Primary pineal malignant melanoma

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Abstract

Primary pineal malignant melanoma is a rare entity, with only thirteen cases reported in the world literature to date. We report a case of a 70-year-old man, who consulted with gait disturbance of six months duration, associated in the last month with dizziness, visual abnormalities and diplopia. No other additional melanocytic lesions were found elsewhere. The magnetic resonance showed a 25 mm expansive mass in the pineal gland that was associated with hydrocephaly, ventricular and transependimary oedema. The lesion was partially excised by a supracerebellar infratentorial approach. The histological examination revealed a melanoma. The patient received radiation therapy, but died of disease 16 weeks later. We herein review the literature on this rare tumour and comment on its clinical, radiological and histopathological features and differential diagnosis.

Introduction

Primary pineal malignant melanoma is a rare entity. The first case was published by Ogle in 1899; since then only thirteen cases have been reported in the world literature. Most of the melanomas arising in the central nervous system (CNS) are metastatic and primary malignant melanoma represents an exceedingly rare malignant primary tumour of CNS, representing less than 1% of primary tumour in this location. The initial symptoms are related to tectal compression and imaging findings can be variable, so frequently diagnosis is made only after surgery when tissue material for pathological exam is obtained. There is no an optimal treatment and neither radiotherapy nor chemotherapy improve survival.

Case Report

The patient was a 70-year-old man, with medical history of diabetes type II treated with oral antidiabetics, who underwent transurethral resection for benign prostatic hyperplasia in June 1997. He was admitted in another Hospital with an approximately six months history of gait disturbance, lower extremities weakness, and progressive inability for walking and standing; in the last month he had also developed dizziness and visual abnormalities with diplopia. Hematologic exams, included full blood examination, electrolytes, hepatic enzyme screen, erythrocyte sedimentation rate and C-reactive protein, were all within normal limits. Magnetic resonance imaging (MRI) showed a 25 mm mass in the pineal gland, hyperintense in FLAIR sequences and isointense in T2 compared to the encephalic parenchyma (Figure 1). The mass was associated with a deformity of the tectum lamina and compression of the Sylvian aqueduct that caused hydrocephaly of the lateral and third ventricles, with signs of transependimary oedema. A MRI of the spine and a computed tomography scan (CT) of the thorax and abdomen discarded widespread dissemination of the tumour. A biopsy of the mass was obtained though an infratentorial, supracerebellar approach, and the mass was partially excised (Figure 2).

Pathology

The entire mass displays a lobular architecture, surrounded by a richly vascularised stroma (Figure 3). Tumour cells are pleomorphic, with fusiform and epithelioid morphology, and marked atypia. Many cells contain abundant intracytoplasmic granules of melanin pigment (Figure 4), and they display a strong immunoreactivity for melanin markers, namely HMB-45 (Figure 5), MelanA (Figure 6) and S100 protein. No other immunoreactivity is found for neuroendocrine and epithelial markers in the neoplastic cells. The tumour shows necrotic areas and the mitotic rate is high, with a Ki-67 proliferative index of 20%. Then the patient was evaluated by an expertise dermatologist and ophthalmologist, without any cutaneous and mucous suspicious lesions found and either on the ocular exam. The CT scans did not reveal any mass other than the pineal. In the absence of clinical skin, mucous and ocular melanic lesions and radiologic evidence of no extracranial disease, diagnosis of primary malignant melanoma of the pineal gland was made.

Discussion

Most of the melanomas arising in the CNS are metastatic. Primary malignant melanoma represents <1% of the malignant primary tumours of CNS1-7 and usually when they arise primarily are localized in the temporal lobe, cerebellum and cerebellopontine angle.[4]

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Pineal melanoma represents an exceedingly rare tumour, with only 14 cases well documented in the world literature[1,2,8-19] (Table 1). Two of these patients were Japanese[8,9] and we have

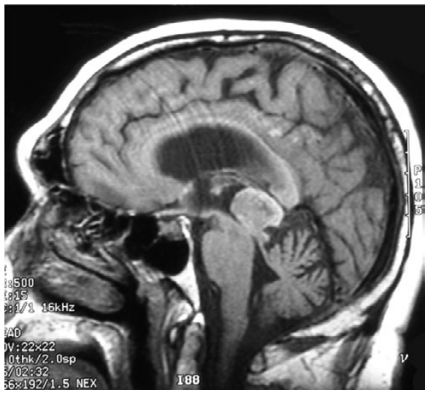

Figure 1. Magnetic resonance imaging evidence a mass in the pineal gland with variables signals in T1 and T2.

