td>
<td>46</td>
<td>No</td>
<td>T12L1</td>
<td>STE</td>
<td>Total laminectomy T11T12L1</td>
<td>Died one day after operation because of bleeding</td>
</tr>
<tr>
<td>Hernández Martínez et al</td>
<td>1F</td>
<td>30</td>
<td>No</td>
<td>L4</td>
<td>NO</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>
Treatment modality of this tumor is usually simple curettage with bone grafting. Recurrence depends on anatomical location. Chondroblastomas of the spine behave more aggressively due adjacent vertebrae destruction and resulting neurological complications with a higher rate of relapse and mortality. Hence, efforts should be directed towards complete excision which is the recommended treatment modality for vertebral chondroblastomas. However, frequent involvement of the spinal canal and paraspinal muscles makes it difficult to completely remove the tumor without neurological deficit. Local recurrence occurs in about one-third of patients and is apparently higher than that of extraspinal chondroblastoma, which is 5-18%. This may be attributed to the frequent extension to adjacent soft tissue and the spinal canal, which hinders complete resection. High recurrence rate and difficult complete resection necessitates the need for follow up over the long-term post surgery.

To summarise this was a case report of chondroblastoma arising in the lumbar spine with a sincere effort to review the relevant literature. For any vertebral mass appearing aggressive on imaging findings chances of it being vertebral chondroblastoma should be kept in mind and a histopathology should be performed to confirm the same. One should not forget that vertebral chondroblastomas may behave differently from those of chondroblastomas of the extremities. Lastly, long-term clinical follow-up is required as far as vertebral chondroblastomas are concerned.

Correspondence
Sharad Pandey
Department of Neurosurgery
P.G.I.M.E.R. DR Ram Manohar Lohia Hospital, New Delhi110001, India
Previously with Department of Neuro Surgery, Sir Sunder Lal Hospital, IMS, BHU,
References

Therapeutic benefit of palmitoylethanolamide in the management of neuropathic pain

I.D. Chaurasia, Kunal Vinayak, Shashikant Tiwari, Prateek Malpani, Sheikh Behram, Mahim Koshariya

Department of Surgery, Gandhi Medical College & Associated Hamidia Hospital, Bhopal, M.P., INDIA

Abstract: Background: Neuropathic pain is defined by International Association for the Study of Pain (IASP) as "Pain caused by a lesion or disease of the somatosensory nervous system". Elderly patients generally have high incidence of chronic neuropathic pain. The safe and effective treatment for chronic pain is a large public health concern. Palmitoylethanolamide (PEA) is an endogenously produced amide cannabimimetic compound with tissue protection and anti-inflammatory activity. Objectives: The aim & objective of this study is to evaluate the effectiveness and safety of Palmitoylethanolamide (PEA) in patients suffering from Neuropathic/Chronic Pain. Study Designed: Prospective Study. Materials and Methods: The Study was conducted in the Neurosurgery unit of Surgery Department in Gandhi Medical College & Associated Hamidia Hospital, Bhopal. A total no. of 150 patients aged 20-78 years were included in the study and divided into two groups, group I (Study group) and the group II (Control group) PEA was given to group I to evaluate the effect of PEA in neuropathic pain. Result: We studied 150 patients with PEA for 60 days in a dose of 354 mg orally three times (TDS) a day for first 10 days and then two times (BID) a day for 50 days. It is available in India by the name of Palmiges. PEA was associated with greater pain reduction in the study group compared to the placebo controlled group. The primary outcome measured was the mean pain reduction evaluated by VAS scale. Conclusion: PEA seems to be useful in the treatment of neuropathic / chronic pain and it is well tolerated in patients in study group. Palmiges PEA reduces the inflammation in neuropathic pain, which results in lowering/reduction of neuropathic pain. Controlled trials are further needed to prove efficacy and reliability and also to find out the adverse reaction associated with the drug.

Key words: PEA, Palmitoylethanolamide, Neuropathic Pain, Analgesics, VAS (Visual Analogue Score)

Introduction

Neuropathic Pain is a complex condition that has its origin in a primary lesion or dysfunction of any part of the nervous system from the peripheral receptor to the brain. Persistent neuropathic pain often interferes with sleep, work, recreational activities and the
emotional state of the individual who suffers from it, thus affecting quality of life [1]. Neuropathic pain is usually described as the perception of strange or unusual painful sensations like burning, stabbing or lancing pains experienced as electrical discharges or other painful sensations [2,3]. Neuropathic pain may be evoked by mechanical, thermal or chemical stimuli.

