



Recurrent Painful Ophthalmoplegic Neuropathy in an 8-Year-Old Boy

Hye Ri Jeon, MD^{1,2}, Young Jun Ko, MD³, Anna Cho, MD², Hunmin Kim, MD²

¹Department of Pediatrics, Seoul National University Children's Hospital, Seoul, Korea

²Department of Pediatrics, Seoul National University Bundang Hospital, Seongnam, Korea

³Department of Pediatrics, Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, Seoul, Korea

Received: September 4, 2024

Revised: September 20, 2024

Accepted: September 22, 2024

Corresponding author:

Young Jun Ko, MD

Department of Pediatrics, Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, 110 Deokan-ro, Gwangmyeong 14353, Korea
Tel: +82-2-2610-6634
Fax: +82-2-2610-6630
E-mail: kjymillennium@cau.ac.kr

Recurrent painful ophthalmoplegic neuropathy (RPON), formerly known as ophthalmoplegic migraine, is diagnosed when a patient experiences at least two episodes characterized by unilateral headache and ipsilateral paresis of the ocular motor nerves [1]. Additionally, RPON is a diagnosis of exclusion, requiring that other disorders, such as inflammatory, vascular, and neoplastic diseases, which may affect the ocular motor nerve, be ruled out first. Thus diagnosing RPON can be challenging, and it is often overlooked. In this report, we describe the case of an 8-year-old boy who presented with ptosis in his right eye accompanied by migraines.

An 8-year-old boy presented to the emergency room with complaints of right-sided ptosis, accompanied by a severe headache and vomiting that had progressively worsened over the previous week. Since the age of three, the patient had experienced headaches three to four times annually, each episode typically accompanied by vomiting. Most of these headache attacks were alleviated with analgesics such as acetaminophen or ibuprofen. However, 4 years prior to this visit, the patient began experiencing more severe headaches and vomiting that were unresponsive to analgesics. Consequently, he was admitted to a local hospital for imaging and pain management. At that time, he exhibited mild exotropia in the right eye but

was discharged a few days later following headache relief and normal magnetic resonance imaging (MRI) results. The mild exotropia in the right eye improved within 1 week of discharge.

The neurological examination revealed no abnormalities in the cranial nerves other than right eyelid ptosis. An ophthalmic examination, including an ice test to rule out myasthenia gravis, yielded normal results. Complete blood tests, serologic tests, and C-reactive protein levels were also within normal limits. While awaiting further evaluation, the patient reported diplopia and a mild restriction in the upward and medial gaze of the right eye. He was admitted for a cerebral spinal fluid (CSF) analysis and brain imaging to investigate potential central nervous system issues. The CSF analysis indicated no pleocytosis and normal protein levels, but showed an increased intracranial pressure (IICP) of 30 cmH₂O. Treatment with mannitol infusion was initiated to manage the IICP. MRI of the brain revealed a 5 mm nodular enhancing lesion at the right crural cistern, raising the possibility of a neurogenic tumor (Fig. 1A). Given his medical history, we reviewed the previous MRI from another hospital taken 4 years earlier. This review confirmed the presence of a nodular, enhancing lesion in the same location (Fig. 1B). Thus, we diagnosed him with ophthalmoplegic migraine and commenced treatment

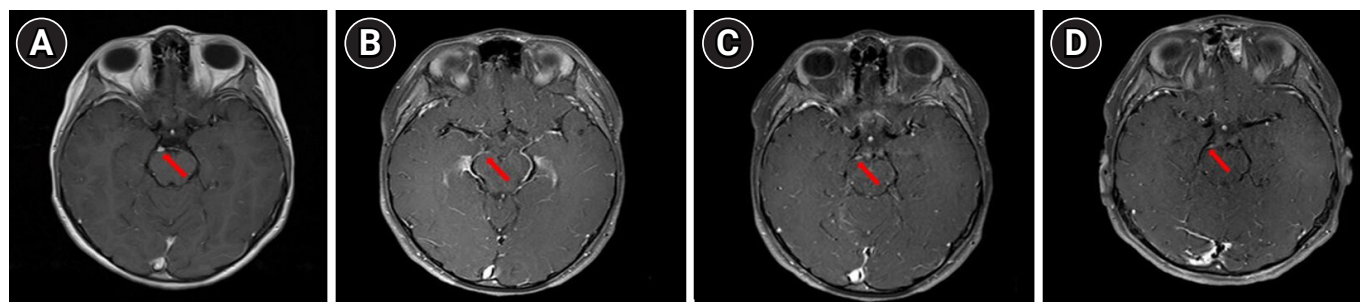


Fig. 1. Axial T1 contrast-enhanced brain magnetic resonance imaging (MRI) features of the patient. (A) Brain MRI performed at the time of the visit, revealing a nodular, enhancing lesion in the cistern segment of the right third nerve (red arrow). (B) A previous MRI examination was performed at another hospital 4 years ago, revealing a nodular, enhancing lesion in the same location (red arrow). (C) Follow-up MRI was performed 3 months after treatment, showing decreases in the intensity and size of the focal enhanced nodular lesion (red arrow). (D) Follow-up MRI at 8 months after treatment, showing further improvement of the lesion (red arrow).

with prednisolone at a dosage of 2 mg/kg/day. In the first 2 days of treatment, his symptoms worsened, showing increased right ptosis, mydriasis, and limited upward and downward gaze, as well as adduction of the right eye. However, his symptoms gradually improved thereafter, and he was discharged on the 8th day with prednisolone. At the outpatient clinic, he continued to recover and was gradually tapered off prednisolone 1 month later. Repeated MRI scans conducted 3 and 8 months post-discharge showed significant reductions in both the intensity and size of the focal enhanced nodular lesion (Fig. 1C and D).

