Idiopathic intracranial hypertension: case report

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Abstract: Idiopathic intracranial hypertension – IIH (synonymous old terms: benign intracranial hypertension - BIH, pseudotumor-cerebri - PTC) it’s a syndrome, related to elevated intracranial pressure, of unknown cause, sometimes cerebral emergency, occurring in all age groups, especially in children and young obese women, in the absence of an underlying expansive intracranial lesion, despite extensive investigations. Although initial symptoms can resolve, IIH displays a high risk of recurrence several months or years later, even if initial symptoms resolved. Results: A 20-year-old male, obese since two years (body mass index 30.9), was admitted for three months intense headache, vomiting, diplopia, progressive visual acuity loss. Neurologic examination confirmed diplopia by left abducens nerve palsy, papilledema right > left. At admission, cerebral CT scan and cerebral MRI with angio MRI 3DTOF and 2D venous TOF was normal. Despite treatment with acetazolamide (Diamox), corticosteroid, antidepressants (Amitriptyline), anticonvulsants (Topiramate) three weeks later headache, diplopia persist and vision become worse, confirmed by visual field assessment, visual evoked potential (VEP). A cerebral arteriography demonstrate filling defect of the superior sagittal sinus in the 1/3 proximal part and very week filling of the transverse right sinus on venous time. Trombophylic profile has revealed a heterozygote V factor Leyden mutation, a homozygote MTHFR and PAI mutation justifying an anticoagulant treatment initiated to the patient. The MRI showed a superior sagittal sinus, right transverse and sigmoid sinus thrombosis, dilatation and buckling of the optic nerve sheaths with increased perineural fluid especially retrobulbar, discrete flattening of the posterior segment of the eyeballs, spinal MRI showed posterior epidural space with dilated venous branches, with mass effect on the spinal cord, that occurs pushed anterior on sagittal T1/T2 sequences cervical and thoracic. The opening pression of lumbar puncture, done with the patient in the lateral decubitus position, was 60 cm H₂O, the cytochemical CSF study were normal. The patient was operated: a lumbo-peritoneal with a variable pressure valve was inserted. Two months after the patient general condition improved: he was without headache, abducens palsy and the visual field assessment, ocular motility examination, ophthalmoscopy were normal. Conclusion: IIH is rare, variable in evolution, and in many cases it disappears on its own within 6 months without affecting life expectancy.
Weight loss, fluid or salt restriction, in conjunction with medical treatment, angioplasty and venous stenting across the sinus stenosis under general anesthesia and surgical treatment (shunting, optic nerve sheath decompression and fenestration, gastric by-pass surgery) are treatment alternatives. Such disorder should be closely monitored because 10 to 25% of cases could be affected by recurrences or by permanent vision loss to those patients with resistant papilledema despite treatment.

**Key words:** idiopathic intracranial hypertension-IIH, benign intracranial hypertension - BIH, pseudotumor-cerebri – PTC, superior sagittal and transverse sinus thrombosis, intracranial pressure, visual evoked potential (VEP)

**Introduction**

Idiopathic intracranial hypertension – IIH (synonymous old terms: benign intracranial hypertension - BIH, pseudotumor-cerebri - PTC) it’s a syndrome, related to elevated intracranial pressure of unknown cause, sometimes cerebral emergency, occurring in all age groups, especially in children and young obese women, with several symptoms including visual loss; without underlying expansive intracranial lesion, hydrocephalus, dural sinus thrombosis; with a recurrence potential months or even years later, even if initial symptoms resolved. (1-12)

**Case report**

A 20-year-old male, obese since two years (body mass index 30.9), was admitted June 2015 in a neurology department for three months intense headache, vomiting, diplopia, progressive visual acuity loss. From his medical records we noticed: left otomastoiditis since childhood, a car accident with cranio-cerebral trauma in 2007 with a 3 mm nonoperated left subdural hematoma and epicranian hematoma. Clinical examination revealed good clinical condition, without motor or sensitive deficits, orientated, no ataxy, ocular motility examination diplopia by left abducens nerve palsy, visual function tests: both eyes 2/3 without corrections, visual field assessment is normal with light colour desaturation for red and green, ophthalmoscopy: papilledema right > left, with peripapillary flame hemorrhages, venous engorgement. Angiofluoroscopy: arteriolar filling at 11 seconds, papillar leakage of contrast substance, both papilla becomes hyperflorescent on late exposures, dilated vessels. The study of visual evoked potentials (VEP) has shown on the right eye latency of P100 wave 145 ms (normal value = 110 ms) and amplitude of 71 mV (normal value > 5 μV). To the left eye, the latency of P100 wave was 121 ms, amplitude of 58 mV.

