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Primary malignant meningeal melanomatosis: a clinical, radiological and pathologic case study

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Abstract

A 40 year-old woman with subacute headache and visual impairment was admitted. Neurological examination revealed meningismus, diminished visual acuity, bilateral sixth cranial nerve palsy, and papillary edema. Dermatologic examination was normal. The brain CT scan showed hydrocephalus and hyperdense edging around fissures and sulci. The CSF study showed an increased protein level, with persistently negative microbiologic and cytological studies. Prior to Gd-DPTA injection, the brain T1-WI MRI revealed leptomeningeal hyperintensity. A dark subpial substance became evident at cerebral biopsy. The histopatological diagnosis was diffuse leptomeningeal melanomatosis. This case report highlights the diagnostic value of the brain MRI findings in primary leptomeningeal melanomatosis, a rare pathologic condition diagnosed in most published cases only after necropsy. Meningeal T1-WI hyperintensity prior to contrast injection is not caused by sarcoidosis or meningeal carcinomatosis, lymphomatosis or gliomatosis.

Key words: Meningeal melanomatosis; melanin; MRI; hydrocephalus.

Introduction

Meninges contain melanocytes of ectodermal origin; their proliferation causes several tumours, which are primarily located in the meninges: a) diffuse melanocytosis and melanomatosis; b) melanocytomas; and c) malignant melanomas (1). Malignant meningeal melanomatosis (MMM) is caused by a proliferation of malignant melanocytes, which spread to the Virchow-Robin spaces and encephalic and spinal leptomeninges; some cases may also invade the dura mater (2). The incidence of primary MMM is very low, and only isolated cases have been reported (3-8). The usual clinical presentation of MMM is a syndrome of intracranial hypertension with cranial nerve palsy, and may also be accompanied by neuropsychiatric symptoms, seizures and impaired consciousness. The diagnosis of MMM is difficult (9), and was achieved in most published cases only after necropsy. The reason for this is that cerebrospinal fluid (CSF) smears are repeatedly negative; on the other hand, the findings in computed tomography (CT) and magnetic resonance imaging (MRI) are not regarded as specific. We present a case of a woman presenting with hydrocephalus and blindness, and diagnosed of MMM. We highlight the diagnostic value of the brain MRI findings.

Case report

A 40 year-old woman was admitted because of headache, neck pain and visual impairment, which had progressed over the previous two months. The neurological examination revealed a diminished visual acuity (she could count fingers with her left eye and could see shapes with the right one), bilateral sixth cranial nerve palsy, bilateral papilledema, meningism and a right Babinski sign. Dermatologic examination was normal. A brain CT scan study showed tetraventricular hydrocephalus and a hyperdense edging around fissures and sulci which was enhanced with intravenous contrast (Figs. 1A and 1B). The CSF opening pressure was 32 cm H_2O, with normal cellularity and cytology, moderately increased proteins (80 mg/dL) and diminished glucose levels (43 mg/dL, simultaneous glycemia 123 mg/dL). Microscopic examination, cultures and different microbiological essays were all negative. The encephalic MRI study, as well as the hydrocephalus, showed a leptomeningeal hyperintensity in T1-weighted images (T1-WI), which was enhanced by intravenous gadolinium (Figs. 1C and 1D). Other studies performed, including a thoraco-