**The Global Prevalence: reported in the literature**

- A review of the epidemiology of chronic pain found that there is still no accurate estimate available for the population prevalence of neuropathic pain (Smith et al.2012). [4]
  - Overall, neuropathic pain affects 7-10% of the general population.
  - In the primary care setting, the prevalence has been reported to be between 2 to 11%.
  - By Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS) criteria, the prevalence of DPN was 29.2%.
  - In cancer patients the prevalence is 19%.
  - In Indian Scenario: -
    - The prevalence of Neuropathic pain in Indian scenario is difficult to establish, as there are many confounding factors that may lead to under reporting of neuropathic pain.
    - The prevalence in males is around 26.1% and females is 33.8%, whereas prevalence of neuropathic pain in cancer patients is 19%.
    - About 1% to 37% of chronic lower back pain patients may have a neuropathic component related to it.
    - Prevalence of neuropathic pain in low backache-related leg pain (LBLP) patients varies from 19% to 80%.
    - A study done by Ind INEP study group in Indian patients in the year 2008 suggests that painful diabetic neuropathy is the most common cause of neuropathic pain (72%).
  - Ind INep study group also suggests that, about 50% of patients reported co-morbid mood disorders, while 67% reported medication-related adverse event in the preceding week.

**Inflammation:**

Inflammation is the response of living tissue to injury. It involves a well-organized cascade of fluid and cellular changes within living tissue. The inflammatory process is of great significance in the development of Neuropathic Pain (NP) [5]. PEA, an endogenously produced amide has been established to work on the inflammatory pathways acting as a pacifier against inflammation. In neuropathic pain, the amount of the amide reduces drastically in the body resulting in aggravated inflammation and furtherance of diseased condition [6]. The endogenously produced FAAH (Fatty Acid Amide Hydrolase) enzyme further degrades the available amide, further reducing its quantity and effectiveness. Palmiges (PEA) is an endogenously produced amide. PEA, Genistein and Daidzein function to counter the action of FAAH enzyme, thereby improving the condition of aggravated inflammation, which is the root cause of neuropathic pain [7].

**Current treatment modalities and their Drawbacks:**

- Current treatment drugs such as gabapentin, pregabalin and duloxetine etc. have annoying side effects such as drowsiness, dizziness, blurred vision, somnolence, peripheral edema etc. Moreover, using these drugs in the long term causes desensitization
of neuron receptors. Therefore, the dose of these drugs has to be increased to elicit the desired response and that leads to more number of side effects. In addition, some drugs require dose adjustment in renal impairment. Hence, the current treatment paradigms have some gaps and require some new arsenal to fight against neuropathic pain. Thus, what is needed at this critical juncture is a solution which corroborates to the core of neuropathic pain with no side effects.

**PALMIGES contains the following components:**

A. Palmitoylethanolamide (PEA):
- PEA is considered an endogenous Peroxisome Proliferator Activated Receptors (PPAR) agonist or activator, interacting with this receptor to inhibit inflammatory pathways & oxidative stress.
- During neuropathic pain, PEA can modulate the PPAR pathway that is able to attenuate Nuclear Factor Kappa B cells (NFKB) induced inflammatory factors or tumor necrosis factor (IL-1 or TNF), inhibit infiltration and activation of MC, reduce mesangial matrix proliferation induced by reactive oxidative stress (ROS) which then resulted in albuminuria [8].

B. Genistein:
- Genistein is a FAAH inhibitor that not only prevents the degradation of PEA from FAAH enzyme in the body but also exerts synergistic effect with PEA to reduce oxidative stress in the over- inflamed neuronal cells.

C. Daidzein:
- Daidzein belongs to the class of isoflavones and serves as a potent FAAH inhibitor in conjunction with Genistein. It works as a competitive binder to FAAH disallowing it to degrade the externally supplemented PEA.

D. MPFAITECH: A technology to ensure the proprietary blend is presented in a form that could be easily absorbed in the human body.

Palmitoylethanolamide (PEA) is a cannabimimetic compound which reduces neuropathic pain. It is a special food for medical purpose in the treatment of chronic pain.

