

Intracranial Meningeal Melanocytoma: Review of the Literature

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Introduction

Primary pigmented tumors of the cerebrospinal meninges are rare and uncommon group of melanin-containing neoplasms. They include pigmented meningioma, malignant melanoma, meningeal melanocytoma, melanotic schwannoma and melanoblastosis. These tumors are different in biological behavior, treatment and prognosis. Valenti was the first to describe pigmented cells normally found in the leptomeninges [1]. Limas and Tio, with their electron microscopic studies, demonstrated that the cell of origin of the so-called pigmented meningiomas is the melanocyte and not the meningothelial cell [2]. So they were the first to speak about the “meningeal melanocytoma”.

The meningeal melanocytoma is often described as a well-encapsulated, nodular, dark brown or black lesion that is firmly attached to the underlying leptomeninges [3]. Histologically they may resemble meningiomas but ultrastructurally they are similar to melanotic tumors of the dermis and uveal tract, thus they are not usually related to abnormalities of cutaneous pigmentation [4]. The differential diagnosis is often so confusing, owing to their similar appearance in CT and MR studies, that is necessary additional diagnostic confirmation with electron microscopy and immunohistochemical analysis. They occur most frequently in the posterior fossa and along the spinal cord, producing neurologic deficits by mass effect rather than by infiltration of adjacent nerve structures, and usually show a benign biological behavior.

Review of the Literature

In 1988 Jellinger et al. [5] reported a case of a 27 year-old woman with a primary localized, partly encapsulated melanotic tumor broadly attached to the occipital dura and tentorium. After developing transient left-sided hemianopia with papilledema headache, a cranial CT demonstrated a lobulated mass of 6 cm in diameter with strong contrast enhancement in the right occipital region so the tumor was removed surgically without postoperative irradiation. A CT performed 44 months after surgery demonstrated a solid mass of 4 cm in diameter in the right posterior fossa and it was necessary remove the tumor a second time. Histology of the first biopsy showed a densely packed oval or elongated cells tumor arranged in bundles and fascicles, with no syncytial pattern, no mitotic figures psammoma bodies or mineral deposits. Immunoperoxidase stains for GFAP, cytokeratin, vimentin, factor VII, NSE were negative, while S-100 protein showed positive staining of tumor cells. Electron microscopy demonstrated a varying number of tumor cells contained mature melanosomes and premelanosomes in various stages of melanization. The results of the histological investigations on the second biopsy revealed a similar pattern with a considerable increase of cellularity and melanin pigment.

In 1995 Maiuri et al. [6] reported a case of intracranial meningeal melanocytoma of the left sphenoid wing in a 69 year-old man with a history of headache, dizziness, severe right-sided hemiparesis and mixed aphasia. A CT study showed a large round hyperdense tumour in the left fronto-temporal region with marked and homogeneous contrast enhancement and slight perilesional edema. The tumor was removed surgically, on the basis of the surgical aspect of the tumor, a meningeal melanoma was suspected. Histologically the tumor was highly cellular, consisting of closely packed spindle-shaped cells, many melanosomes at varying stages of development and absence of mitotic figures. Immunoperoxidase staining was performed using antibodies against Fibrillary Acidic Protein (GFAP), vimentin, S-100 protein, antimelanoma antibody (HMB-45), Epithelial Membrane Antigen (EMA) and Neuron-Specific Enolase (NSE). Immunohistochemical studies showed negative staining of the neoplastic cells with GFAP, NSE and EMA. Stains for S-100 protein, vimentin and HMB-45 were strongly positive on the majority of cells. The histologic, electron microscopy and immunohistologic studies proved that the neoplasm was a meningeal melanocytoma.

In 2000 Painter et al. [7] described the case of a 35-year-old man with a history of remote closed head injury who presented with new neurologic deficits. A non-contrast CT study showed hyperdensity involving both temporal lobes, frontal lobes, basal meninges and cerebellum. A subsequent contrast-enhanced MR scan of the brain showed enhancement in the basal cisterns extending into the upper cervical spine and throughout the spinal canal. An elective right pterional craniotomy was performed, including biopsy and partial debulking. Light microscopic examination showed the typical appearance of a pigmented lesion. Immunohistochemical stains were positive for S-100 protein, HMB-45 and vimentin, suggesting a pigmented neoplasm of melanocytic origin.

In 2003 Rahimi-Movaghar, et al. [8] reported a rare case of parietal convexity meningeal melanocytoma associated with oculodermal melanocytosis (Nevus of Ota) in a 17-year-old man presented with headache, blindness, progressive lethargy, periods of confusion and disorientation. A CT scan of the brain with IV contrast showed a non-homogeneously enhancing lesion located in the left parietal region, with shift of ventricles ad midline structures to the right. So the mass was removed surgically. The lesion -a black and encapsulated mass- was distinct from the brain but firmly attached to the dura. Light microscopic examination showed sheets of tumor tissue with focal areas of whorled pattern but no pleomorphism, necrosis or abnormal mitosis. Immunohistochemistry revealed positive reactions to HMB-45 and S-100 protein in neoplastic cells and focally positive Epithelial Membrane Antigen (EMA), suggesting the diagnosis of meningeal melanocytoma.