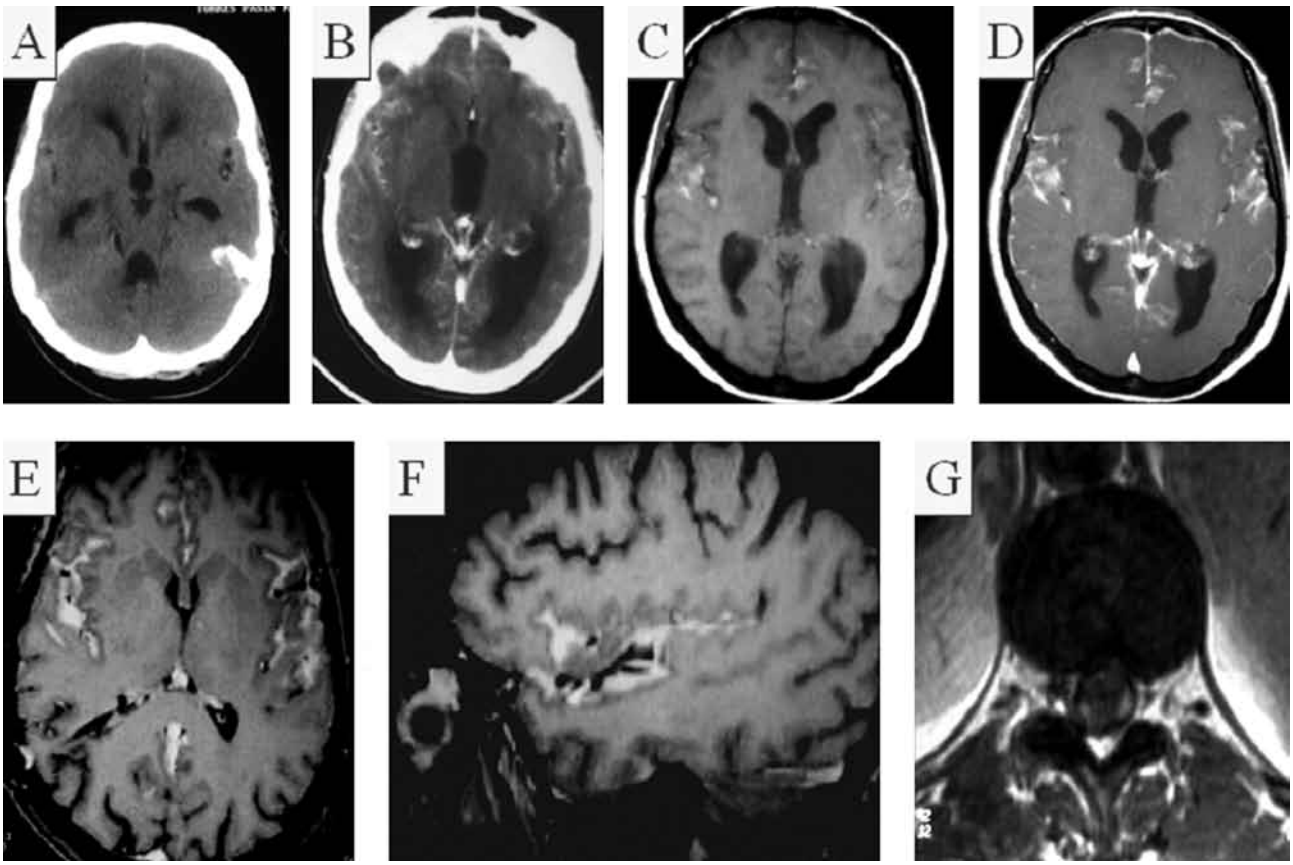

FIG. 1. — A: appearance of sulci and fissures upon opening of the dura mater. B: macroscopic aspect of a biopsy fragment. C (H&E: original magnification ×2) and D (inmunohistochemistry for HMB-45: original magnification ×4): diffuse neoplastic proliferation involving the meninges and the Virchow-Robin spaces with invasion of the cerebral parenchyma in some areas.