**Material and Methods**

The study includes patients with neuropathic pain and pain due to various causes like chemo-therapy induced neuropathic pain, chronic pain, trigeminal neuralgia, lower back pain and cervical spondylosis pain etc. These patients reported in the outpatient department (OPD) of Neurosurgery of Hamidia Hospital Bhopal. In a period of four months total 150 patients with neuropathic pain between age group of 20-78 years were studied. Male patients were 94 and female patients were 56. They were divided into two groups each consisting of 75 patients. The control group received usual conventional treatment like NSAID’s, antiepileptics (Carbamazepine, Gabapentin or Pregabalin etc.), SNRIs (Duloxetine), Opioids (Acetaminophen, tramadol, tapendol etc.) or TCAS (Amitriptolene, Nortreptolene). The study group patients received PEA (Palmiges) daily, three times a day for 10 days (TDS), and then two times a day (BID) for 50 days. Patients were allowed to continue with their usual treatment if they had other comorbidities. Pain reduction was more evident in group I (study group) treated with
Discussion

Neuropathic Pain can be treated with neuroepileptics, antidepressants and opioids whereas musculoskeletal pain can be treated with acetaminophen and non-steroidal anti-inflammatory (NSAID) drugs. Chronic use of analgesics is often limited by side effect, toxicity and diminished patient compliance and is a problem, especially in older patients.

Neuropathic pain results from damage or disease affecting the somatosensory system. Up to 7-8% of the western population is affected and in 5%, it may be severe also. Treatment of neuropathic pain is challenging because about 50% of patients with neuropathic pain get partial relief from treatment which currently comprises of opioids, NSAIDS, and antiepileptics etc. So the choice of treatment for neuropathic pain should always be taken into consideration, besides efficacy, safety and tolerability of the treatment and interaction with other concomitant treatments.

The drawbacks of current drugs in neuropathic pain and need of new solution: Current treatment options for neuropathic pain are mainly focused on neuronal system suppressing GABA or other inhibitory receptors. Most of the drugs used for neuropathic pain cause drowsiness, dizziness, blurred vision, somnolence, peripheral edema, psychomotor slowing and paresthesia and many more. Moreover, using these drugs on long term basis causes desensitization of receptors. Therefore, there is an increase in the dose of these drugs to elicit the desired response and that leads to more number of side effects. In conclusion, the current treatment paradigms have some gaps and require some new arsenal to fight against neuropathic pain.

The second described treatment is PEA. PEA has high affinity to the nuclear peroxisome proliferator activated receptors α (PPAR-α) and PEA has indeed analgesic and anti-inflammatory effects in clinical trials. Biosynthesis of PEA in tissues, live neurons and glial cells occurs in inflammatory and chronic pain states [9]. When given orally, PEA has almost no side effect, though it has clear pain reducing properties in various pain states [10].

It seems that PEA reduces pain via the natural modulation pathway and besides modulation of the central nervous system, through the release of endorphins, serotonin, norepinephrine and dopamine. Pain reducing effects of acupuncture can also be explained by suppression of activated glial cell [11]. PEA may have a synergistic effect in modulating glial cells, mast cells and neurons [12s]. We often observe pain reduction when we add PEA to our treatment. PEA also enhances the analgesic effect of compounds such as pregabalin and amitriptyline.

In 1986, the famous neuroscientist professor Erminio Costa delivered a key note lecture in Washington, bearing the title "To follow where nature leads". In this speech Costa talked with great vision about how
nature itself can become our tutor in developing new drugs. PEA is one of these molecules entering clinical use and developed according to Costa’s vision. That is why PEA seems such a good compound to combine with other treatment modalities.

**Result**

PEA (palmitoylethanolamide) generally provided better pain relief than placebo in a comparison that includes three different chronic neuropathic pain conditions (trigeminal neuralgia, diabetic neuropathy and cervical pain). There was some indication of pain improvement, mainly over the short term, but with poorly defined outcome. The mean decrease on the VAS was largest in the study group: a reduction from 7.1 to 2.1 which is more than 50% pain reduction. In the control group, the VAS score decreased from 6.6 to 4.6.

PEA resulted in a significant reduction in pain symptoms in neuropathic pain after 7 weeks (49 days). The median values obtained from TSS (Total Symptom Score) and NSPI (Neuropathic Pain Symptoms Inventory) were compared to base level at many observation points until the end of treatment at 60 days confirming a significant attenuation (P<0.001) in the intensity and presence of symptoms. After completion of treatment i.e. after 60 days the same significant reduction (P<0.001) was seen in relation to the frequency and intensity of symptoms like pain, burning, numbness and paresthesia.

