Meningioma association with Three Different Cell Types Tumors: Report of Clinical Cases and Review of the Literature

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Abstract
Most primary intracranial tumors occur as solitary lesions; multiple locations of one tumor, the occurrence of two different tumors or even collision tumors have been described only in a few patients. Multiple primary brain tumors rarely originate in different tissues. Cases not associated with von Recklinghausen's neurofibromatosis constitute only 0.3% of all primary brain tumors. The association of two primary intracranial tumors of different histogenesis in the same individual is rare, except in cases of phakomatosis or radiation-induced tumors. We present three cases with simultaneous occurrence of meningioma with glioblastoma, pituitary adenoma, and acoustic schwannoma respectively, as shown by MRI on admission. In two cases (meningioma/glioblastoma, and adenoma/meningioma associations) both tumors have been approached in one operation, both tumors being completely removed. In the meningioma/acoustic schwannoma association case only the schwannoma was approached surgically due to poor patient status and meningioma being completely clinically silent. Postoperative recovery was good for all three patients and the 1 year follow up showed no growth for the remnant meningioma. Although the particular tumors diagnosed in all three presented cases represent common primary intracranial tumors, the simultaneous occurrence of each two tumors is rare. Previous reported results failed to consistently show a common genetic mark that could explain the development of two different tumors. However, based on our cases and previous literature, we believe that increased research effort could provide significant insights in the appearance and development of multiple brain tumors.

Introduction
The occurrence of multiple neoplasms in the central nervous system is well documented. In von Recklinghausen's disease, patients frequently present with multiple neurofibromas and/or meningiomas at different sites within the spinal axis. However, the presence of multiple, histologically different spinal tumors outside this inherited single-gene disorder or other particular clinical situations as phakomatosis or radiation therapy. Meningioma, one of the most common primary brain tumor (20% in hospital-based statistics, and up to 30% in autopsy-based statistics) 1, is presented in the literature as being associated with a variety of other tumors, both intracranial or of different origins (breast cancer for example) 2. Nonetheless its association with other primary intracranial tumors outside the aforementioned cases is a rare clinical finding. We present 3 cases where meningiomas are associated with 3 different types of primary intracranial tumors:
glioblastoma, pituitary adenoma, and acoustic schwannoma. We present the particularities of each association, looking at the individual contribution of each tumor to the clinical picture, the way they influence the therapeutical decision, and last but not least, the alteration of the outcome and adjuvant therapy in each case.

Case I – Cavernous sinus meningioma and pituitary adenoma

A 56-year old woman was admitted with a six months history of diplopia, intermittent headache of moderate intensity, progressive exophthalmia of the right eye, hypoesthesia of the right half of the face, also progressive. The clinical exam revealed the paresis of the right sixth cranial nerve, hypoesthesia with paresthesia in the territory of the right trigeminal nerve. The patient presented right axial exophthalmia, not painful, irreducible, and non-pulsating. She also presented a minimal palpebral ptosis on the right. No sensory loss or motor deficit were identifiable. The MRI showed a well-delineated mass lesion filling the cavernous sinus area, homogeneous, and a mass lesion occupying the sella turcica suggestive of a pituitary neoplasy (Figure 1A). The surgical goal was to remove both tumors in one intervention. An extended right temporo-pterional approach was used to reach access to both tumors, followed by the partial resection of the adenoma and complete resection of the endocranial portion of the meningioma, on the superior, lateral, and medial walls of the cavernous sinus. The patient underwent a uneventful recovery with no noticeable neurological deficit. The CT follow-up examination at one year showed no obvious sign of reminiscent tumor in a clinically silent patient.

Case II – Tuberculum sellae meningioma and frontal glioblastoma

A 69-year old female was admitted accusing episodes of spatial-temporal disorientation, confusion, and fatigue. All symptoms started 10 days prior to admission and improved on cortisone. The neurological examination shows no motor or sensory deficits, and no cognitive deficits, except a slight frontal behavior (correlated with relatives description of her becoming euphoric and slightly disinhibited). Head MRI was performed and it showed two independent mass lesions, both infiltrative, one frontal and one pervading the tuberculum sellae and pituitary stalk. The surgery was performed through a left fronto-pterional paramedian approach with macroscopically complete resection of both tumors. Postoperatively a motor deficit in the right limbs was recorded in the context of a mixed epidural and subdural hematoma. A second surgery was performed for hematoma evacuation. Evolution after the second surgery was good with a degree of motor deficit still present at discharge.

Case III – Acoustic schwannoma and frontal meningioma

The third case presents a 67-year old woman with a 5 months history of progressive hearing loss in the right ear and vertigo. A week before admission a syndrome of increased intracranial pressure (mostly headache and nausea) completed the clinical picture. Head MRI
showed a mass lesion highly suggestive of a right side acoustic schwannoma but also a frontal meningioma with no clinical manifestations. Surgery was performed for the ablation of the schwannoma which resulted in complete macroscopic resection of the acoustic tumor. The frontal meningioma was not approached surgically because it had no clinical or imagistic mass manifestations. At one year MRI follow-up it showed no increase in size at one year.
Disscussion

We present, for the first time to our knowledge, multiple associations of meningioma with different cell type intracranial tumors: glioblastoma, pituitary adenoma, and acoustic schwannoma. Although the fact that all patients were females, in their sixth or seventh decade of life corresponds to the predominance of meningioma in women, the diversity of the associated tumors presents a theoretical challenge on the causes and predisposing factors for tumor appearance and growth. Meningiomas were clinically salient and caused part of the symptoms except for the third case that can be considered an imagistic discovery.

Although a recent study\(^2\) nominates as a confirmed risk factor, other than increasing age, ionizing radiation, none of our patients were subject to this type of exposure. Also, none of the patients presented a family history of meningioma or any other brain tumor, less so inherited genetic syndromes (like NF2). However, no genetic study was performed in these three patients.

Another risk factor present in previous literature on meningiomas, i.e. hormones,
are unlikely to play any role in the biological status of our patients. The reasoning behind this affirmation is two folded. First, our patients were at menopause and presented no gynecological pathology. Second, recently, no associations with reproductive or hormonal factors were observed in a case–control study of 151 meningiomas in female patients (6).

The probability of having any of the two tumors simultaneously is extremely low. Taking the incidence of glioblastoma and meningioma for instance as base for calculus the probability of both of them appearing at the same time in the same patient would be about 1.5 in a billion. However our patients presented in a period of 3 years (2005–2007), among the 4000 patients treated in our clinic, from a population of around 4 millions. This raises the question of environmental factors and mutations present in the genetic background that involves multiple mutations appearing with a higher frequency.

References