Ocular Dipping in a Patient With Hemiplegic Migraine

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ABSTRACT

A 5-year-old girl presented with acute, rapidly progressive encephalopathy following minor head trauma and was found to have ocular dipping. Her encephalopathy was secondary to a channelopathy caused by a CACNA1A mutation. This is the first reported case of ocular dipping in an encephalopathic child with CACNA1A-confirmed hemiplegic migraine. **[*J Pediatr Ophthalmol Strabismus*. 2018;55:e4-e6.]**

INTRODUCTION

Severe hemiplegic migraine is a rare subtype of migraine with aura associated with a neurologic disturbance, with nystagmus being a frequent neuro-ophthalmic manifestation. A unique case is reported of sporadic hemiplegic migraine with ocular dipping as one of the presenting clinical features during the initial acute attack.

CASE REPORT

A 5-year-old girl presented with acute onset vertigo, right-sided hemiplegia, and altered mental status after a minor fall without loss of consciousness. She was admitted to an outside hospital, where her mental status continued to deteriorate, and she was intubated and placed on mechanical ventilation. There was no preceding illness. She had no medical or ocular history and there was no family history of neurologic or ocular disease.

Extensive infectious and toxic work-up was noncontributory, including negative cerebrospinal fluid studies. Magnetic resonance imaging of the head and spine was without significant abnormalities, but was remarkable for gyral swelling in the left cerebral hemisphere (**Figure 1A**). Electroencephalography showed diffuse cerebral dysfunction and the erythrocyte sedimentation rate was elevated to 120 mm/hr. The patient improved rapidly and was extubated, but her course was complicated by a fever spike during an intravenous immunoglobulin infusion that was administered due to concern for autoimmune encephalitis. She again rapidly deteriorated neurologically and developed status epilepticus that was refractory to multiple medications. The patient was transferred to our facility 10 days after her initial presentation. Magnetic resonance imaging showed worsening of the left-sided gyral swelling and right midline shift (**Figure 1B**), for which a 5-day course of intravenous methylprednisolone was administered.

On ophthalmologic evaluation, afferent function could not be evaluated because the patient was intubated and sedated. Pupils were round and reactive without an afferent pupillary defect and motility was full during an oculocephalic maneuver with intact horizontal eye movements. Continuous but irregular episodes of a slow downward deviation of both eyes followed by a quick return to primary position, consistent with ocular dipping, were observed (**Video 1**, available in the online version of this article). Undilated examination revealed mild pallor of both optic nerves.

A repeat work-up was performed with unclear etiology of her encephalopathy, and included unre-

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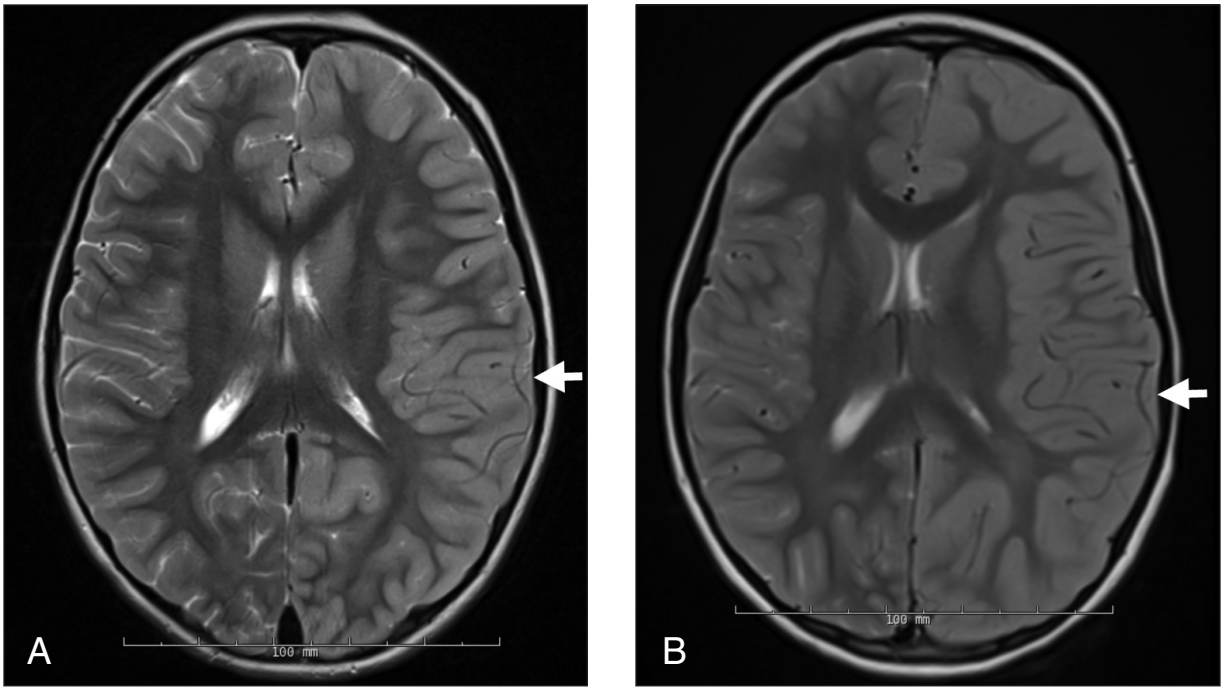