What we have is an indication that PEA can produce good level of pain relief for some patients with distressing chronic painful conditions.

![Figure 1 - 50% decrease in VAS in study and control groups](image-url)
Figure 2 - The mean decrease on the VAS was largest in the study group: a reduction from 7.1 to 2.1 which is more than 50% pain reduction. In the control group the VAS score decreased from 6.6 to 4.6.

Figure 3 - Effect of PEA on painful neuropathy evaluated by Michigan Neuropathy Screening Instrument (MNSI), Neuropathic Pain Symptoms Inventory (NPSI) and Total Symptom Score (TSS). Analysis of variance shows a significantly decreased pain intensity and symptom scores observed by MNSI, TNPSI and TSS ($P < 0.0001$) during the treatment period.
In this study the important observation is that a clinical and statistical difference was found that after 7 weeks (49 days) and onset of pain reduction was at 2 weeks (14 days) but the pain reduction at 7th week was satisfactory. These observations support the recommendation to use PEA for at least 2 months before evaluating the result.

Overall completeness and applicability of evidence available include:
• Limited Size
• Short Duration
• Inadequate Outcome
• Incomplete Outcome Assessment

In order to be sure that PEA works in neuropathic/chronic pain and to be confident of the magnitude of the effect, the ideal would be several large randomized double blind studies comparing PEA at sensible doses with placebo over 8 to 12 weeks.

**Conclusion**

Chronic pain management remains a challenge for the clinician. PEA induced pain relief is progressive, age and gender independent and not related with the etiopathogenesis of chronic pain. PEA also controls the mechanism common to different conditions where neuropathic pain is associated e.g. neuro inflammation.

PEA is safe and well tolerated treatment for control/reduction of chronic neuropathic pain and can be combined with other standard/routinely used analgesic medications. PEA possesses intrinsic efficacy towards syndromes co-morbid with chronic pain e.g. depression and anxiety. PEA also lacks acute and chronic toxicity and is not associated with gastric mucosal lesions. That is why it has become possible to include PEA in
new class of therapeutic agent called food for special medical purposes "FSMP". PEA is safe and well tolerated treatment for the reduction of neuropathic pain and can easily be combined as well added to classical medication without fear of negative interactions.

Correspondence
Dr. I.D. Chaurasia MS, MCh,
Associate Professor Neurosurgery
Email: chaurasiaid@gmail.com

References
44th Congress of the Romanian Society of Neurosurgery Considerations

The 44th Congress of the Romanian Society of Neurosurgery (RSN) in association with the 5th Danube Carpathian Region Congress took place between the 5th and the 8th of September, in Timișoara. The location was the Regional Business Centre (CRAFT), an exquisite academic ambience, with all the possible facilities in use.
The opening of the congress was the 23d French Course in Neurosurgery, a major contribution of the French speaking neurosurgeons, who manage each time to present in a very exciting and educational way an entire series of elements of neurosurgical pathology, addressing especially the young neurosurgeons. The Francophone Course focused mainly on cerebral vascular pathology, but there were many exchanges between the French and Romanian teams concerning this very difficult and frequent issue.

The Congress of Neurosurgery was structured in parallel sessions in several halls because of the number of various elements of neurosurgical pathology discussed: Sellar and Parasellar Tumors, Neurotrauma, Functional Neurosurgery, Trigeminal Neuralgia, Tumor Pathology and Degenerative Spine Pathology, Pediatric Neurosurgery, Intracerebral and Skull Base Neurosurgery. We mention also the 2 sessions regarding epilepsy surgery, endovascular treatment for vascular cerebral malformations at the centres in Timișoara and Iași, and the outstanding works of the young neurosurgeons at the „Young Neurosurgeons Corner”. During the congress, the 2nd Symposium of Nurses in Neurosurgery also took place.

From the works sustained at the congress, at the category „Sellar and Parasellar Tumors” we mention the contribution of F. Tomasello (Italy), G. Rosseau (United States), I. Kannan (Saudi Arabia). At the „Craniocerebral Trauma” section we mention W. I. Steudel (Germany) and S. Florian (Romania), „Functional Neurosurgery”. At „Functional Neurosurgery” section we mention P. Mertens and M. Sindou (France), A. Brinzeu (Romania). In the „Spine Surgery” section worth mentioning are C. Popescu (Romania), G. Zapuhlih (Moldova) and M. Ivanon (Great Britain). At the „Pediatric Neurosurgery” section S. Ferraresi (Italy) and D. Nica (Romania) stood out with their works; For „Cerebral Tumors”, H. Pleș (Romania), I. Solaroglu (Turkey) and V. Sinha (India); for „Skull Base Tumors”, F. Tomasello (Italy), M. Gorgan, A. V. Ciurea, D. Teleanu (Romania).