An immunologic screening demonstrate CRP positive, ANA positive, Ac anti DNA dc, Ac anti SM, Ac anti Ro, Ac anti La, cANCA,pANCA, Ac anti U1RNP, Ac anti GP1beta. An infectious screening was negative for Ac anti HIV, Ac anti HCV, Ag HBS, Ac anti CMV, Ac anti EBV, Ac anti HSV, Ac anti
Borrelia, Ac anti Mycoplasma, Ac anti Chlamydia, Ac anti Toxoplasma. The RIA-screening for TSH, FSH, LH, PRL and GH found normal levels.

At admission, cerebral CT scan was normal (Figure 1). Cerebral MRI with angio MRI 3DTOF and 2D venous TOF showed: supra and infratentorial structures with normal morphology and normal MRI signal, no acute cerebral lesions visible in diffusion. On T2 EG sequence no hemorrhages supra or infratentorial, ventricular system with normal dimensions, shapes, topography. Selar and parasellar region, orbital region and optic nerves with normal MRI signal, no vascular malformations, normal dural sinuses.

The patient was put on a low calories diet, corticosteroid therapy was initiated and consisted of a bolus methypredisolone - 1g/d for 5 days, followed by an oral corticosteroid dose decreasing over three weeks), associated with acetazolamide (Diamox 1g/d), antidepressant (Amitriptyline), anticonvulsivant (Topiramate).

Three weeks later headache, diplopia persist and vision become worse (1/10 on the right side and 3/10 on the leftside). A cerebral arteriography demonstrate normal arteriography on right side - arterial time; filling defect of the superior sagittal sinus in the 1/3 proximal part and very week filling of the transverse right sinus on venous time. On the left side cerebral angiography was normal (Figure 2)

The opening pression of lumbar puncture, done with the patient in the lateral decubitus position, was 60 cm H2O, the cytochemical CSF study were normal (protein concentration: 0.23 g/ l, CSF glucose: 0.42 g/ l and 3 white cell /mm³).
Trombophylic profile has revealed a heterozygote V factor Leyden mutation, a homozygote MTHFR and PAI mutation justifying an anticoagulant treatment initiated to the patient.

A new cerebral and spinal MRI revealed (Figure 3):
perineural fluid especially retrobulbar, discrete flattening of the posterior segment of the eyeballs
D: cerebral MRI (TOF sequence) confirming filling defect of the 1/3 anterior part of the superior sagittal sinus (SSS)

A week after, headache increased and the patient was transferred and operated to the Neurosurgery Department. A lombo-peritoneal shunt with a variable pressure Medtronic valve was performed. At operation the opening pressure of lumbar puncture, done with the patient in the lateral decubitus position was 85 cm H2O. Two months after, the patient general condition improved: he was without headache, abducens palsy and the visual field assessment, ocular motility examination, ophthalmoscopy, visual evoked potentials were normal.

The peculiarity of this case lies in the progressive emergence of a severe idiopathic intracranial hypertension syndrome at a young male, age of 20 years, obese - recently instaled, not leated to a endocranial cause, with normal hormonal tests, to which trombophylic profile has revealed a heterozygote V factor Leyden mutation, a homozygote MTHFR and PAI mutation; also the opening pressure of lumbar puncture, done with the patient in the lateral decubitus position, was initial 60 cm H2O and at operation 85 cm H2O. The medical treatment failed, but lombo-peritoneal shunt with a variable pressure Medtronic valve was beneficial.

