

LETTER TO THE EDITOR**TO THE EDITOR****Embryonal Tumor with Multilayered Rosettes Presenting with Intermittent Third Nerve Palsy****Keywords:** Tumors, Pediatric neurology, Oculomotor nerve palsy

Embryonal tumors with multilayered rosettes (ETMR) are highly malignant neoplasms of infancy and childhood. They include tumors formerly known as primitive neuroectodermal tumor such as ependymoblastoma, embryonal tumor with abundant neuropil and true rosettes as well as some cases of medulloepithelioma. A hallmark of these neoplasms is their amplification of the *C19MC* cluster on chromosome region 19q13.42. High levels of LIN28A and low levels of OLIG2 are specific for this tumor subtype¹ and may serve as useful biomarkers. We report a case of ETMR presenting with intermittent episodes of oculomotor nerve palsy (OMP).

A 14-month-old girl was referred for intermittent ptosis of the right upper eyelid. The patient had undergone a full-term uncomplicated delivery. Her past medical history was unrevealing and she had met all developmental milestones. Over a period of 2 months, her parents noticed intermittent ptosis of the right upper eyelid. Those episodes lasted for a few seconds to a few minutes and recurred several times daily. A constant increase in frequency was noted over the preceding few weeks. Simultaneous to the ptosis were right eye exotropia and mydriasis, suggesting the diagnosis of intermittent episodes of complete OMP. No trigger zone or synkinesis was identified. There was no visual complaint. Assessment of eye movements revealed limitation of right eye elevation in all fields of gaze, even when ptosis was minimal. Ptosis fluctuated during and in between exams (Figure 1). Examination of the eyes did not reveal any other abnormalities. Central and peripheral visual acuity was preserved in each eye. There was no evidence of other cranial nerve palsies. The rest of the neurological examination did not show any localizing signs such as hemiparesis, ataxia or other cranial neuropathy. To exclude a posterior communicating artery (PCOM) aneurysm, a computed tomography (CT) and computed tomography angiography (CTA) of the head were prescribed but revealed no such anomaly (Figure 2). However, there was a non-enhancing hyperintense lesion emerging from the right pontomesencephalic junction. Magnetic resonance imaging showed extension of the lesion into the interpeduncular fossa. There was again no enhancement but a restriction of diffusion was present (Figure 3). The patient underwent a subtotal resection which led, postoperatively, to a persistent and complete OMP of the right eye. Histopathological and genetic examinations of the specimen were consistent with ETMR with *C19MC* amplification. The cerebral fluid analysis was positive for



Figure 2: CT scan of the head showing a slightly hyperdense space occupying lesion in the pontomesencephalic junction.

malignant cells. She started intensive chemotherapy with weekly intrathecal cytarabine, vorinostat from day 1 to 4, isotretinoid from day 1 to 4, vincristine on day 4, 11, 18, etoposide on day 4, 5, 6, cisplatin on day 4 and cyclophosphamide on day 5, 6. Stem cells were collected since high dose chemotherapy was planned. Unfortunately, after two cycles there was a significant tumor progression with leptomeningeal spread to spine and brainstem. The patient was transitioned to palliative care and died 5 months after diagnosis.

In this report, we describe a case of brainstem ETMR presenting with an intermittent oculomotor palsy. This rare tumoral entity occurs in infancy with a median age of 2.3 years at diagnosis. It shows a slight predilection for girls with a female to male ratio of 1.1 to 1. These neoplasms have a dismal prognosis with a recurrence rate of 91% and a median overall survival of 12 months. Most of them are located supratentorially (70%) rather than infratentorially (30%) with 60% of the latter having a brainstem location.² Clinical presentation is not well described in the literature. Rarely, embryonal tumors have been reported to involve the third cranial nerve³ and one case was treated in our institution (author, personal observation).

Oculomotor nerve palsies are rare in childhood. Congenital OMP is the most common presentation followed by traumatic etiologies. Neoplasms are found in about 10%-20% of cases. The usual clinical course is a steady progression from a partial to a complete palsy. Stepwise progression and temporary improvement can also be seen.⁴ As opposed to their adult counterpart, pupillary involvement is not associated with an increased probability of a compressive etiology.⁵

Intermittent third nerve palsy has seldom been reported in the literature. Case reports describing such a finding point to various etiologies. These include acquired palsies such as PCOM aneurysms, lesions close to the cavernous sinus, idiopathic intracranial hypertension,⁶ schwannomas⁴ and recurrent painful

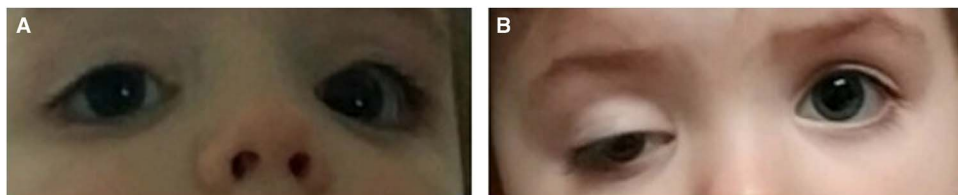


Figure 1: Photographs showing intermittent oculomotor nerve palsy: patient only a few minutes before (a) and after (b), she had one of her episodes of increased right third nerve palsy.

