Meningeal melanocytosis: a challenging diagnosis

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A 22-year-old woman with a history of gradually worsening headache, who had developed nausea, vomiting, and diplopia within the past month, was referred to the Department of Neurosurgery of Hospital de Santo António (Porto, Portugal) in June, 2017. Initial neurological examination and cerebrospinal fluid (CSF) studies were unremarkable. Lumbar puncture opening pressure was elevated. The patient had no lesions evoking a congenital phakomatosis or neurocutaneous melanosis, including no nevus of Ota. MRI of the neuroaxis showed mild hydrocephalus and discrete disperse leptomeningeal enhancement of the cranial and spinal nerves (figure, A). Complete physical examination, including observation by ophthalmology and dermatology, followed by whole-body CT scan and scintigraphy, excluded the presence of other lesions. She was proposed for ventricle–peritoneal shunt placement and open brain biopsy. Biopsy analysis showed leptomeningeal thickening, with melanin-containing cells, low mitotic count, and no cellular atypia or brain invasion. Staining was positive for HMB45 and Melan-A, but she tested negative for the *BRAF*^{V600E} mutation. These findings were consistent with meningeal melanocytosis. Her symptoms improved with shunting.

3 months later, she was admitted to the hospital with shunt obstruction, and CSF collected during shunt revision showed cells with nuclear atypia, dark macronucleoli, and positive for melanic pigment, suggestive of melanoma. Off-label treatment with immune checkpoint blockade was considered in combination with radiotherapy, but rapid progression with biplegia and sphincter anomalies, followed by tetraplegia and respiratory depression, ensued. MRI at this stage showed syringobulbia, strong leptomeningeal enhancement of the cranial and spinal nerves, with exuberant filling of the spinal subarachnoid spaces and lumbar cistern (figure, B). She died 4 months after disease presentation.

Primary CNS malignant melanoma is a rare disease. It can be divided into nodular intraparenchymal and diffuse leptomeningeal patterns. The differential diagnosis for a diffusely disseminated leptomeningeal disease includes leptomeningeal carcinomatosis; disseminated primary brain tumours, such as diffuse leptomeningeal glioneuronal tumour; lymphoma; infectious meningitis; and inflammatory conditions, including sarcoidosis. Primary leptomeningeal melanocytosis is an extremely rare and aggressive type of primary CNS melanoma, and few published reports exist. Classically described treatments include radiotherapy and chemotherapy, but recent successes with BRAF inhibitors and immune checkpoint inhibitors in metastatic CNS melanoma suggest the potential of these drugs to treat CNS melanoma.

Clinical awareness of this condition and its aggressive course is fundamental for prompt discussion and expeditious initiation of treatments.

Contributors

CN contributed to data collection, literature search, data analysis, writing, and figure editing. LR contributed to critical review, writing, and figure editing. Written informed consent to publication was obtained.

Declaration of interests

We declare no competing interests.

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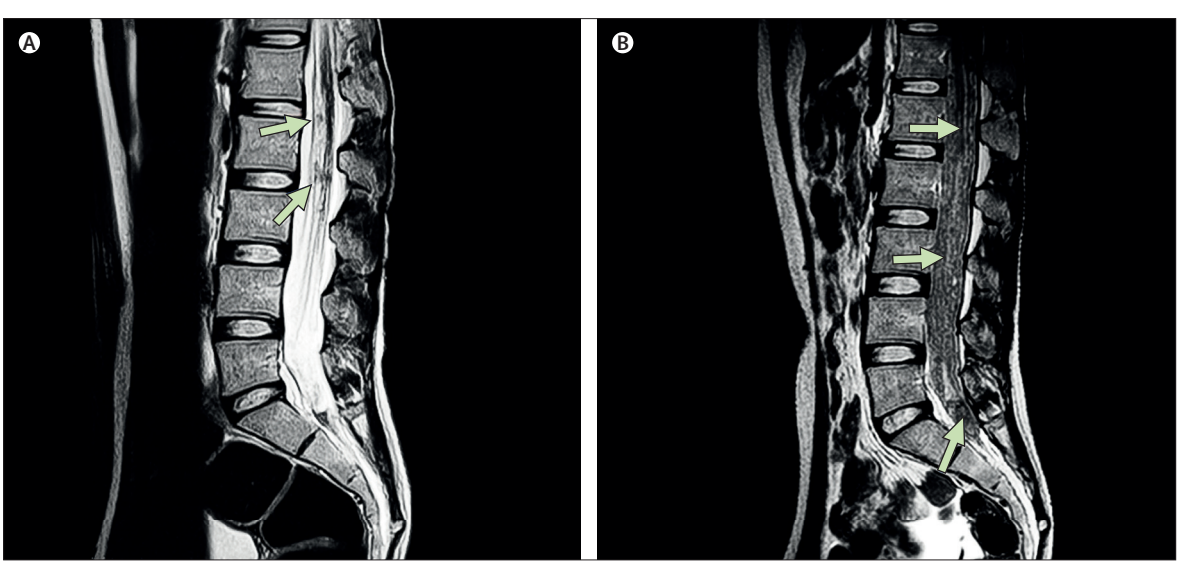

Figure: **Lumbar MRI progression in a patient with meningeal melanocytosis**
(A) Lumbar MRI at admission showed diffuse leptomeningeal enhancement of the spinal nerves. (B) Upon progression, exuberant filling of the spinal subarachnoid spaces and lumbar cistern was observed.