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Letter to the Editor

Primary diffuse leptomeningeal melanomatosis: A case report of an unusual presentation in a pediatric patient

Yamila Basilotta Marquez, Agustin Ruiz Johnson, Romina Argañaraz, Beatriz Mantese

Department of Neurosurgery, Hospital Prof Juan P. Garrahan, Buenos Aires, Argentina.

E-mail: *Yamila Basilotta Marquez - yamibasilottamarquez@gmail.com; Agustin Ruiz Johnson - agustinrj86@gamil.com; Romina Argañaraz - rominatuki@gmail.com; Beatriz Mantese - mantesebeatriz@gmail.com

***Corresponding author:**
Yamila Basilotta Marquez, Department of Neurosurgery, Hospital Prof Juan P. Garrahan, Buenos Aires, Argentina.

yamibasilottamarquez@gmail.com

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Dear Editor,

Melanocytic tumors that involve the central nervous system may be primary or metastatic. Primary melanocytic tumors of the meninges are extremely rare.[2,15] Malignant melanocyte-derived lesions that diffusely affect the leptomeninges without extracranial metastases are termed primary diffuse leptomeningeal melanomatosis (PDLM).

This type of neoplasm is rare in adults but even more so in children.[1,3] The clinical signs and symptoms are nonspecific and may mimic other disorders. Few patients with this rare and aggressive tumor have been reported in the literature. In this study, we describe the case of a 14-year-old patient diagnosed with PDLM in whom no pigmentation of the meningeal lesion was observed in the biopsy.

CASE REPORT

A 14-year-old female patient with no relevant history of disease presented to the hospital due to several days of headache associated with vomiting and photophobia. Brain computed tomography (CT) without contrast was performed, and no abnormalities were observed. The symptoms persisted, and the patient developed limb paresthesia. Fundoscopy showed bilateral papilledema. Magnetic resonance imaging (MRI) of the brain and spine showed interhemispheric leptomeningeal inflammation with intense contrast enhancement without ventricular enlargement. Lumbar puncture showed elevated cerebrospinal fluid (CSF) pressure. Tuberculous meningitis was suspected, and empirical antitubercular treatment was started. The tumor marker disialoganglioside GD2 was positive on CSF flow cytometry, and therefore, it was decided to perform a biopsy. For the biopsy, an interhemispheric approach with a left frontal craniotomy was used. A wedge specimen was taken from the leptomeninges and brain, and macroscopically, no pigmented area was observed [Figure 1].

Histopathological analysis showed neoplastic proliferation of cells with round nuclei and scant cytoplasm, with focal areas of brownish pigment. Immunohistochemistry was positive for HMB45 and variable for Ki67, which was higher in nests of intracortical tumor infiltration. PDLM was diagnosed.

The patient developed hydrocephalus, and a ventriculoperitoneal shunt was placed. Two shunt revisions were required due to obstruction of the proximal catheter. Temozolomide and

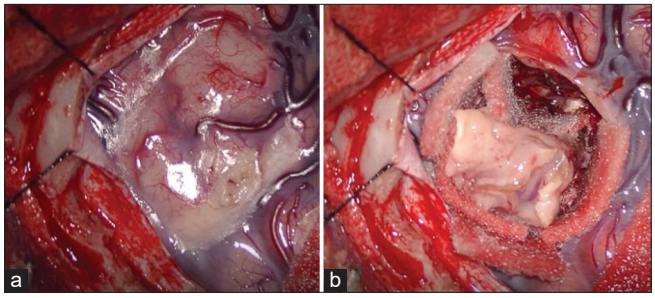

Figure 1: (a) The intraoperative image shows a hypopigmented frontal cortical area from which the sample for pathological anatomy was taken. (b) Image of the wedge segment that was resected.

dexamethasone were given. Subsequently, the patient started with seizures that were difficult to manage. The last brain CT scan revealed more lesions with marked perilesional edema. Due to the impossibility of curative treatment, palliative care was administered. She died four months after diagnosis.

DISCUSSION

The World Health Organization classifies primary leptomeningeal melanocytic neoplasms into circumscribed and diffuse lesions.[4,5] The former group includes melanocytoma (low-grade lesion), intermediate-grade melanocytic tumor, and melanoma (malignant). Melanocytosis, a histologically benign lesion that is often associated with neurocutaneous melanosis, is included among the diffuse lesions.[6,14] The malignant variant is called PDLM and is characterized by diffuse invasion of the leptomeninges by neoplastic cells. In the course of the disease, parenchymal infiltration occurs.[3] PDLM originates from melanocytes, which derive from neural crest cells.[5,11] Very few cases of PDLM in children have been reported in the literature [Table 1].

