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Sporadic hemiplegic migraine with permanent neurological deficits

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Abstract

By definition, the neurologic impairments of hemiplegic migraine are reversible. However, a few cases of permanent neurologic deficits associated with hemiplegic migraine have been reported. Herein we present the case of a patient with permanent impairments due to hemiplegic migraine despite normalization of associated brain MRI abnormalities. Cases like these suggest the need to consider aggressive prophylactic therapy for patients with recurrent hemiplegic migraine attacks.

Keywords

hemiplegic migraine; migraine; persistent neurologic deficits

Introduction

Hemiplegic migraine (HM), a subtype of migraine with aura, consists of fully reversible motor weakness and at least one other aura symptom [1]. Although neurological impairments may last days to weeks, by definition the impairments are reversible. However, permanent neurological deficits have been previously observed. [2, 3] The case reported herein provides further evidence that permanent neurological deficits may occur in patients with HM, even in the absence of brain infarction.

Case Report

A 22-year-old right-handed woman with sporadic hemiplegic migraine (SHM) was initially evaluated in our headache clinic in February 2013. Her first attack of HM was in 2006 at the age of 15. Between 2006 and 2009, she had recurrent HM attacks approximately 4 times each year. Attacks consisted of severe left-sided headache, photophobia, and hemiplegia with a variable combination of confusion, mixed motor and sensory aphasia, and right hemisensory symptoms, but never with visual aura. In the past, neurologic deficits generally resolved within 2 hours and the headache resolved within 1 day. She had no family history of hemiplegic migraine and genetic testing for the CACNA1A and ATP1A2 mutations were

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The patient described herein provided signed consent for reporting of this case.

negative. Brain magnetic resonance imaging (MRI), head and neck magnetic resonance angiography, and electroencephalography, all performed within two weeks of symptom onset of her first attack were normal. Laboratory investigations in the past showed only a mildly positive antinuclear antibody. A full thrombosis evaluation revealed no evidence of a genetic or acquired coagulopathy. Transthoracic echocardiogram with bubble contrast was normal.

The patient had been treated with several migraine prophylactic medications over the years, all with limited to no benefit: valproic acid 750 mg daily, levetiracetam 1000 mg daily, lamotrigine 50mg daily (developed rash requiring immediate discontinuation), topiramate 175 mg daily, zonisamide 300 mg daily, and coenzyme Q10 300mg daily.

In May 2012, after being deprived of sleep while studying for an examination, she experienced her most severe attack. Symptoms included severe recurrent headaches with photophobia over one week, marked hemiplegia, hemisensory loss and cognitive dysfunction for 4 weeks, and severe aphasia lasting 6 weeks. The initial brain MRI, completed within 24 hours of symptom onset, was normal. Repeat brain MRI performed 10 days after the onset of symptoms showed increased signal of the entire cortical ribbon over the left hemisphere on FLAIR and restricted diffusion within the same distribution on DWI sequences. A follow-up MRI, performed 5 months after onset of symptoms, was essentially normal. (see Figure 1)

Despite normalization of brain MRI abnormalities, the patient reported persistent language impairment, right side hemianesthesia and memory deficits when she was evaluated in our clinic 9 months after initial onset of her severe HM attack. Neurological examination revealed sensory loss to light touch and temperature involving the right face, arm, leg, and trunk, splitting the midline. Severe deficits in vibration and loss of proprioception were present up to the right elbow and right hip. Tendon stretch reflexes were symmetric. Cognitive evaluation showed impairments in immediate memory, delayed recall, and calculation. Speech and language examinations were normal. Because of her ongoing cognitive and subjective receptive language impairment and slowed information processing, she has been unable to resume her university studies.

The final diagnosis was SHM with persistent neurologic deficits. Treatment with acetazolamide was initiated.

Discussion

SHM is a subtype of HM characterized by episodes of gradual progression of hemiparesis and at least one other neurological symptom/sign, in the absence of a first-degree relative with similar attacks. Although according to formal diagnostic criteria neurologic symptoms are fully reversible within 24 hours, many cases have been reported in which neurological deficits last up to several weeks. [1–2, 4–5] A few reports have illustrated irreversible neurological deficits. [3, 6] The main two types of permanent deficit described include cerebellar signs and cognitive deficits. [7] In this case, the patient had persistent cognitive deficits, but no cerebellar signs such as nystagmus, ataxia and dysarthria. This patient also

had severe and persistent hemisensory deficits in all domains, including proprioception. Although sensory symptoms are common during attacks of HM, such deficits are typically reversible. [7–8]

The pathophysiological mechanisms of HM are unclear. Cortical spreading depression (CSD) is considered to play an important role in the aura symptoms of HM. [9–10] Mutations in the ion transportation genes CACNA1A, ATP1A2, and SCN1A can cause FHM. [7, 11–12] As a result of these mutations, there is altered membrane polarity, a lowered threshold for depolarization, and neuronal and/or glial excitability. [13] These ionic channelopathies result in a large and sustained depolarization-induced rise in extracellular synaptic glutamate through increased release and/or reduced removal or reuptake. A sustained and excessive rise in synaptic glutamate may result in neuronal death as a result of excitotoxicity. [7, 14]

After 7 years of recurrent HM attacks our patient developed persistent cognitive and sensory impairments following her most severe HM attack. There was no evidence of cerebral infarction and no evidence of cerebellar atrophy, the latter of which has been previously reported in patients with HM. [15] Glucose hypometabolism and cerebral hypoperfusion have been reported in patients with HM. [3, 6, 9–10] However, fluorodeoxyglucose positron emission tomography, single photon emission computed tomography, and perfusion studies were not performed in the evaluation of this patient. Nonetheless, the patient's persistent symptoms and continued abnormalities on neurologic examination suggest that irreversible neuronal damage accounts for the persistent symptoms.