Among the activities was also the presentation of the book „Principles of Neurological Surgery”, the 4th edition (edited by Ellenbongen RG, Sekhar LN, Kitchen ND, Elsevier 2018), the first Romanian edition is coordinated by Prof. Dr. Ioan Stefan Florian and published at Hipocrate publishing house.

At the end of the congress the new President of the General Assembly RSN was chosen for the next 2 years: Conf. Dr. Horia Pleș, Timișoara and Vice Presidents Dr. Vicențiu Sâceleanu, Sibiu, Chief of Lectures, Prof. Dr. Mircea Gorgan, Bucharest, Prof. Dr. Ion Poeata, Iași; Conf. Dr. Constantin Costea, Timișoara, was appointed General Secretary of the General Association of Neurosurgery. All the above mentioned were voted unanimously.
During the General Assembly it was also established that Prof. Dr. Grigore Zapuhlih, the representative of the Association of Neurosurgeons in Moldavia, be made a member of the Romanian Society of Neurosurgery.

The next congress, the 45th Congress of the Romanian Society of Neurosurgery will take place at Sibiu, in October 2019.

The entire event took place in a special academic and cultural environment, in Timișoara, Romania. 387 participants were registered. There were 37 lecturers from abroad who represented 17 countries on 4 continents.

The scientific schedule was comprised of a total of 20 lectures, 3 sessions of the young neurosurgeons, 2 sessions of the nurses, 144 spoken presentations and 17 poster presentations. For these 3 days, the neurosurgical activity in Romania was presented exhaustively, receiving unanimous appreciations and showing that, right now, the Romanian neurosurgery is perfectly aligned to the European standards. The congress proceedings were in the English language.
The administrative-organizational part, as well as the social program, including The Opera Concert on the 6th of September, were in agreement with the congressional requirements, made by the exceptional team “MedEvents”.

Finally, we conclude that the Romanian Society of Neurosurgery is in the European trending of real growth of the quality of the surgical act. This is reflected, on one hand, by the multiple efforts to implement the neuro-imaging diagnostic apparatus and, on the other hand, by even extraordinary endowment of the neurosurgical operating rooms at the university centers.

Andreea-Anamaria Idu, MD, PhD Student, ”Carol Davila” University of Medicine and Pharmacy, Neurosurgery Resident, Emergency University Hospital of Bucharest, Romania
Prof. Alexandru-Vlad Ciurea, MD, PhD, MSc, Dr. h. c. Mult., Sanador Medical Center, Bucharest, Romania
The three princes authors, well known in the neurosurgery world, Ellenbongen RG, Sekhar LN, Kitchen ND, have the merit of publishing this monography, comprising the experience of an entire team of neurosurgeons, radiologists, radiotherapists, geneticists, anesthetists, from the United States but also from Canada, Australia, Brazil and Great Britain.

The publishing of a complete monography in any specialisation is not only obligatory, but well necessary. Such world wide recognized monographies have appeared everywhere in medical literature, like „Harrison’s Principles of Internal Medicine” (originally published in 1950) for internal medicine. In neurosurgery, for years, the specialised literature was dominated by the successive publishing of „Youman’s Neurological Surgery” (originally published in 1973). The same happened in pediatric neurosurgery and, even today, A. Leland Albright and his collaborators’ works, especially „Principles and Practice of Pediatric Neurosurgery” (originally published in 1999), in various editions, have been the conduite guides in this discipline, detailing some particularities related to pediatric age.


The authors framed their work under the precise denomination „Principles of Neurological Surgery”. The material in the 4th edition addresses especially neurosurgery
residents, practitioners, but also all the medicine students with inclinations for neurosciences. The three authors are renowned both for their extremely precise written works in neurosurgery, but also for their numerous neurosurgical interventions they developed over time, with personal upgrades and procedures.