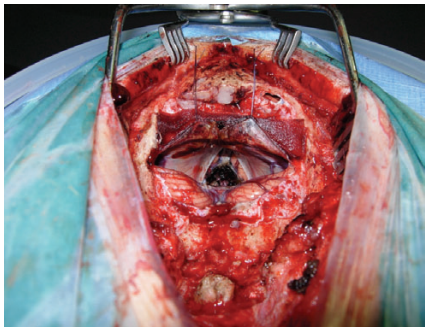

Figure 2. Macroscopic appearance of the melanic tumor in the chirurgic approach.

found no information regarding the race of the other cases. The age at presentation ranged from 20 to 77 years (average 48.2 years), with an equal sex distribution.

The first case was published by Ogle[10] in 1899; since then only fourteen further cases have been reported for more than one century, with our case.

Two origins have been postulated. The first one was proposed by Ogle, he hypothesized an origin from Wagner Meissner corpuscles and Merckel-Ranvier bodies. The second was proposed by Gibson *et al*., who claimed that melanoblasts are present through all the pia-arachnoid CNS and that these melanocytic cells could undergo malignant transformation.[11] These cells are located in the leptomeninges and the stroma of the pineal gland only during the prenatal period.[2,9,12] It seems reasonable to think that melanocytic cells located in the leptomeninges,[5] that form the capsule which surrounds the gland, might undergo malignant transformation, proceed to invade the gland and eventually substitute and blur its structure.[2] We have confirmed this hypothesis in all the slices we evaluated, in which we did not find any remaining normal pineal parenchyma.

It can be questioned if this tumour arose in the pineal gland and disseminated to meninges or just the other way around. Our tumour was located in the pineal gland, and no lesions were detected in the meninges by MRI or in the cytological exam of cerebrospinal fluid. Without clinical and radiological evidence of melanocytic lesions on the skin and ocular exam at the time of presentation, the diagnosis of primary pineal malignant melanoma can be considered certain. The symptoms can vary widely, including headache, nausea, vomiting and paralysis. Ataxia has also been reported, but all these symptoms can be related to obstructive hydrocephaly due to Sylvian aqueduct and superior tectal compression. In an advanced stage of the disease there could be seizures, aphasia and hemiparesia. In magnetic resonance images, the tumour is frequently hypointense in T1-weighted MRI and hyperintense in T2-weighted MRI. However, these typical features can be lacking in some cases.[9] A fact that can be attributed to intratumour haemorrhage, melanin paramagnetic free radicals and different concentrations of melanin.[2,9] Woodruff *et al*., reported a series of 13 patients with CNS melanoma. They found hyperintense T1 and hypointense T2 lesions, which consistently had more hemorrhagic areas than melanin pigment.[20] Other MRI studies by Escott divide intracranial melanomas in those with a melanotic MRI pattern and with amelanotic MRI pattern.[21] The melanotic pattern corresponds to tumours with high melanin content, with a hyperintense T1 and hypointense T2 MRI signals. The amelanotic pattern represents tumours with less than 10% of melanin containing cells, which were hypointense in T1 and hyperintense in T2 weighted MRI. In the present case the MRI signals corresponded to the melanotic pattern described by Woodruff, as was posteriorly confirmed by histopathology analysis, for the tumour cells contained high quantities of melanin intracytoplasmic pigment and showed intense immunoreactivity

Table 1. Summary of the fifteen cases of primary pineal melanoma.

Series (ref.)	Age (years)/sex	Time since onset of symptoms (weeks)	Melanic pigment	Therapy	Survival (weeks)
Ogle ,[10] 1899	32/F	3	NR	None	13
Stoerck,[13] 1904	31/M	8	NR	None	12
Foot and Zeek ,[14] 1931	40/M	2	Present	None	4
Gibson,[11] 1952	68/F	8	Present	None	8
Enriquez,[15] 1973	43/M	32	Present	None	37
Arland,[12] 1977	32/M	40	Present	Radiation	56
Carlson,[16] 1987	77/F	1	NR	VP shunt, craniotomy, biopsy	5
Weindling,[17] 1988	59/M	2	Present	Biopsy	NR
Rubino,[18] 1993	60/M	4	Present	Radical resection	>52
Yamane,[8] 1994	53/F	2	Present	Resection, chemotherapy	>208
Mitchell,[19] 1998	49/M	12	Present	Biopsy	NR
Suzuki,[9] 2001	50/F	16	Present	Partial resection, radiation	92
Bookland,[2] 2006	20/F	3	Present	Biopsy, VPs, radiation and chemotherapy	>37
Barron,[1] 2007	73/F	NR	Present	Radiation	69
Present case	70/M	24	Present	Partial resection, radiation	40