Figure 1. Magnetic resonance imaging (MRI) of the head of the patient at the time of presentation. (A) Axial T2-weighed MRI shows asymmetric diffuse increased T2/FLAIR hyperintensity in the left cerebral hemisphere cortex, with suggestion of mild swelling of the gyri (arrow). (B) Repeat MRI shows interval worsening of the gyral swelling in the left cerebral hemisphere (arrow), with interval increase in mass effect and shift of midline structures.

markable Epstein–Barr virus polymerase chain reaction, *Bartonella*, *Mycoplasma*, herpes simplex virus, human immunodeficiency virus, Lyme IgM/IgG, paraneoplastic panel, thyroid, and cerebrospinal fluid studies (analysis including paraneoplastic panel, N-methyl-D-Aspartate receptor antibody, Epstein–Barr virus, enterovirus, herpes simplex virus, and West Nile IgM testing). Her seizures resolved with therapeutic dosing of valproic acid and lacosamide, the ocular dipping stopped, and she slowly regained consciousness. Verapamil was administered due to suspicion for hemiplegic migraine. Genetic testing was positive for an S218L CACNA1A mutation, confirming the diagnosis of hemiplegic migraine. No family members tested positive for the mutation. The patient continued supportive measures and was discharged to an inpatient rehabilitation facility 1 month after admission, where she regained the use of her right arm and leg, began to walk, and was advanced to a full diet. The patient was discharged home, where she continued to make significant progress. On subsequent follow-up, her expressive language was 85% of baseline.

Repeat ophthalmologic examination showed excellent visual acuities of 20/30 and 20/25 in the right and left eyes, respectively. Motility examination was unremarkable without nystagmus or nystagmoid eye movement, and she was orthophoric on alignment testing.

DISCUSSION

Hemiplegic migraine is a rare subtype of migraine with aura characterized by motor weakness or severe neurologic disturbance that accompanies a migraine headache attack.[1] It can occur with highly variable natural history and clinical manifestations.[2] This can vary from pure hemiplegic migraine to recurrent, severe attacks that occur in a small subset of patients[3] and may include encephalopathy, seizures, fever, cerebellar ataxia, and cerebral edema.[4] Mutations in CACNA1A, which encodes a neuronal calcium channel, have been identified in familial[5] and sporadic[6] cases. The S218L CACNA1A mutation in particular has been described to confer the highest risk for a severe clinical phenotype consisting of acute hemiplegic migraine attack, cerebral edema, and potentially fatal coma after minor head trauma.[7]