abdominal CT, a whole body positron-emission tomography (PET) and a gallium gammagraphy, were normal. A ventriculo-peritoneal shunt was placed, which improved the headache and neck pain. The CSF cytological studies were repeated, including HMB-45 and S-100 tagging, and were consistently negative. Further MRI studies showed a progressive increase in infiltration (hyperintense in T1-WI and iso-intense in T2-WI) around sulci and fissures and also perimedullary (Fig. 1E and 1F). In the brain biopsy, upon opening of the dura mater, a blackish subpial substance was found (Fig. 2A and 2B). The histopathological examination revealed a diffuse neoplastic proliferation involving the meninges and the Virchow- Robin spaces (Fig. 2C and 2D). Oval and spindle-shaped melanin-containing cells were seen in short fascicles and a storiform arrangement. In some regions an invasion of the cerebral parenchyma was evident. Immunohistochemistry showed a diffuse and strong reaction in the tumour for vimentin, S-100 protein, Melan A and HMB-45. MiB-1 showed nuclear staining in more than 10% of the cells. The diagnosis was made of diffuse leptomeningeal melanomatosis derived from a malignant melanoma. In view of the poor prognosis, antineoplastic therapy was not initiated. The patient died a year after the onset of the symptoms.

Discussion

Primary malignant meningeal melanomatosis (MMM) is caused by a proliferation of malignant melanocytes (meninges contain melanocites of ectodermal origin), which spread to the Virchow- Robin spaces and encephalic and spinal leptomeninges; in some cases they may also invade the cerebral parenchyma and the dura mater. A quarter of patients with MMM and melanocytomas, often children and adolescents, have wide pigmented cutaneous nevi, among them the Ota nevus (pigmentation of sclera and skin adjacent to the eye) (10,11). Cases of pure MMM, i.e. without an intraparenchimal tumoral nodule or melanoma outside the nervous system, are very rare. From the last half of the 20th century isolated cases of primary MMM have been reported (3-8). In the absence of cutaneous nevi, the diagnosis

