Case Report

Melanoma Originating from the Dura-Mater: A Case Report and Review of the Literature

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ABSTRACT: Melanomas originating from the dura-mater are extremely rare tumors. The diagnosis is complex, and usually only made after excluding other entities. The prognosis is poor, with average free-disease survival of 20 months, after treatment with complete surgical excision and adjuvant therapy. We report the case of a 41-year-old asymptomatic patient, presenting with a subcutaneous mass in the left parieto-occipital region, later diagnosed as a primary dura mater melanoma. Treatment included complete microsurgical excision, radiotherapy and adjuvant immunotherapy. Therefore, due to the rare nature of the disease and its high lethality, correct diagnosis and treatment are medical challenges.

KEYWORDS: *Central nervous system, primary malignant melanoma, melanoma, tumor, dura mater.*

Introduction

In the central nervous system (CNS), besides the meningeal layers, the melanocytes, cells originated from the neural crest and that produce melanin, can be found in the brain hemispheres, medulla oblongata, cervical spinal cord and, occasionally, in the olfactory bulbs [1,2,3].

Extra-cutaneous melanomas are rare, representing only 4-5% of all the primary melanomas, and have a worse prognosis when compared with the cutaneous forms [4,5].

It is more common in children and in most cases is related to the concomitant presence of pigmented nevus.

Primary CNS melanomas represent only 1% of all melanomas, and 0,07% of brain tumors [4,6,7].

Meningeal melanomas grow more frequently from the leptomeninges (arachnoid and pia-mater), since these structures have the higher concentration of melanocytes in the CNS [7] and are rarely detected in the dural layer.

The clinical scenario varies widely and depends on the affected site.

The most common symptoms include intracranial hypertension (43%); focal neurological deficits (35%); subarachnoid haemorrhage (14%); and seizures (12%).

Headache, diplopia, dysarthria, aphasia and decline in cognitive function are also reported [4,6].

In these cases, complete surgical excision is the treatment of choice, preferably followed by adjuvant therapy with radiation or immunotherapy, demonstrating a better prognosis when compared to those originating from the leptomeningeal layers [3,6,8].

This article aims to report a rare case of melanoma involving exclusively the dura mater and adjacent skull in an adult patient, as well as describe a brief review on the subject.

Case Presentation

A 41-year-old male patient presents with a slow-growing subcutaneous mass, in the posterior cranial region, with three months of progression. A consent from the patient has been obtained for publication of this case report.

When the patient was admitted to our neurosurgery service at the Hospital of the Clínicas de Passo Fundo he had no associated neurological symptoms or risk factors for chronic exposure to sunlight.

There were no signs or symptoms of systemic disease, and, as previous medical background, there was only a positive history of toxoplasmosis during childhood, developing convergent strabismus as a sequela.

On physical examination, his clinical performance was excellent (ECOG 0/Karnofsky scale 100%).

A palpable subcutaneous nodulation in the left parieto-occipital region was identified, measuring approximately 5cm in diameter, with hard consistency, adherent to the deep subcutaneous tissue, without any modification in the skin colour.

There was also apparent erosion of the adjacent bone.

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No neurological deficits were identified.

Neuroimaging obtained by Magnetic Resonance Imaging (MRI) showed a heterogeneous solid mass, with lobulated margins and hematic appearance, centred on the cranial vault, in the parieto-occipital region, measuring 3 x 2.8 x 2.7cm (Figures 1 a,b,c) with destruction of the adjacent bone.

The lesion expanded into the intracranial compartment, compressing the brain tissue, as well as into the subcutaneous tissue, projecting through it.

After gadolinium infusion, there was a heterogeneous enhancement on T1WI, that extended to the adjacent dura-mater.