Considering all of the above, the president of the Romanian Society of Neurosurgery, with the support of Hipocrate publishing house, appreciated that the Romanian Society of Neurosurgery and all the practitioners in this field should possess the Principles of Neurosurgery in Romanian, in order to study in depth the clinical and operative details of the challenging neurosurgical pathology. Considering, furthermore, that often the information in English is not perfectly assimilated, the coordinator of this edition in Romanian, Prof. Dr. Ioan Ștefan Florian, made the translation as correct and appropriate as possible. Moreover, some chapters were revised by specialised translators so that nothing unclear or interpretable would appear, especially not in the operative procedures.

The treatise „Principiile Chirurgiei Neurologice” has 9 parts: Part 1 - General considerations; Part 2 - Pediatric Neurosurgery; Part 3 - Vascular Neurosurgery; Part 4 - Cranial-Cerebral Trauma; Part 5 - Spine and Medulla Pathology; Part 6 - Intracranial Tumors; Part 7 - Radiosurgery and radiotherapy; Part 8 - Functional Neurosurgery. Pain; Part 9 - refers to several issues that were not covered in the previous parts, such as the pathology of Peripheral Nerves.

Each chapter is structured beginning with several clinical notes, then a framing of the issue, its history, its epidemiology, genetic and etiological factors, anatomical-pathologic observations, clinical diagnostics evaluation and imagery; after that, the surgical procedures are described thoroughly, with operative timing, advantages and disadvantages for every procedure, then results, complications and future progress. The bibliography at the end of each chapter is carefully selected and comes mainly from actual data. As a whole, this monography firstly answers the major challenges of the specialists in this field regarding the correct diagnosis, and secondly it gives the recommended operative procedures of today.

The Romanian edition „Principiile Chirurgiei Neurologice”, coordinated by Prof. Dr. Ioan Ștefan Florian, published at Hipocrate publishing house (translation of the 4th edition in English edited by Ellenbogen RG, Sekhar LN, Kitchen ND, Elsevier 2018), supported by Fundația Transilvania Leaders, is extremely interesting, clear and efficient, with an exceptional scientific and educational quality.

The translation of the documents was the result of a collective effort attended by 58 physicians, alongside highly experienced teachers from all traditional university centers, including resident physicians with major inclinations for English language, for whom this approach was an intense educational exercise.
Reading the treatise in detail we see that the main topics in neurosurgery pathology are discussed, but some modern elements as well, such as the endovascular treatment of vascular cerebral malformations. Furthermore, radiotherapy and radiosurgery are also thoroughly discussed, with a focus on the recent aspects of proton therapy.

The image-guided neurosurgery procedures are detailed and explained very clearly and very educationally, which contributes to a deeper understanding of the value and importance of image-guided surgery by magnetic resonance when diagnosticating neurosurgical traumas, in pre- or post-operative.

The first chapter is extremely interesting and is dedicated entirely to the history of neurosurgery, starting from the first trepanations and leading to more and more sophisticated approaches. The many progresses in this difficult field are all presented in short.

Furthermore, this monography is also an efficient guide book for extremely difficult cases, complications or malpraxis in neurosurgery, with medical-legal interpretations.

The presentation of each chapter is extremely clear, with exceptional illustrations, demonstrating the professionalism and dedication of the 3 authors, exceptional neurosurgical personalities.

The monograph is done in nearly 900 pages, with an alphabetical index of pathology at the end.

We consider this neurosurgery treatise is edited at an international level by a complex team from the United States and Great Britain and also other personalities from different parts of the world, and as such it deserves a place on the main shelf of neurosurgical and adjacent specialties education (neurology, psychiatry, anesthesia etc.).

The effort of the entire team of neurosurgery residents in Romania, coordinated by Prof. Dr. Ioan Ștefan Florian, in translating this book contributes immensely to the upgrade of the neurological knowledge in this country. Most of all, publishing this treatise in Romanian represents a great opportunity for the neurosurgery experts in this country to have access to a modern and renowned international neurosurgical treatise.

Andreea-Anamaria Idu, MD, PhD Student, ”Carol Davila” University of Medicine and Pharmacy, Neurosurgery Resident, Emergency University Hospital of Bucharest, Romania
Prof. Alexandru-Vlad Ciurea, MD, PhD, MSc, Dr. h. c. Mult., Sanador Medical Center, Bucharest, Romania
Instructions for Authors on References (APA style)

Authors
Authors should provide complete, correct and properly structured references, as instructed by the editors.

