Paediatric Meningioangiomatosis PD-L1+: A Case Report

Meningioangiomatose Pediátrica PD-L1+: Um Caso Clínico

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Palavras-chave: Angiomatose; Criança; Inibidores de Checkpoint Imunológico; Meningioma

Dear Editor,

It is now well established in the literature that immune checkpoints (including in particular PD-1, PD-L1 and CTLA4) play an important role in the 'molecular communication' between cells/tissues and the surrounding immune microenvironment, modulating the continuous function of self/non-self-recognition. This awareness has led to the increasingly widespread use of immune checkpoint inhibitors in oncology, with the aim of preventing the immunoescape of neoplastic cells and enabling the immune system's effector cells to recognize and fight them. However, the status of immune checkpoints in non-neoplastic and/or pre-neoplastic disease is still poorly explored: the case we present belongs to this context.

We present the case of a 6-year-old girl who was born at term with no perinatal problems except for the presence of a slowly growing midline occipital swelling. The ultrasound examination showed a swelling in the middle occipital area measuring 13 x 18 mm, without any vascular signal. A subsequent brain magnetic resonance imaging (MRI) (Fig. 1A) showed and confirmed the presence of a midline occipital meningocele with a large craniolacunia (cranial bone or skull bone discontinuity). Also noted were the presence of normotensive hydrocephalus, subcortical fronto-parietal ischemic lesions, probably occurring during pregnancy, resulting in severe atrophy of the corpus callosum. Other associated malformations included: cyst of the septum pellucidum and microgyria in the parieto-occipital regions, vermian hypoplasia and secondary right convex thoracolumbar scoliosis with hemispondilus at C2-C3 left and somatic fusion at C4-C5. This was associated with the presence of a meningocele at the level of the external occipital protuberance. Surgical *en bloc* excision of the lesion with removal of the dystrophic skin allowed histological examination: microscopy showed angiomatoid and fibrous/fibroblastic areas with scattered meningothelial cells in clusters or surrounding vessels, without atypia or mitosis or a significant presence of lymphocytes/macrophages around the lesion, immunohistochemically epithelial membrane antigen+, progesterone+ and PD-L1+ (Fig. 1B), leading to the diagnosis of meningioangiomatosis (MAM), PD-L1 positive (the positivity rate, calculated as the number of PD-L1-positive pathological cells out of the total number of pathological cells, was 10%). The patient underwent surgical, clinical/epileptological and radiological follow-up, with nothing to report two years after surgery.

Meningioangiomatosis is a lesion with almost 200 histologically confirmed cases, typically affecting children and young adults, often presenting with seizures, headaches, neurological deficits or developmental defects including meningocele and/or encephalocele.[1,2] Neuroimaging (MRI) can show cortical lesions, but a definitive diagnosis usually requires biopsy. Previously, MAM was widely considered in the literature to be a non-neoplastic lesion (although sometimes associated with neurofibromatosis type 2, as in meningiomas), a view we considered reliable at the time. However, recent findings by Tauziède-Espariat *et al* challenge this view and show that MAM may represent a pre-neoplastic or neoplastic lesion. Their study revealed genetic alterations, including 22q homozygous deletions, and epigenetic profiles that closely align MAM with pediatric meningiomas,

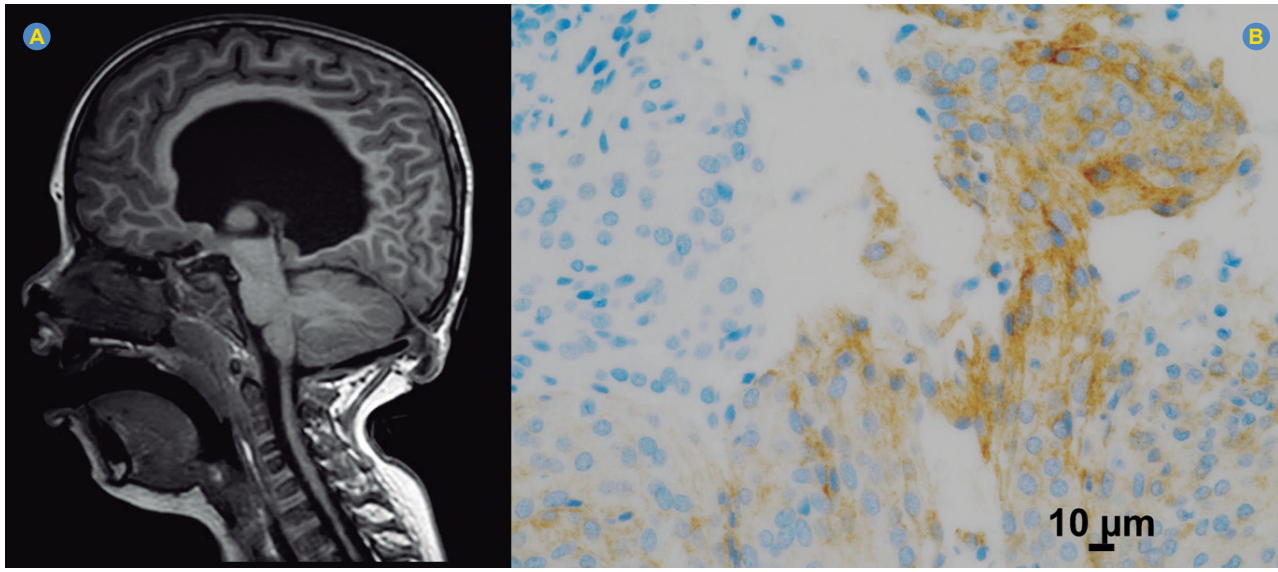

Figure 1 – Neuroimaging (MRI, sagittal plane, T1-weighted): defect of the occipital bone with herniation of mainly meningeal tissue (meningocele) with associated voluminous hydrocephalus (A). Microphotograph showing expression for PD-L1 in pathological cells (40x) (B).

suggesting a histomolecular continuum between these entities.[3]

To the best of our knowledge, this is the first described case of MAM/PD-L1+. Nevertheless, our observation of PD-L1 positivity could serve as an indirect confirmation of Tauziède-Espariat *et al*'s conclusions. Indeed, PD-L1 is an immune checkpoint associated with the immunoescape of many tumors, including meningiomas, which are targeted by specific therapies with anti-tumor effects,[4-6] thus supporting the hypothesis of a neoplastic potential in MAM. This raises important questions: does PD-L1 expression indicate that all MAM lesions have neoplastic potential, or does it identify a specific subset of MAM that may progress to a neoplastic state through mechanisms such as immune escape? These considerations highlight the need for further studies to delineate the molecular subgroups of MAM and to explore the role of PD-L1 as both a biomarker and a therapeutic target in such a disease, potentially broadening the ever-expanding landscape of lesions treatable with anti-immune checkpoints.

AUTHOR CONTRIBUTIONS

GG: Study design, data interpretation, literature search, writing of the manuscript.

SB: Data interpretation, literature search, writing of the manuscript.

AR: Data interpretation.

CM, MP: Writing and critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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