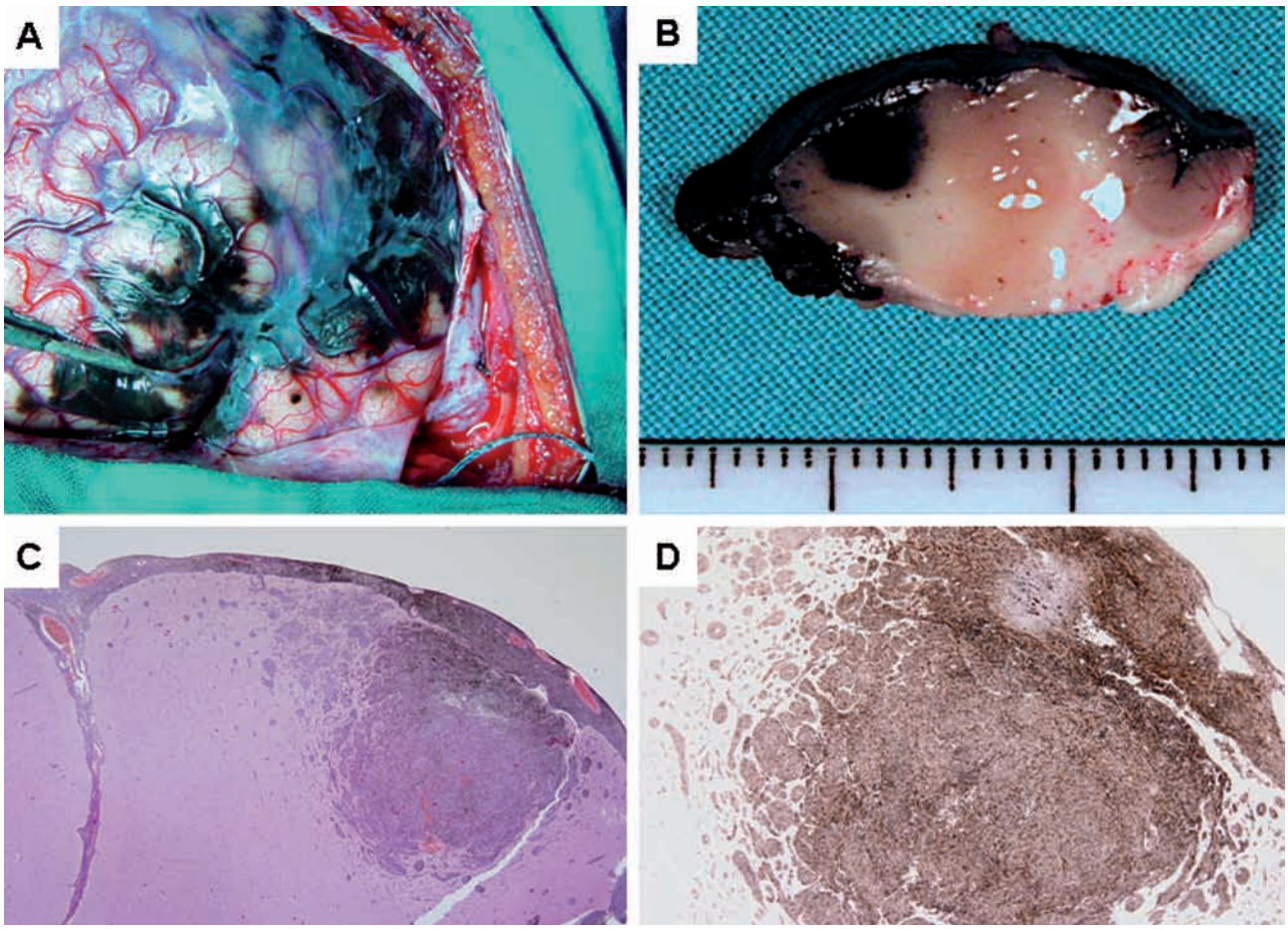

FIG. 2. — A and B: cranial CT study at admission showing hydrocephalus and discrete hyperdense edging around fissures and sulci, which was enhanced with intravenous contrast. C and D: cranial T1- WI MRI study at admission showing hyperintense areas around sulci and fissures before Gd-DPTA injection (mimicking enhancement by contrast medium). E, F, G: T1-WI MRI cranial and spinal study two months later, showing an increase of the hyperintense areas without Gd-DPTA injection.

of primary MMM may prove difficult, as the neuroimaging of the neoplastic infiltration in skull base, brainstem and spinal meninges may closely resemble – especially with contrast medium – other conditions, including sarcoidosis, tuberculosis, carcinomatosis, lymphomatosis or gliomatosis (6). The melanoma signal intensity, as compared to encephalic and spinal parenchyma, has classically been said to be hyperintense in T1-WI and iso/hypointense in T2-WI (12-14). This particular behaviour is caused by the paramagnetic action of the free radicals contained in melanin, combined in case of bleeding, with those derived from hemoglobin degradation (oxyhemoglobin, deoxyhemoglobin, hemosiderin). Rare amelanotic melanomas without bleeding could be an exception and would appear hypo- or isointense in T1-WI. Our case, a confirmed diffuse melanoma with no evidence of bleeding, behaved isointense in T2-WI and hyperintense in T1-WI MRI. Slow flow and hypermyelinization, as well as the presence of substances like calcium, fat, proteins and peptides or paramagnetic substances, will result in T1-WI hyperintensity. Most reported cases of MMM do not mention the results of T1-WI MRI, although a more or less diffuse leptomeningeal hyperintensity would be expected considering the histological description. In one published case, we found that a clear tumour implant (hyperintense in T1-WI-MRI) had been described as a hemorrhage (7). There are no histopathological features that help differentiate primary and metastatic melanoma in the meninges and this is achieved only upon clinical and radiological examinations, as well as evolution (our patient died one year later without evidence of any other lesion anywhere in the body).

The response of leptomeningeal melanomatosis to a conventional intrathecal chemotherapy and radiotherapy is poor. One of the longest-surviving patients was treated with intrathecal interleukin-2 (15). The distribution of the lesions, their MR character-

istics and the absence of systemic disease as in our case, is highly suggestive of primary MMM.

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