In patients with HM, the changes on MRI during the attack can be dramatic. Most reports state that images become normal when neurological deficits resolve. [2, 4–5] A few reports have illustrated irreversible brain damage. [3, 6] In this case, the FLAIR sequences and DWI sequences showed changes consistent with cortical edema of the left hemisphere.

This case provides further evidence that HM may be associated with persistent neurological deficits in the absence of cerebral infarction. Thus, unlike the typical recommendations guiding the use of migraine prophylactic treatment for those with migraine with or without aura, a more aggressive approach to the use of prophylactic medications in patients with ongoing attacks of HM, regardless of attack frequency, may be recommended.

References

1. The International Classification of Headache Disorders 2nd edition. Cephalalgia. 2004; 24(Suppl 1): 1–160.
2. Oberndorfer S, Wober C, Nasel C, et al. Familial hemiplegic migraine: follow-up findings of diffusion-weighted magnetic resonance imaging (MRI), perfusion-MRI and [99mTc] HMPAO-SPECT in a patient with prolonged hemiplegic aura. Cephalalgia. 2004; 24:533–539. [PubMed: 15196295]
3. Dodick D, Roarke M. Familial hemiplegic migraine: permanent attack-related neurologic deficits. Headache. 2007; 47:1210–1212. [PubMed: 17883529]
4. Lindahl AJ, Allder S, Jefferson D, et al. Prolonged hemiplegic migraine associated with unilateral hyperperfusion on perfusion weighted magnetic resonance imaging. J Neurol Neurosurg Psychiatry. 2002; 73:202–203. [PubMed: 12122185]

5. Chakravarty A, Sen A. Sporadic hemiplegic migraine in children: a report of two new cases. *Neurol India*. 2010; 58:648–650. [PubMed: 20739815]
6. Hayashi R, Tachikawa H, Watanabe R, et al. Familial hemiplegic migraine with irreversible brain damage. *Intern Med*. 1998; 37:166–168. [PubMed: 9550598]
7. Dichgans M, Freilinger T, Eckstein G, et al. Mutation in the neuronal voltage-gated sodium channel SCN1A in familial hemiplegic migraine. *Lancet*. 2005; 366:371–377. [PubMed: 16054936]
8. Gardner K, Barmada MM, Ptacek LJ, Hoffman EP. A new locus for hemiplegic migraine maps to chromosome 1q31. *Neurology*. 1997; 49:1231–1238. [PubMed: 9371899]
9. Pelzer N, Stam AH, Haan J, et al. Familial and sporadic hemiplegic migraine: diagnosis and treatment. *Curr Treat Options Neurol*. 2013; 15:13–27. [PubMed: 23203776]
10. Russell MB, Ducros A. Sporadic and familial hemiplegic migraine: pathophysiological mechanisms, clinical characteristics, diagnosis and management. *Lancet Neurol*. 2011; 10:457–470. [PubMed: 21458376]
11. 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. [PubMed: 8898206]
12. De Fusco M, Marconi R, Silvestri L, et al. Haploinsufficiency of ATP1A2 encoding the Na⁺/K⁺ pump alpha2 subunit associated with familial hemiplegic migraine type 2. *Nat Genet*. 2003; 33:192–196. [PubMed: 12539047]
13. Moskowitz MA, Bolay H, Dalkara T. Deciphering migraine mechanisms: clues from familial hemiplegic migraine genotypes. *Ann Neurol*. 2004; 55:276–280. [PubMed: 14755732]
14. Whetsell WO Jr, Shapira NA. Neuroexcitation, excitotoxicity and human neurological disease. *Lab Invest*. 1993; 68:372–387. [PubMed: 8479146]
15. Vincent M, Hadjikhani N. The cerebellum and migraine. *Headache*. 2007; 47:820–833. [PubMed: 17578530]

Figure 1.

Brain MRI performed 10 days after symptom onset showed restricted diffusion within the entire cortical ribbon over the left hemisphere on DWI sequences (A) and increased signal within the same distribution on FLAIR (C). No abnormality was definitively seen on ADC maps (B and E), possibly due to the low resolution of ADC sequences or to the likelihood that the abnormal signal on diffusion and FLAIR sequences is not related to ischemia. A

follow-up MRI, performed 5 months after symptom onset, showed normalization of the DWI (D) and FLAIR (F) sequences.