

## CASE REPORTS

# Recurrent sixth nerve palsy in childhood ophthalmoplegic migraine: A case report

Chaudhry Neera MD DM, Patidar Yogesh MD DM, Puri Vinod MD DM, Geeta A Khwaja MD DM

Department of Neurology, G.B. Pant Hospital, New Delhi, India

### Abstract

Ophthalmoplegic migraine is a rare disorder characterized by childhood onset recurrent attacks of migraineous headaches with paresis of ocular cranial nerves. The third cranial nerve is commonly involved. Involvement of fourth and sixth cranial nerve is uncommon. We present a child with ophthalmoplegic migraine with recurrent sixth cranial nerve palsy on two occasions.

### INTRODUCTION

Migraine is second commonest cause of primary headache after tension-type headache.<sup>1</sup> Migraine can begin at any age, but the initial attack most commonly occurs during adolescence, and the peak prevalence being between ages of 25-45 years. Although migraine is common, migraine with ophthalmoplegia is rare, with an incidence of approximately 0.7 per million.<sup>2</sup> Ophthalmoplegic migraine is commonly seen in pediatric age group and majority of patients are <5 years with a female preponderance.<sup>2,3</sup> The International Classification of Headache Disorders (second edition) (ICHD-II, 2004) defines ophthalmoplegic migraine as recurrent attacks of headache with migrainous characteristics associated with paresis of one or more ocular cranial nerves in the absence of any demonstrable intracranial lesion, other than MRI changes within the affected nerve.<sup>4</sup> Ophthalmoplegia usually involve third cranial nerve. Involvement of fourth, sixth or multiple cranial nerves is rare and occurs more in adults than in children.<sup>5-10</sup>

Here we describe a case of a 13 year old female who presented with two episodes of migraine with ophthalmoplegia, involving the sixth cranial nerve each time.

### CASE REPORT

A 13 year old female presented with a 3 years history of episodic migraineous headaches. Headaches were unilateral, alternating sides left more than right, throbbing in character, moderate to severe in intensity, associated with

nausea, vomiting, photophobia and phonophobia. There was no history of aura. The headaches usually lasted for few hours, and were relieved by analgesics and sleep; and used to occur 2-4 times a month. There was no history of any precipitating factors.

After two and a half year of onset of these headaches she experienced daily left sided, severe headaches of similar character, and within a week of this increasing severity and frequency, developed double vision on looking to her left side. This was accompanied by a reduction in headache severity. She presented to us within 4 days of onset of double vision and on examination had isolated left sixth nerve palsy. She was started on propranolol 40 mg daily. This lead to a decrease in the headache frequency and severity, and the sixth nerve palsy completely recovered over 2-3 weeks. The patient took prophylactic treatment for 6 months and then discontinued it on her own. This was accompanied by an increase in severity and frequency of headaches. The headaches again attained a daily frequency and this time these were predominantly right sided and within a week she also developed double vision on looking to the right side. The double vision was persistent when she presented to us, almost 6 weeks after its onset. There was no history of any other cranial nerve involvement, motor weakness, sensory, cerebellar or systemic involvement. There was no significant past, personal or family history.

Her general examination was normal. Nervous system examination revealed right sided 6<sup>th</sup> nerve palsy (Figure 1a). Fundus examination was normal. Rest of neurological and systemic



Figure 1a,1b. Before and after treatment with prednisolone.

examination was normal. All her routine investigations were normal. Contrast enhanced MRI brain T1 axial and coronal images showed gadolinium enhancing cisternal part of right sixth nerve (Figure 2a,b). CSF opening pressure was not raised. CSF examination showed increased proteins (118 mg%) with normal sugar (55 mg%) and no cells. Her CSF TB PCR and cryptococcal Ag were negative and there were no abnormal cells.

She was started on prednisolone 30mg per day along with propranolol 40mg per day. The ophthalmoplegia completely recovered (Figure 1b) in the following 3 weeks and she remained asymptomatic at a follow up of 6 months.

## DISCUSSION

Ophthalmoplegic migraine was first described by Charcot in 1890.<sup>11</sup> The first headache classification of the International Headache Society (ICHD I, 1988) included ophthalmoplegic migraine in

the classification, as a variant of migraine. It incorporated the criteria first proposed by Walsh and Hoyt that included: a) established history of typical migraine headaches, b) increasing severity of migraine (crescendo migraine) prior to the ophthalmoplegic attack, c) development of recurrent ophthalmoplegia with migraine pain, and d) exclusion of other causes of painful ophthalmoplegia with appropriate investigations, including a normal angiogram.<sup>12</sup>

In the revised International Classification of Headache Disorders (ICHD II, 2004), the syndrome is reclassified under the cranial neuralgias to reflect evolution in thinking about its etiology; however, the migraine appellation was still retained.<sup>4</sup> The ICHD-II defines ophthalmoplegic migraine as at least two attacks characterized by a “migraine-like” headache followed within 4 days by paresis of the third, fourth, and/or sixth cranial nerves, including ophthalmoparesis, ptosis, or mydriasis. Structural causes of painful ophthalmoparesis, such as tumor, infection, and thrombosis, must