Discussion

Idiopathic intracranial hypertension – IIH occurs in about 1-2 per 100,000 people, each year, with severe visual loss in 10-30% of patients, at a median age of 20-45 years and affects women four to nine times more frequent than men (6, 12, 13). In young obese women, the incidence of IIH has been shown
Several conditions have been associated with IIH (2, 3, 5, 10, 11, 15, 22)

- obesity: obese women of childbearing age are more likely to the disorder due to elevate intraabdominal pressure, venous and even intracranial venous pressure. In our case obesity was recently instaled, not leated to a endocranial cause, with normal hormonal tests.
  - onset of menstruation (menarche)
  - pregnancy - at any stage
  - medications (no fully clarified causal relation with this disorder) including: high-dose vitamin A > 100,000 U/day - see isotretinoin for acne, long-term antibiotherapy with penicillin, cyclosporine, minocycline, tetracycline, nalidixic acid, nitrofurantoin, carbidopa, levodopa, indomethacin, ketoprofen, corticosteroids - topical and systemic, phenytoin, growth hormone, oral contraceptives, tamoxifen, lithium and anabolic steroids
  - diseases such as: Addison, Cushing’s, Behcet’s (23), polycystic ovary syndrome, systemic lupus erythematosus, multiple sclerosis, herpetic encephalitis, Reye syndrome, sleep apnea, chronic kidney disease, chronic respiratory insufficiency, familial mediterranean fever or others disorders, such as iron deficiency, anemia, uremia, thrombocytopenic purpura, hypothyroidism, hypoparathyroidism, psittacosis, metabolic, toxic causes
  - disorders of cerebral venous drainage: secondary thrombosis due to coagulopathy, relative stenosis due to a venous flow anomaly or even extravascular tumors that may impare due absorption of CSF; increased venous red
blood cell (RBC) aggregation and relatively elevated fibrinogen concentrations.

To explain the pathogenesis of IIH, starting from 4 evidences: a high rate of occurrence in obese women during the childbearing years, CSF outflow has reduced conductance, normal ventricular size, no hydrocephalus and no histologic evidence of cerebral edema, several theories have been advanced, generating pathological conditions acting simultaneously as follows: (1-3, 11, 13, 24-26)

- the increased production of cerebrospinal fluid was the first hypothesis to be proposed, but later dismissed following experimental data (27)
- the increased resistance to cerebrospinal fluid absorption (13, 24)
- the increased blood flow to the brain or cerebral tissue was suggested using phase contrast MRA studies and biopsy samples. IIH is only an incomplete intracranial hypertension syndrome initial: increased intracranial pressure is very important, up to 60–80 mmHg, but the brain vascular auto regulation compensates the increase in intracranial pressure and maintains cerebral blood flow (24)
- restricted venous drainage, by narrowing or stenosis of two large sinuses in the brain low grade stenosis of the SSS and transverse sinus
- a condition which could be an effect or a cause of IIH: raised intracranial pressure causes venous narrowing in the transverse sinuses, resulting in venous hypertension (raised venous pressure), with decreased cerebrospinal fluid resorption via arachnoid granulations and further lead to a rise of intracranial pressure and cerebral oedema (4, 17, 28-33)
- obesity increases intra-abdominal pressure, raises cardiac filling pressures and impedes venous return from the brain due to the valveless venous system that exists from the brain to the heart, with a subsequent elevation in intracranial venous pressure, chronic interruption of the axoplasmic flow of the optic nerves and ensuing papilledema as a consequence of this pressure, leading to irreversible optic neuropathy (2)

IIH diagnosis (1, 3), is based on the criteria devised by Dandy in 1937 (20) and subsequently modified by:

- Smith 1985 (34) replaced ventriculography with CT scan
- Digre and Corbett 2001 (3) added the requirement that the patient is awake and alert, no other cause for the raised ICP is found, including exclusion of venous sinus thrombosis as an underlying cause
- Friedman and Jacobson 2002 (35) MR venography is only required in atypical cases: men and woman with normal weight age over 44 years, prepubertal children.
- the lumbar puncture should be performed with patient lying sideways

Current diagnostic IIH criteria (1-3, 5, 15, 29, 35, 36) require the following:

1. signs and symptoms of intracranial hypertension syndrome
- moderate to severe headaches in 92–94% of cases, revealing, progressive, starting retroorbital, worsening with eye movement, generalized in character and throbbing in nature, especially in the morning or during
physical activity; exacerbated by coughing and sneezing