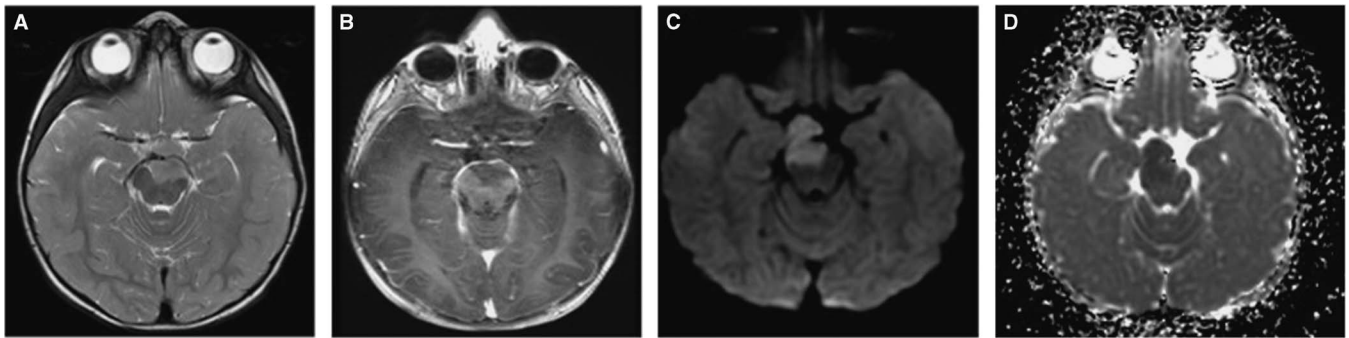


Figure 3: MRI of the pontomesencephalic junction showing the space occupying lesion measuring: $1.5 \times 2 \times 2$ cm in each plane and extending into the interpeduncular fossa. It is isointense to the cerebral cortex in the T2 sequence (A) and has marked restriction diffusion as can be seen by the hyperintense DWI (C) and hypointense ADC map (D). There is no contrast enhancement (B). There is no significant mass effect.

ophthalmologic neuropathy.⁷ The fluctuating symptomatology of these conditions lasted from days to years. We found only one other case with episodic third nerve palsy lasting a few minutes and it was related to a cryptococcal meningitis in an adult patient. No case related to a tumor has been reported in the pediatric population.⁶

This case highlights the fact that a brainstem tumor can cause intermittent OMP, drawing attention to the importance of conducting early neuroimaging.

*Luis André Leal Ferman**
Department of Neurology
Centre Hospitalier Universitaire de Sherbrooke
Sherbrooke, Quebec, Canada

*Patrick Daigle**
Department of Ophthalmology
Centre Hospitalier Universitaire de Sherbrooke
Sherbrooke, Quebec, Canada

Alexander Weil
Department of Surgery, Division of Neurosurgery,
Centre Hospitalier Universitaire Sainte-Justine
Montreal, Quebec, Canada

Benjamin Ellezam
Department of Pathology
Division of Neuro-pathology
Centre Hospitalier Universitaire Sainte-Justine
Montreal, Quebec, Canada

Patrick Hamel
Department of Ophthalmology
Centre Hospitalier Universitaire Sainte-Justine
Montreal, Quebec, Canada

Sébastien Perreault
Department of Pediatrics, Division of Child Neurology
Centre Hospitalier Universitaire Sainte-Justine
Montreal, Quebec, Canada

*Luis André Leal Ferman and Patrick Daigle contributed equally to the manuscript.

Correspondence to: S. Perreault, M.D., M.Sc., FRCSC,
Department of Pediatrics, Division of Child Neurology,
Centre Hospitalier Universitaire Sainte-Justine, 3175
Chemin de la Côte-Sainte-Catherine, Montréal, QC,
Canada, H3T 1C5. Email: s.perreault@umontreal.ca

DISCLOSURES

The authors have nothing to disclose. None of the authors have financial or proprietary interests in any of the material or method mentioned.

STATEMENT OF AUTHORSHIP

LALF and PD are responsible for study concept and design, acquisition of data; AW and BE carried out revision of the manuscript; PH and SP are carried out study supervision, revision of the manuscript.

REFERENCES

1. Ceccom J, Bourdeaut F, Loukh N, et al. Embryonal tumor with multilayered rosettes: diagnostic tools update and review of the literature. *Clin Neuropathol.* 2014;33:15-22.
2. Korshunov A, Ryzhova M, Hovestadt V, et al. Embryonal tumor with abundant neuropil and true rosettes (ETANTR), ependymoblastoma, and medulloepithelioma share molecular similarity and comprise a single clinicopathological entity. *Acta Neuropathol (Berl).* 2014;128:279-89.
3. Ferri Niguez B, Martínez-Lage JF, Almagro MJ, et al. Embryonal tumor with abundant neuropil and true rosettes (ETANTR): a new distinctive variety of pediatric PNET: a case-based update. *Childs Nerv Syst.* 2010;26:1003-8.
4. Shin RK, Mejico LJ, Kawasaki A, et al. Transient ocular motor nerve palsies associated with presumed cranial nerve schwannomas. *J Neuroophthalmol.* 2015;35:139-43.
5. Lyons CJ, Godoy F, ALQahtani E. Cranial nerve palsies in childhood. *Eye Lond Engl.* 2015;29:246-51.
6. Azran MS, Waljee A, Biousse V, et al. Episodic third nerve palsy with cryptococcal meningitis. *Neurology.* 2005;64:759-60.
7. Kim R, Kim J-H, Kim E, et al. Oculomotor nerve tumors masquerading as recurrent painful ophthalmoplegic neuropathy: report of two cases and review of the literature. *Cephalalgia.* 2015; 35:825-30.