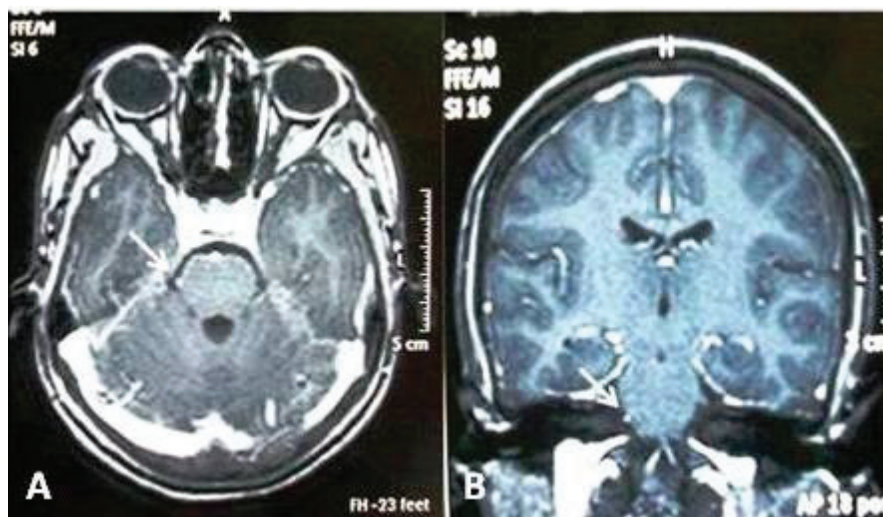


Figure 2a,b. MRI brain contrast T1 axial and coronal images showing enhancing cisternal part of right sixth nerve (arrow).

have been excluded by imaging. There are two explanations given for this shift of classification: firstly the headache often lasts for a week or more and secondly, there is a latent period of up to four days from the onset of headache to the onset of ophthalmoplegia.

The pathophysiology of ophthalmoplegic migraine is not completely understood. With the increasing reports of MRI showing gadolinium uptake in the cisternal part of the affected cranial nerve, it has been suggested that the condition may be a recurrent demyelinating neuropathy.<sup>3,13,14</sup> Although, a post-viral demyelination hypothesis for ophthalmoplegic migraine have been suggested, still there is no clear evidences for the association between viral infection and ophthalmoplegic migraine.<sup>3,13,14</sup> Also, the term “migraine” may be a misnomer as a significant proportion of children do not have characteristic “migraine-like” headaches.<sup>13</sup>

Sixth nerve palsy in children is uncommon. The commonest underlying cause is neoplasm, followed by raised intracranial pressure (non-tumor), trauma, congenital, post inflammatory, and other causes.<sup>15,16</sup> In our patient there was no history of trauma, preceding infection, raised intracranial pressure and the neuroimaging and CSF study excluded these possibilities.

Third cranial nerve is the commonest nerve to be involved in ophthalmoplegic migraine. In the largest recent review of 84 cases of ophthalmoplegic migraine by Gelfand *et al.*<sup>13</sup>, the third cranial nerve was involved in the vast majority of cases (83%), 93% of which were characterized by isolated third nerve involvement. The sixth cranial nerve was involved in 20% of cases (77% of those cases having an isolated sixth). The fourth nerve was only involved in 2% of cases (with only a single case of an isolated fourth nerve deficit) and multiple cranial nerves in 6% of which, the third nerve was involved in all. In this study the patients included were in the age group of 1-74 years. Two-thirds of ophthalmoplegic migraine cases were in females and one-third in males. The site of involvement was evenly distributed between the right and left sides. The interval between headache onset and ophthalmoparesis ranged from immediate to up to 14 days, with a median (interquartile range) of 1.6 days (0.5-3 days). The headache component typically lasted on the order of several days to a week, while the ophthalmoplegia tended to last longer, often on the order of 2-3 weeks to 2-3 months.<sup>3</sup>

In a study of 62 adult patients (> 15 years)

of ophthalmoplegic migraine by Lal *et al.*, sixth nerve was the commonest nerve to be involved (56.5%); followed by third (33.9%), fourth (8.1%) and combined sixth and third nerve involvement (1.6%).<sup>14</sup> They noticed certain differences between childhood and adult ophthalmoplegic migraine. In children it was characterized by severe migraine, recurrent third nerve palsy with pupillary involvement and enhancement on Gd-MRI; while in adults there was severe migraine with single attacks of sixth nerve palsy. The third nerve involvement was less common, was pupillary-sparing and there was lack of enhancement on Gd-MRI. Also, there are many case reports of isolated sixth nerve palsies in adults, but very rare in childhood ophthalmoplegic migraine.<sup>5-10</sup> Our patient, a 13 year old child, had involvement of sixth cranial nerve twice in association with migraine, a rare occurrence to the best of our knowledge.

Recurrent episodes have been noted to have a greater likelihood of 1) longer time for symptom resolution, 2) more severe or pronounced ocular symptoms and 3) resulting in permanent neurological sequelae.<sup>17</sup> In our case also the ophthalmoplegia in the second attack persisted for around 9 weeks. The definitive treatment of ophthalmoplegic migraine is not yet established. Most patients have single attacks that recover completely within days to weeks, but some may have recurrent attacks with persistent neurologic deficits.<sup>3,13,14</sup>

Recently, a few studies reported beneficial effect of steroids in the treatment of acute attack as well as prevention of recurrences.<sup>3,13,14,17,18</sup> We resorted to steroid therapy in the second attack as there had been no spontaneous resolution over 6 weeks, and observed a good persistent response. This probably supports the demyelinating cranial neuropathy hypothesis.

## DISCLOSURE

Conflicts of interest: None

Source of support: None

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