Discussion

Primary melanocytic neoplasms are rare lesions arising from normally occurring leptomeningeal melanocytes and not from the meningothelial cell. Embryologic evidence suggests a common origin of melanocytes of the basal layer of the epidermis and the leptomeninges covering the base of the brain and the brain stem. The most commonly involved anatomical regions are: cerebellum, cerebral peduncles, medulla, interpeduncular fossa and inferior surfaces of the frontal, temporal and occipital lobes. Cases in cervical and thoracolumbar regions are also described [9]. These neoplasms are generally divided into three main types, including diffuse melanosis, meningeal melanocytoma and primary malignant melanoma. These tumors usually behave as a benign, single, often encapsulated, nodular brownish lesion, with the tendency to compress the adjacent tissues rather than to infiltrate nerve structures [3]. A meningioma may

mimic this gross appearance if large amounts of hemosiderin are present within the lesion from previous episodes of hemorrhage [7,10]. A variety of neurological symptoms may be seen with meningeal melanocytoma like recurrent headache, hydrocephalus, seizures, chronic basal meningitis, multiple cranial nerve palsies, psychiatric disturbances, intracranial hemorrhage of the meninges. The preoperative diagnosis is made by neuroradiologic studies with CT, MRI and angiography. CT scan are characterized by iso/hyperdensity lesions with variable contrast enhancement. The MRI appearance is influenced by the content of melanin which causes shortening of T1 and T2 relaxation times. Generally these tumors have a high signal on T1-weighted studies and a diminished signal on T2-weighted images, with enhancement after contrast administration [11-13]. The angiography shows scarce or no vascular stain. The ultrastructural and immunohistochemical characteristics of these lesions are unique.

	Meningeal Melanocytoma	Melanocytic Schwannoma	Melanocytic Meningioma	Melanoma
HMB-45	+	+/-	-	++
S-100 PROTEIN	+	++	-	+
VIMENTIN	+	+	+	-
EMA	-	-	+/-	-
GFAP	-	+/-	-	-
Leu7	-	+	-	-

Table 1: Immunohistochemical features of pigmented tumors of the meninges.

Authors	Age/Sex	Location	Symptoms/signs	Radiologic diagnosis	Treatment	Pathologic diagnosis	Follow-up
Jellinger et al. [5]	27 F	Right occipital region	Headache, left-sided hemianopia, papilledema	CT	Complete removal	Light and electron microscopy	Recurrence at 44 months, reoperation
Maiuri et al. [6]	69 M	Left sphenoid wing	Headache, dizziness, right-sided motor weakness, speech disturbances	CT, angiography	Partial removal and irradiation	Light and electron microscopy, immunohistochemistry	No recurrence
Painter et al. [7]	35 M	Basal cisterns extending into the upper cervical spine	Recurrent headache, cortical blindness	CT, MRI	Partial removal	Light microscopy, immunohistochemistry	No recurrence
Rahimi-Movaghgar [9]	17 M	Left parietal convexity	Headache, blindness	CT	Complete resection	Light microscopy, immunohistochemistry	No recurrence

Table 2: Data on the reported cases of meningeal melanocytoma.

Histologically, the tumor is composed of oval or elongated cells, may be organized in shape from spindle or fusiform to polygonal; the nuclei are usually large and prominent nucleoli are often described. Necrosis and hemorrhage are generally absent, though O'Brien et al. reported minimal necrosis, and the mitotic figures are also described as few, scanty, occasional or single [14-16]. The tumor cells may present different degrees of melanization. However the pigment stains negatively for iron. These signs and the absence of cytological signs of malignancy contradict the diagnosis of melanoma while the lack of desmosomes and interdigitating cytoplasmic processes contradict the diagnosis of meningioma. Immunohistochemical analysis is

important to differentiate meningeal melanocytoma from other similar lesions. Meningeal melanocytoma is positive to anti-melanoma antibody (HMB-45), S-100 protein, vimentin antibodies (rarely present in malignant melanoma) and by a negative reaction to Epithelial Membrane Antigen (EMA). Melanocytic meningioma is characterized by a positive reaction to EMA and vimentin, and by a negative reaction to HMB-45 and S-100 protein. A positive reaction to HMB-45 and S-100 protein in the absence of a reaction to EMA provides a reliable diagnostic criterion for the diagnosis of a pigmented lesion, excluding meningioma [10,17,18] (Table 1). The best therapeutic treatment is a complete surgical removal and, if it is

not possible, an incomplete tumor resection combined with a postoperative radiotherapy or stereotactic radiosurgery. However the effectiveness of radiation therapy is not completely clear for this type of lesions. Rades, et al. showed that complete resection was superior to incomplete resection with statistical significance at 1-, 2-, 3-, and 4-year follow-up intervals ($p < 0.05$). Incomplete resection with radiotherapy was superior to the incomplete resection alone at 2-year follow-up ($p < 0.05$). The survival rates related to different therapeutic approaches were not statistically significant ($p > 0.47$) [19]. Gamma knife radiosurgery has shown to reduce the tumor size and improve clinical outcome. Intrathecal methotrexate or interleukins too have been tried in few cases. Currently, Gross Total Resection (GTR) with adjuvant RT provides the best local control and survival [20] (Table 2).

Conclusion

Meningeal melanocytomas are benign tumors, but they may present with aggressive behaviors. Complete surgical resection can be curative for most cases. Radiation therapy is important to prevent relapse of the tumor when complete surgical resection is not possible. However the management of melanocytoma has no definite guidelines. The prognosis of meningeal melanocytoma is better than their malignant counterparts [21]. Local recurrences, in spite of the apparently complete surgical removal, suggest that these neoplasm have the possibility of malignant change. For this reason patients should be followed closely to prevent recurrences or the rare event of malignant transition.

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