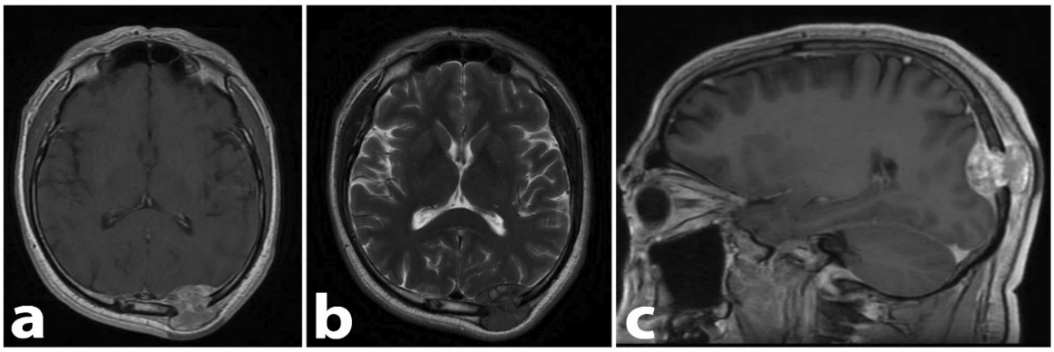

Figure 1. Preoperative MRI. a) T1WI with gadolinium, axial image, evidencing a left occipital lesion, extending from the intracranial to the extracranial compartment, eroding the adjacent bone, with heterogeneous enhancement by contrast. b) T2WI, axial image, evidencing the hypointense left occipital lesion, with apparent cleavage plane from the brain tissue. c) T1WI with gadolinium, sagittal image, evidencing a left occipital lesion, extending from the intracranial to the extracranial compartment, eroding the adjacent bone, with heterogeneous enhancement by contrast.

Then, an excisional biopsy was performed, with complete resection of the lesion.

For better oncological control, the infiltrated and eroded bone of the parieto-occipital region and the occipital dura mater were also resected.

There were no signs of infiltration of the leptomeningeal planes, neither of the brain tissue (Figure 2 a-f).

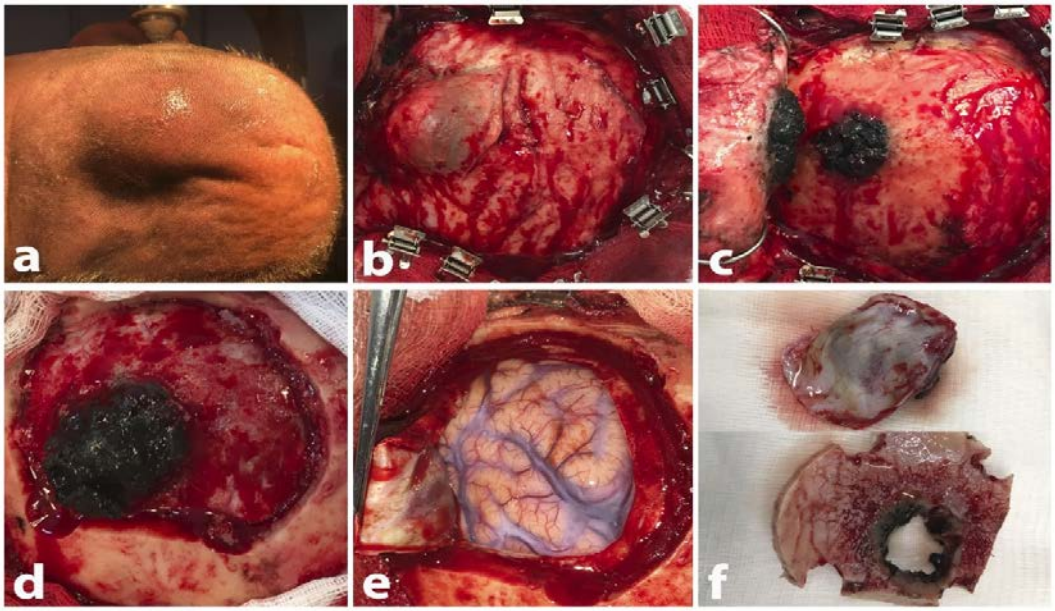

Figure 2. Surgical procedure findings. a) Pre-operative aspect of the scalp, evidencing a subcutaneous nodulation in the left occipital region. b) After initial incision of the skin, exposure of the bone and pericranium, evidencing the compromise of the latter. c) After dissection of the pericranium, dark colored tumor expanding from the affected occipital bone. d) Post-craniotomy aspect, showing that the lesion compromises the dural layer. e) After dural incision, no evidence of leptomeningeal layers was found, and dural compromise was confirmed. f) Surgical specimens after resection, evidencing bone erosion by the tumor, as well as dural involvement.

Immunohistochemical analysis were performed at the Institute of Pathology and Molecular Biology of Passo Fundo using histological sections previously fixed in buffered formalin 10% processed and paraffin embed.

Monoclonal or polyclonal antibodies are used under the BenchMark ULTRA platform combined with detection system of Ventana following these steps: deparaffinization; antigenic retrieval; blocking of nonspecific reactions; incubation in a panel of antibodies described below, detection and amplification (when necessary) of the reactions and development.

Individualized positive controls are used to attest to the fidelity of the reactions.

The anatomopathological examination confirmed the diagnosis of melanoma (Figure 3 a-d), and immunochemistry assay showed positivity to Sry-related HMg-Box Gene 10 (SOX10), Melan A (A103), Human Melanoma Black (HMB45) e microphthalmia transcription factor (MITF) antibodies.