To our knowledge, this is the first reported case of ocular dipping described in a patient with the S218L CACNA1A mutation and severe rapidly progressive phenotype during an acute hemiplegic attack. The sequence of slow downward followed

by fast repositioning eye movements and its asynchrony distinguish ocular dipping from vertical nystagmus and would be classified as an ocular oscillation or nystagmoid eye movement. Ocular dipping is thought to be a marker of diffuse rather than focal brain damage and is a non-localizing phenomenon. It is most often seen in patients with anoxic brain injury, encephalitis, status epilepticus, and metabolic encephalopathy. In contrast, ocular bobbing is characterized by a rapid downward movement followed by a slower return to primary position, and horizontal palsies often coexist. Although the exact underlying pathophysiologic mechanism is unclear, ocular bobbing is localized to intrinsic pontine lesions and tends to portend a poor prognosis for neurologic recovery.[8]

Nystagmus is recognized as a frequent neuro-ophthalmic manifestation found in patients with CACNA1A-associated hemiplegic migraine with neurologic signs.[2] Recently, it has been observed that eye movement disorders such as paroxysmal tonic up gaze, abnormal saccades, and nystagmus are common presenting features and early manifestations of CACNA1A mutations in children.[9] Therefore, it has been suggested that eye movement disorders such as ocular motor apraxia or strabismus in infancy may be early presenting features and diagnostic clues for the diagnosis of hemiplegic migraine. Our case is the first to report ocular nystagmoid movements during an acute presentation of hemiplegic migraine attack and suggests that careful ophthalmic examination and recognition of a motility disorder may provide important diagnostic clues.

Evidence from small studies has shown that the calcium channel blocker verapamil is typically used as a first line prophylactic and abortive agent in both familial and sporadic forms of the disease.[10] Management and treatment of severe hemiplegic migraine also often includes hospitalization and close monitoring with supportive measures. Our patient continues to do well with verapamil and close monitoring for recurrence, particularly in the setting of minor injury or head trauma.

REFERENCES

1. Thomsen LL, Olesen J. Sporadic hemiplegic migraine. *Cephalalgia*. 2004;24:1016-1023.
2. Ducros A, Denier C, Joutel A, et al. The clinical spectrum of familial hemiplegic migraine associated with mutations in a neuronal calcium channel. *N Engl J Med*. 2001;345:17-24.
3. Thomsen LL, Eriksen MK, Roemer SF, Andersen I, Olesen J, Russell MB. A population-based study of familial hemiplegic migraine suggests revised diagnostic criteria. *Brain*. 2002;125:1379-1391.
4. Russell MB, Ducros A. Sporadic and familial hemiplegic migraine: pathophysiological mechanisms, clinical characteristics, diagnosis, and management. *Lancet Neurol*. 2011;10:457-470.
5. Ophoff RA, Terwindt GM, Vergouwe MN, et al. Familial hemiplegic migraine and episodic ataxia type-2 are caused by mutations in the Ca2+ channel gene CACNL1A4. *Cell*. 1996;87:543-552.
6. Vahedi K, Denier C, Ducros A, et al. CACNA1A gene de novo mutation causing hemiplegic migraine, coma, and cerebellar atrophy. *Neurology*. 2000;55:1040-1042.
7. Stam AM, Luijckx GL, Poll-Thé BT, et al. Early seizures and cerebral oedema after trivial head trauma associated with the CACNA1A S218L mutation. *J Neurol Neurosurg Psychiatry*. 2009;80:1125-1129.
8. Liu G, Volpe N, Galetta S. *Neuro-ophthalmology: Diagnosis and Management*, 2nd ed. Amsterdam, Netherlands: Elsevier; 2010.
9. Tantsis EM, Gill D, Griffiths L, et al. Eye movement disorders are an early manifestation of CACNA1A mutations in children. *Dev Med Child Neurol*. 2016;58:639-644.
10. Yu W, Horowitz SH. Treatment of sporadic hemiplegic migraine with calcium-channel blocker verapamil. *Neurology*. 2003;60:120-121.