Complete data contains:
For article in a journal: Author(s), Title of the article, Journal name (full name or abbreviation according to ISO standard), Volume, Issue, Publication date, pagination.
For a book: Author(s), Title, Publisher, Publication place and date
If the article/book has DOI number, the author should include it in the references. DOIs are very easy to find. Most publishers, if they have them, place them at the top of the article front page. Please keep in mind that the DOI number will automatically make the active link!
All data in the reference must be correct. Most common errors are incorrect abbreviations of journal titles or wrong navigation data (like volume number or article pages) of the cited article.
Finally, the author ought to prepare references in a format chosen by the journal. The journal editors must instruct the author as appropriate (see below).

APA style
Article in a journal:

Book:

This document describes standards for preparing the references in the APA style. The following sections give detailed instructions on citing books, journal articles, newspaper articles, conference papers, theses, webpages and others.
Please provide all the required elements in the references to your paper. Please pay particular attention to spelling, capitalization and punctuation. Accuracy and completeness of references are the responsibilities of the author. Before submitting your article, please ensure you have checked your paper for any relevant references you may have missed.
A complete reference should give the reader enough information to find the relevant article. And most importantly, complete and correct references may allow automatic creation of active links by the MetaPress technology that we use for making the electronic version of our journal. Active reference linking is regarded as the greatest benefit of electronic publishing and it adds a lot of value to your publication.

1. Book
   a. Book (one author)
      Format:
      Author. (Year of publication). *Book title*. Place of publication: Publisher.
      Example:

   b. Book (two or more authors)
      Format:
      Author1, Author2 & Author3. (Year of publication). *Book title*. Place of publication: Publisher.
      Example:

   c. Book chapter or article in an edited book
      Format:
      Author(s) of chapter. (Year of publication). Chapter title. In Editors of the book (Eds.), *Book title* (Chapter page range). Place of publication: Publisher.
      Example:

   d. Proceedings from a conference
      Format:
      Author(s). (Year of publication). Title. In Conference name, Date (Page range). Place of publication: Publisher.
Example:

e. ebook
Format:
Author(s). (Year of publication). Title. Publisher.
Retrieving date, http address. DOI.
Example:

f. Thesis
Format:
Author(s). (Year of publication). Title. Information, Place of publication.
Example:

g. Report
Format:
Author(s). (Year of publication). Title. Place of publication: Publisher. (Report number)
Example:

h. Government publication
Format:
Institution name. (Year of publication). Title. Place of publication: Publisher.
Example:

2. Article
a. Journal Article (one author)
Format:
Author. (Year of publication). Article title. Journal Title. Volume (issue), range of pages. DOI.
Example:

b. Journal Article (two or more authors)
Format:
Author1, Author2 & Author3. (Year of publication). Article title. Journal Title. Volume (issue), range of pages. DOI.
Example:

c. Journal article from an online database
Format:
Author(s). (Year of publication). Article title [Electronic version]. Journal Title. Volume (issue), range of pages. Retrieved date of access, from name of database. DOI.
Example:

d. Newspaper article (no author)
Format:
Article title. (Publication date). Journal Title. page.
Example:

e. Encyclopedia article
Format:
Example:

3. Other formats
a. Web page
Format:
Author/Sponsor. (last update or copyright date). Title. Retrieved date of access, from URL.
Example:

b. Lecture note
Format:
Author(s). (Date of presentation). Lecture title. Lecture notes distributed in the unit, at the name of the teaching organisation, the location.
Example:
Liffers, M. (2006, August 30). Finding information in the library. Lecture notes distributed in the unit Functional Anatomy and Sports Performance 1102, University of Western Australia, Crawley, Western Australia.

c. Patent
Format:

d. Standard
Format:

e. Video
Format:
Producer, P. P. (Producer), & Director, D.D. (Director). (Date of publication). Title of motion picture [Motion picture]. Country of origin: Studio or distributor.

f. Audio recording
Format:
Songwriter, W. W. (Date of copyright). Title of song [Recorded by artist if different from song writer]. On Title of album [Medium of recording]. Location: Label. (Recording date if different from copyright date).
Example:

g. Mailing list
Format:
Author. (Exact date of posting). Subject line of message. Message posted to followed by name of mailing list, archived at followed by address for the archived version of the message

h. Computer software
Format:
Author(s). (Year). Title [computer software]. The location: Company.

APA style1
Article in a journal:

Book:

1Read more: http://www.library.uwa.edu.au/education_training_and_support.guides/how_to_cite_your_sources/apa_style