- radicular pain - uncommon symptom, usually in the neck and shoulders
- nausea, vomiting
- dizziness
- pulsatile tinnitus in one or both ears (64–87%), synchronous with the pulse (37)
- visual disturbances (80% of cases): blurred or distortion (metamorphopsia) of central vision - caused by macular wrinkling and subretinal fluid spreading from the swollen optic disc, often predominantly orthostatic, initially in the periphery, in the nasal inferior quadrant but progressively towards the center of vision; loss of color vision; visual obscurations affecting one or both eye – seconds lasting episodes or blindness in 30% of cases; photopsia - light flashes; sudden visual loss in 91% of cases due to ischemic optic neuropathy or a retinal vascular occlusion associated with the papilledema; diplopia by abducens palsy uni or bilateral. Rarely, patients presenting with increased ICP with related optic nerve edema may be asymptomatic. Visual acuity is usually normal until significant peripheral visual field loss with progressive postpapilledema by optic atrophy has occurred (23). In children, numerous nonspecific signs and symptoms may be present: numbness of the extremities, generalized weakness, loss of smell and coordination; rarely third, fourth or even facial nerve nerve palsy uni or bilateral may appear (15, 35), papilledema in addition to subretinal hemorrhages are poor visual prognostic signs. Uncontrolled papilledema results in progressive peripheral visual field constriction or nerve fiber bundle defects (11).

2. normal neurological examination excepting diplopia by abducens palsy, uni or bilateral
3. the patient is awake and alert
4. normal cranio-cerebral and spinal investigations (1-3, 36, 38-42)
   - CT with and without contrast, angio-CT venous time
   - emergency MRI including the following sections: native in sagittal T1, axial: T2 flair, diffusion T2*; with contrast (Gadolinium) T1 fat sat on orbits, axial cuts T1 on the brain; using axial and coronal sections 2 mm thick centered on orbits FSE T2
   - MR venography, a cerebral angio MRV with gadolinium and manometry to exclude the possibility of an intracranial mass, a cerebral venous sinus thrombosis, venous sinus stenosis/obstruction or a dural fistula, to explain physiopathology or even for therapeutic interest to implant a stent (4, 5, 15, 32, 35).

IIH commonly presents with: normal or small (slit-like) and symmetric lateral ventricles, tortuous optic nerves, dilatation and buckling of the optic nerve sheaths with increased perineural fluid (42), minimal flattening of the posterior segment of the eyeballs, bulging optic discs, possible moderate to severe smooth-walled venous stenosis affecting the longitudinal or transverse sinus; "empty sella sign" (flattening of the pituitary gland due to increased pressure) and enlargement of Meckel's caves (41). Occasionally: T2 signal intensity of the optic nerve, discreet ptosis of cerebellar tonsils
(40). Follow-up MRI or CT scans may be needed to rule out hidden cancer.

5. increased opening pressure of lumbar puncture, performed with the patient in the lateral decubitus position, CSF pressure > 25 cmH2O with normal biochemical and cytological composition of CSF

6. no other explanation for the raised intracranial pressure as metabolic, toxic or hormonal

In addition to IIH diagnostic criteria the following investigations should be performed (1-3, 11, 15):

Visual function tests, visual field assessment, ocular motility examination, ophthalmoscopy (funduscopy) are mandatory to diagnose and monitories patients with IIH. At ophthalmoscopy: papilledema is seen in 95% of cases, without correlation with visual impairment severity, absent or unilateral especially in young children, sometimes bilateral, asymmetric; peripapillary flame hemorrhages, venous engorgement, hard exudates, telangiectatic vessels on the disc surface, opticiliary shunt veins. Chronic papilledema is associated with optic disc pallor, Paton lines (arc-shaped retinal wrinkles concentric with disc margin) along the temporal side of inferior pole of disc. Late chronic optic atrophy can also be seen: decreased visual acuity with significant peripheral visual field loss especially in the inferior nasal quadrant of the visual field, diffuse pallor of disc and absence of small arterial vessels on surface are noted, with very little disc elevation. Disc margin in the upper and lower poles and nasal margin is obscured by some residual edema in nerve fiber layer and gliosis that often persists even after all edema has resolved. In general the impact of idiopathic HIC on visual function is usually appreciated by repeated studies of the visual field, also by altered visual evoked potential (VEP) - see our case too (41).