RPON is a rare disorder characterized by paralysis of the third, fourth, or sixth cranial nerves following a headache. The headache may occur up to 14 days before ipsilateral paresis of the ocular motor nerves. Repeated episodes can suggest the diagnosis, which is confirmed by MRI evidence of nerve thickening during an episode [1]. The prevalence of RPON is estimated at approximately 0.7 cases per million [2]. Although most cases begin in childhood, with an average age of onset at 8 years, the early onset of the first attack in infancy or childhood makes RPON challenging to diagnose in this population [3].

RPON is diagnosed by ruling out other disorders, and a diagnosis can only be confirmed when at least two attacks meet the specified criteria. Brain imaging plays a crucial role in excluding structural lesions in the orbital, parasellar, or posterior fossa regions. However, brain imaging alone is insufficient to determine whether the condition is related to metabolic issues, neoplasms, systemic inflammation, or infections. Differentiating neoplastic diseases such as schwannoma, which can be easily mistaken for RPON, is challenging. This is because tissue biopsy, which is highly invasive and often not feasible due to the risk of permanent disability, is the primary method for differentiation [4]. Consequently, lesions that enhance and show progressive growth over time on follow-up imaging may provide better indications of neoplastic diseases [5].

Nevertheless, the clinical practice does not always allow sufficient time to wait for verification of follow-up images, making the patient's medical history crucial for diagnosing RPON. In this instance, the patient was diagnosed with RPON after a thorough review of his medical history and previous MRI scans.

The thickening and enhancement of one or more of the ocular cranial nerves, most commonly the oculomotor nerve, observed in brain imaging, coupled with a history of a previous attack, can aid in diagnosing RPON [6,7]. In most cases of RPON, if symptoms improve, follow-up brain MRI typically shows a reduction or complete resolution of focal enhancement in the cisternal portion of the involved nerve, a finding that is uncommon in schwannoma. In the case of our patient, MRI confirmed a reduction in size following treatment, supporting the diagnosis of RPON.

In most cases of RPON, ophthalmoplegia resulting from cranial nerve palsy tends to improve following the resolution of headache attacks. However, with repeated recurrences, permanent neurological sequelae such as ptosis or exotropia can persist in up to 30% of patients [8]. In such instances, surgical intervention may be necessary. Indeed, in our case, the exotropia did not resolve even after 21 months, leading to the patient undergoing a right rectus muscle resection operation.

In conclusion, we have reported a case of RPON characterized by ptosis and exotropia, followed by a severe headache attack. The diagnosis was challenging due to the similarity of the imaging findings to those of a schwannoma. Treatment options may vary based on the accurate diagnosis. Therefore, it is crucial for clinicians to thoroughly review the patient's medical history when diagnosing RPON.

This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB No. B-2203-742-702). The review board waived the need for informed consent owing to the study's retrospective nature.

Conflicts of interest

Anna Cho is a managing editor of the journal, but she was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

ORCID

Hye Ri Jeon, <https://orcid.org/0009-0001-3685-2497>

Young Jun Ko, <https://orcid.org/0000-0002-1680-720X>

Anna Cho, <https://orcid.org/0000-0001-7500-5955>

Hunmin Kim, <https://orcid.org/0000-0001-6689-3495>

Author contribution

Conceptualization: YJK, AC, and HK. Visualization: HRJ, AC, and HK. Writing - original draft: HRJ and YJK. Writing - review & editing: HRJ and YJK.

References

1. Headache Classification Committee of the International Headache Society (IHS). The International classification of headache disorders, 3rd edition (beta version). *Cephalalgia* 2013;33:629-808.
2. Hansen SL, Borelli-Moller L, Strange P, Nielsen BM, Olesen J. Ophthalmoplegic migraine: diagnostic criteria, incidence of hospitalization and possible etiology. *Acta Neurol Scand* 1990;81:54-60.
3. Gelfand AA, Gelfand JM, Prabakhar P, Goadsby PJ. Ophthalmoplegic "migraine" or recurrent ophthalmoplegic cranial neuropathy: new cases and a systematic review. *J Child Neurol* 2012;27:759-66.
4. Kim R, Kim JH, Kim E, Yang HK, Hwang JM, Kim JS. Oculomotor nerve tumors masquerading as recurrent painful ophthalmoplegic neuropathy: report of two cases and review of the literature. *Cephalalgia* 2015;35:825-30.
5. Yan Y, Zhang B, Lou Z, Liu K, Lou M, Ding M, et al. A case of recurrent painful ophthalmoplegic neuropathy. *Front Neurol* 2020;11:440.
6. Nandana J, Nair SS, Girdhar S, Sundaram S. Recurrent painful ophthalmoplegic neuropathy: a cause for recurrent third nerve palsy in a child. *BMJ Case Rep* 2021;14:e246179.
7. Dhoot R, Sengupta S. Recurrent painful ophthalmoplegic neuropathy with headache and oculomotor palsy 18 years apart. *Headache* 2022;62:1434-6.
8. Ghosh PS. Recurrent right-sided ptosis in a child. Recurrent painful ophthalmoplegic neuropathy. *JAMA Pediatr* 2015;169:693-4.