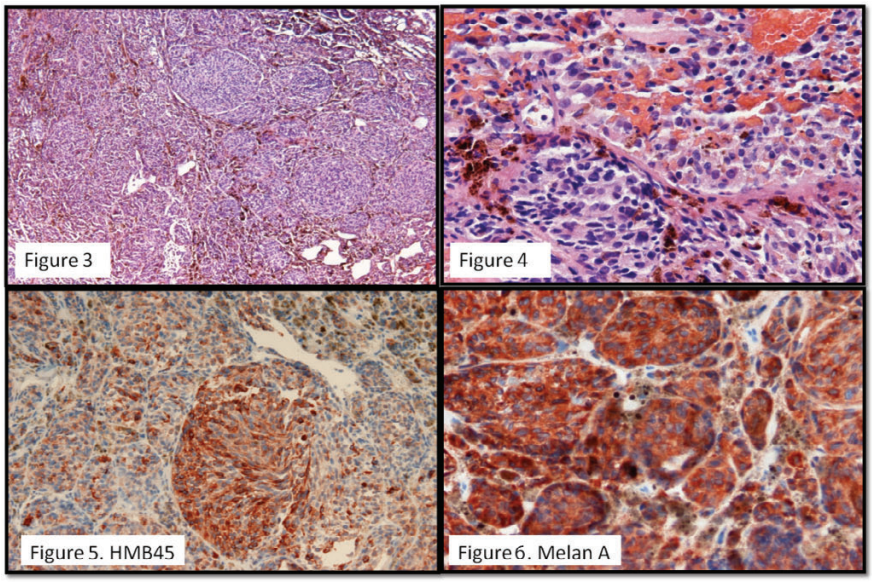

Figure 3. Melanic neoplam swith a nodular pattern. Figure 4. The neoplastic melanic cells are pleomorfic and show variable intracitoplasmic brown pigment and haemorrhagic areas. Figure 5. Malignant melanic cells were positive for HMB-45. Figure 6. MelanA cytoplasm caption in of melanic malignant cells.

for HMB-45 and MelanA.[20]

Isiklar *et al.*, studied 42 cases diagnosed as intracranial melanomas. They found that 38% corresponded to the amelanotic pattern and 24% to the melanotic one. However approximately 38% of their cases fell into another category with varying T1 and T2 weighted signals on MRI, that could be related to the presence of haemorrhage.[22]

The morphology of these tumours varied from nodular to a diffuse pattern. In our case, nodular proliferation was the dominant pattern. This morphology could also be found in other primary parenchymal tumours of the pineal gland, such as melanocytoma, a tumour consisting of well-differentiated melanocytic tumour cells in the pineal gland. Melanoma displays a broad spectrum of cell differentiation, from areas with well-differentiated cells that resemble melanocytoma to areas with higher degrees of cytological atypia and pleomorphism, variable pigmentation, from dense to amelanotic, mitotic figures and necrosis. There are no cases reported of pure primary pineal amelanotic melanoma. Pineal melanomas show frequent foci of haemorrhage and necrosis in association with intraparenchymal, ventricular and leptomeningeal invasion and dissemination through the cerebrospinal fluid (CSF).

The prognosis of these patients is poor and survival has ranged from 4-13 weeks for patients that did not receive any therapy and 56 weeks to 4 years for those patients who received some kind of therapy [surgery, chemotherapy and/or radiotherapy (RT)] with a relatively longer survival as expected, and reported by Barron.[1] A study by Kiel *et al.*, classified these tumours in discrete and diffuse leptomeningeal tumours. As expected, the tumours with dissemination show a worse prognosis, with a mean survival of 6-7 months compared with 20.7 months for patients with discrete lesions.[23]

The absence of meningeal dissemination and the degree of tumour differentiation seem to be an important factor that contributes to a longer survival. It seems obvious that any therapy is associated with a benefit in the survival. Suzuki el al. reported a case of a well-differentiated tumour with a 4.7 year survival.[9]

Our case has a single mass without leptomeningeal dissemination, received RT after partially tumour resection, and died after 16 weeks. The survival was only 40 weeks since the initial symptoms.

The optimal treatment remains unsettled but any therapy appears to improve survival, as already discussed.

Conclusions

Primary pineal melanoma is a rare tumour with an adverse outcome. Due to its low frequency and varying symptoms and imaging characteristics, it is difficult to suspect this diagnosis on both clinical and radiological grounds. Pathological diagnosis is based on the exclusion of other primary tumours of the pineal gland and metastatic melanoma. It is clear that therapy improves the survival in these patients but, actually, there is no consensus about the optimal one.

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