- blood tests to patients with IIH (1, 2, 5) are necessary for ruling out systemic lupus erythematosus, collagen-vascular diseases, to identify the procoagulant profile, etcetera. They include: complete blood count, erythrocyte sedimentation rate, serum iron, iron-binding capacity, full procoagulant profile regardless to those patients of previous history of thrombosis or MRI - including protein S, protein C, homocysteine levels, antithrombin III, factor V Leiden variant, antiphospholipid/anticardiolipin antibodies, lupus anticoagulant and platelet aggregation studies; also antinuclear antigen (ANA) profile (eg, anti-dsDNA and anti-ssDNA), Lyme screening test - enzyme-linked immunosorbent assay ELISA to those patients who have a history of exposure to Lyme in areas of endemic disease.

- cerebrospinal fluid studies (2, 11) include the following: opening pressure, white blood cell and differential counts, red blood cell count, total protein, quantitative protein electrophoresis, glucose, bacterial culture and sensitivity, Cryptococcal antigen - especially in patients with HIV, Syphilis markers - eg, rapid plasma reagin- RPR, tumor markers and cytology (in patients with a history of cancer or with clinical features suggesting occult malignancy)

IHH treatment goals are (2, 3, 15, 23, 31, 39, 43, 44): the prevention of visual loss and
blindness, symptom control, weight loss, fluid or salt restriction.

Medical treatment (1-3, 7, 43, 44) is based on: acetazolamide (Diamox) for six months - in conjunction with a low-sodium weight-reduction diet modestly improved vision, reduced intracranial pressure, improved quality of life and reduced papilledema; furosemide; digoxin (reduces CSF production by as much as 78% in humans, probably by inhibiting the Na-K-ATPase pump); analgesics: primary headache prophylaxis with antidepressants (Amitriptyline), anticonvulsivants (Topiramate); corticosteroids – as in our case is useful especially in patients with papilledema (reducing CSF production by as much as 78% in humans, probably by inhibiting the Na-K-ATPase pump binder). Repeated lumbar punctions to control ICP should be abandoned due to questionable results and infectious risks (11).

For patients with raised ICP due to severe transverse sinus stenosis, angioplasty and venous stenting across the sinus stenosis under general anesthesia, may improve CSF resorption, decrease and even cure IIH symptoms as well as papilloedema (28, 38, 45, 46).

Surgical treatment of IIH (1-3, 43) is recommended if: medical therapy proves unsuccessful or is not tolerated, vision deteriorate; as in our case. In the absence of randomized controlled trials, surgical treatment include: shunting – lombo-peritoneal or ventriculo-peritoneal with ventricular cateter inserted stereotactically preferably with a variable pressure valve (42, 47-51), optic nerve sheath decompression and fenestration (52, 53), gastric bypass surgery for obese patients (5). IIH may resolve after initial treatment, may go into spontaneous remission (although it can still relapse at a later stage) or may continue chronically (5, 35).

Conclusion

IIH is rare, variable in evolution, and in many cases it disappears on its own within 6 months without affecting life expectancy (2). Weight loss, fluid or salt restriction, in conjunction with medical treatment, angioplasty and venous stenting across the sinus stenosis under general anesthesia and surgical treatment (shunting, optic nerve sheath decompression and fenestration, gastric by-pass surgery) are treatment alternatives. Therefore a long term follow up of these patients is essential to improve the prognosis, because 10 to 25% of cases (5, 23) could be affected by recurrences or by permanent vision loss to those patients with resistant papilledema despite treatment.

References

2. Gans M.S. - Idiopathic Intracranial Hypertension, emedicine, medscape, overview, 2014, 02.05
6. Iencean S.M., Ciurea A.V. - Intracranial hypertension:
17. Mihorat T.H. - Classification of the cerebral edemas with reference to hydrocephalus and pseudotumocerebri, Childs Nerv Syst. 1992, 8, 301–306
21. Symonds C.P. - "Otitic hydrocephalus", Brain 1931, 54 (3705), 55–71
38. Bracard S., Schmitt E. et al. - Hypertension intracrânienne "bénigne": imagerie et thérapeutiques
endovasculaires, Neurochirurgie 2008, 54, 6, 721-723
42. Peter P, Philip N, Singh Y. - Reversal of MRI findings following CSF drainage in idiopathic intracranial hypertension, Neurol. India 2012; 60, 267-268