Our patient presented with nonspecific symptoms, consistent with other reports in the literature. Imaging studies showed an interhemispheric pattern of contrast enhancement with little involvement of the basal cisterns. The initial presumptive diagnosis was tuberculous meningitis since this is an endemic disease in our environment. The presence of hyperintense signals in T1-weighted sequences due to the paramagnetic properties of melanin is helpful in the differential diagnosis.[2] On the other hand, melanin is spontaneously hyperdense on a CT scan, which was not seen in this case.

CSF samples were positive for disialoganglioside GD2, prompting biopsy. This type of sphingolipid is associated with tumor development and malignant phenotype.[9,10] This finding pointed to a neoplastic disease.

At the time of surgery, macroscopic examination did not reveal any pigmented areas. The patient also did not present skin lesions suggestive of a melanocytic cell-derived tumor. As these tumors originate from darkly pigmented cells (melanin),

Table 1: Summary of reported cases of patient under 18 years of age with diffuse malignant melanocytic tumors from 1995 to 2021.

Author	A	G	Symptoms	Location	Differential diagnosis	Surgery	H	Treatment	Survival
Xinke Xu[15]	13	M	Headache and vomiting	Left temporal	Hemorrhage	Gross total resection	No	None	5
Lee HJ[7]	17	M	Headache and vomiting	Right temporal	Hemorrhage and Tuberculous meningitis	Open biopsy	No	Radiotherapy and chemotherapy	Not specified
Kelsey[5]	5	M	Vomiting, weight loss, headache, hemiparesis and seizure	Difusse meningeal	Tuberculosis	Biopsy	No	Dexamethasone and chemotherapy	Not specified
Angelino[1]	2	F	Squint and vomiting	Difusse meningeal	Encephalitis	Spinal biopsy	Yes	Chemotherapy	11
Szathmari[13]	5	F	Headache, vomiting and seizure	Left parietal	Other tumors	Biopsy	Yes	Chemotherapy	10
Baumgartner[3]	14	M	Headache and vomiting	Difusse meningeal spinal and cranial	Hydrocephalus	Open biopsy	No	Chemotherapy	7
Tavana Rad[14]	14	F	Vomiting, diplopia and weakness in lower limbs	Diffuse spinal and cranial	Carcinomatosis and meningitis	Open spinal biopsy	No	None	6

A: Age expressed in years, G: Gender, F: Female, M: Male, H: Hydrocephalus. Survival expressed in months A.

most of them are blackish in appearance. In our case, these features were not evident during surgery; therefore, we believe this may have been a non-pigmented variant.

Given that PDLM may mimic a wide variety of conditions, early diagnosis is important.[4,7] Delayed diagnosis and inappropriate treatment, including tuberculostatic agents, may have a negative impact on survival time. An accurate diagnosis allows for the timely initiation of oncologic therapy and palliative care to treat the symptoms.

Hydrocephalus generally occurs in the late stages of the disease.[4] In this case, we chose to place a ventriculoperitoneal shunt instead of endoscopic treatment as the hydrocephalus was communicating in nature. It should be noted that in these cases, there is a higher risk of shunt obstruction due to the presence of tumoral cells and elevated CSF protein levels. Some authors recommend the use of filters in shunt systems.

The behavior of these tumors is aggressive, and survival is <1 year after diagnosis. Treatments with different drugs and radiotherapy have been tried, but currently, there is no curative therapy.[12,13] Pembrolizumab is a monoclonal antibody against the programmed death cell receptor. It is indicated as adjuvant therapy in adult patients with stage 3 unresectable or metastatic melanoma. It has been tried in adult patients with melanomatosis, and, in one case, disease stability was observed for two years.[8,9]

CONCLUSION

PDLM is a neoplastic disease with a poor prognosis for which no curative treatment has been found so far. Here, we report a pediatric patient with a macroscopically nonpigmented PDLM that presented a poor outcome in spite of medical treatment. We believe that CSF levels of tumor markers such as GD2 may aid in the diagnosis, excluding infections. Further study of this disease is important to improve therapeutic options and thereby prolong survival.

Ethical approval

Not applicable.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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