The study of mutation in the B-RAF Proto-Oncogene (BRAF) gene, by the cobas technique, evidenced the variant V600E.

Surgical recovery was uneventful, and the patient continued treatment with radiotherapy on surgical site, and adjuvant anti-BRAF therapy for 12 months, associated with serial CSF analysis and close oncological follow-up with neuroimaging.

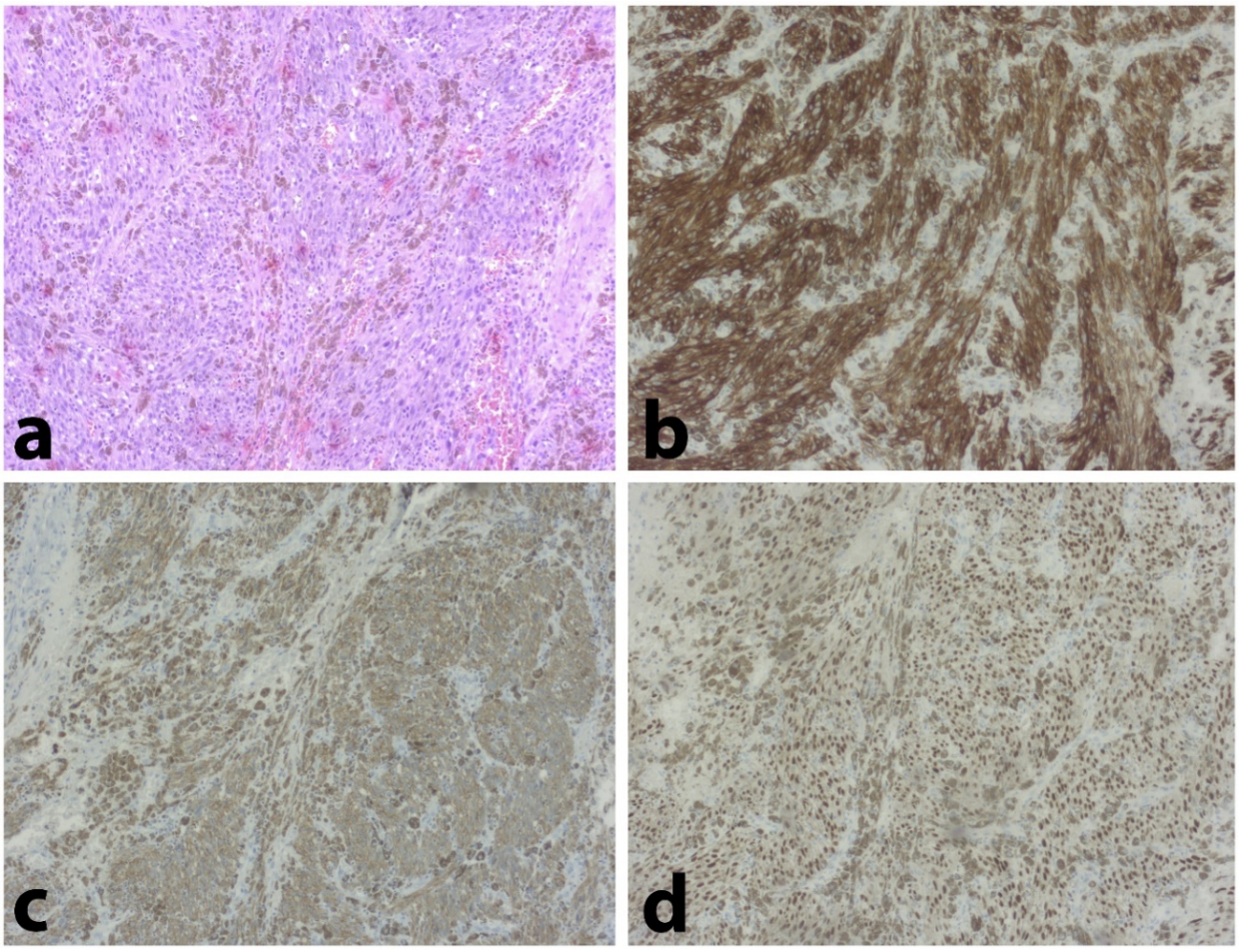

Figure 3. Pathology findings. a) H&E (x20), evidencing pleomorphic tumor cells organized in nests. The cells are round and pigmented, and present mitotic figures. b) Melan A immuno-histochemical staining (×5) revealing positivity in the tumor cells. c) HMB-45 immuno-histochemical staining (×5) revealing positivity in the tumor cells. d) SOX10 immuno-histochemical staining (×5) revealing positivity in the tumor cells.

Discussion

Melanocytic tumors originating from the meningeal layers form a wide tumoral spectrum.

Primary CNS melanoma has an incidence of around 0,005/100.000 inhabitants [9], and can be divided in two subtypes, according to the pattern of involvement: the first subtype invades the meningeal layer in a diffuse pattern, with greater involvement of the leptomeninges; the second subtype forms an intraparenchymal nodular pattern [2].

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They have an incidence peak in the fourth and fifth decades of life, with male predominance, and, as occurs in all melanomas is less frequent in dark-skinned populations [7].

Melanomas are composed of biologically distinct subtypes, and various histological theories have been proposed about its origin.

Mutations in the BRAF gene have significant importance in its development, since they lead to activation of the RAS (Rat sarcoma virus), RAF (Rapidly accelerated fibrosarcoma), MEK (Mitogen-activated protein kinase kinase), ERK (Extracellular signal-regulated kinase) pathways that regulate cellular circles.

BRAF mutations are the most frequent (50%) in melanomas, positive in the histochemical findings of our patient, and NRAS (Neuroblastoma RAS viral oncogene homolog) mutations represent 20%, these latter oncogenes are responsible for induction melanocyte proliferation and development of congenital melanocytic lesions [6,7,10].

Pathological markers such as tyrosine kinase, S-100, HMB-45, MART-1 (Melan A) and SOX10, confirm the melanocytic origin of the tumors [6,11], with the last three identified in our case.

The HMB-45 antibody, for example, has high specificity for melanocytic tumors, being positive in 86-97% of cases [2].

The histological pattern of these tumors consists of large, pigmented atypical cells with bizarre pleomorphic nuclei, which grow form nests or loose sheets.

There is high mitotic activity and high MIB-1 index (around 8.1%), often presenting invasive and necrotizing behaviour [12].

The typical presentation of melanomas in the magnetic resonance imaging (MRI) is a hypersignal in T1-weighted image (T1WI) and hyposignal in T2-weighted image (T2WI), due to the paramagnetic effect of melanin present in these tumors.

The absence of leptomeningeal melanosis, associated with extensive melanosis of the dura-mater, strongly suggests the dural origin of the tumor [3], both evidenced in our patient.

The occurrence of bone metastasis in the primary CNS melanomas is not uncommon, although radiological demonstration is infrequent.

Primary CNS melanocytic tumors have better outcomes when primary neurosurgical therapy is indicated, followed or not by adjuvant treatment [6].

Adjuvant radiotherapy and targeted therapy/immunotherapy are important in the post-operative care, especially in those cases where total resection was not possible, despite the relative resistance of melanomas to these therapies [6,11].

When dealing with a focal single lesion, without cranio-spinal dissemination, treatment can be performed through complete excision of the lesion, associated with whole-cranial or focal (tumor and margin) radiotherapy.

Therefore, this was the procedure indicated for our patient.

Literature data on prognosis are scarce, considering the rare nature of this pathology, and that such data are mainly based on case reports and retrospective studies.

Life expectancy in meningeal melanomas depends on factors like the type of lesion, if there is involvement of the leptomeningeal layers, if complete resection of the lesion was achieved and, especially, MIB-1 pattern.

When compared to metastatic melanomas to the CNS, primary tumors present higher survival rates.

The diffuse subtype has a mean life expectancy of 6 months, while in the nodular types the life expectancy is around 20 months after complete surgical excision [4,8,13].

In the differential diagnosis, metastasis plays the main role since the CNS is the most commonly affected site.

The differentiation is based on neuroradiological examination and surgical excision, with subsequent histological analysis.

Metastatic dissemination occurs mainly from the primary cancers of breast, lungs and cutaneous melanoma, the latter presenting in about 16%, with 70% affecting the leptomeningeal layers [3].

Due to this high association, arbitrarily, to confirm a primary meningeal site it is necessary to exclude involvement of any other side [2,6].

Other differential diagnoses are the meningeal melanocytoma, a rare benign tumor, arising from the leptomeningeal layers, usually in the posterior fossa or superior spinal cord [4] and meningiomas, since both have isointense aspect in T1WI, become homogenous after contrast enhancement and present as a single mass with dural infiltration.

Besides, schwannomas, ependymomas, lymphomas and pineoblastomas should also be remembered [11].

Immunohistochemistry protocol

Study performed on histological sections fixed in 10% buffered formalin, processed and embedded in paraffin.

Monoclonal and/or polyclonal antibodies were used in the BenchMark ULTRA equipment in combination with VENTANA detection systems through steps of: deparaffinization, antigenic recovery; blocking of nonspecific reactions; incubation in antibody panel (SOX10, Melan A, HMB45, MITF), detection and amplification of reactions and exposure.

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Conflict of interests

None to declare

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