Child Neurology: Migraine with aura in children

ABSTRACT

The differential diagnosis for an acute hemiparesis in a child includes stroke, Todd paralysis, and hemiplegic migraine. In the context of an illustrative case, this review highlights the differences in clinical presentation among these entities and an approach to the diagnostic workup. Migraine with aura in children is reviewed, including migraine equivalents such as abdominal migraine and the particular presentation of hemiplegic migraine. An approach to the prophylactic and acute treatment for children with migraine with aura is offered. Neurology® 2010;75:e16–e19

CASE: PART 1

A 14-year-old boy with Crohn disease was admitted for a presumed flare. On the second hospital day, his abdominal pain acutely increased. Shortly thereafter, he experienced tingling starting in his shoulder and spreading over his left hemibody over 10 seconds. This was accompanied by 7/10 pounding left-sided head pain. Several minutes later, the tingling gave way to diminished sensation and weakness on the left. These symptoms persisted into the next morning, at which time a neurologic consultation was requested.

Now 20 hours into the attack, he had 5/10 pounding head pain. Neurologic examination revealed a left hemiparesis in a pyramidal distribution, with face and arm affected more than leg. Sensation was also diminished over the left face and hemibody. Reflexes were normal and there was no neglect. Complete blood count, electrolytes, erythrocyte sedimentation rate, liver function tests, lactate, amylase, and lipase were normal.

Differential diagnosis. The differential diagnosis for acute onset hemiparesis in a child includes stroke, Todd paralysis, and migraine with aura, specifically hemiplegic migraine. Demyelinating disease, brain tumor, and metabolic disturbances such as hypoglycemia or hypocalcemia should also be considered.

Patients with inflammatory bowel disease are often hypercoagulable, increasing their risk of ischemic stroke.1 Positive symptoms such as tingling are more suggestive of migraine, while stroke is classically associated with negative symptoms. However, children with ischemic and hemorrhagic stroke can complain of tingling paresthesias.

In this case, there was no witnessed seizure activity or change in mental status. Postictal paralysis is also usually not so prolonged. In a study of adults in an epilepsy monitoring unit, Todd paresis resolved within 22 minutes,2 though in one pediatric case report it lasted 24 hours.3

Migraine with prolonged aura would be a diagnosis of exclusion given this was his first presentation, and that children often complain of headache at the ictus of both hemorrhagic and ischemic strokes.4

Recommended workup. Additional history important to elicit includes whether there is a family history of epilepsy, migraine, or hypercoagulability. The presence of migraine markers, such as motion sickness and ice cream headache (throbbing head pain when eating something cold),5 should also be sought.

Given that migraine with prolonged aura is difficult to differentiate from acute stroke, on first presentation these patients should be imaged with MRI and intracranial magnetic resonance angiography to rule out ischemia. Imaging also rules out vasculitis or moyamoya disease, which may present with headache with a migrainous phenotype, probably as a comorbid activation of the patient’s underlying tendency to migraine.

CASE: PART 2

MRI with diffusion-weighted imaging, which is highly sensitive for acute infarction, was normal. Magnetic resonance angiography and venography were also normal. By 26 hours after symptom
onset, the patient’s weakness began improving, and by the next morning his neurologic examination was normal.

Further history revealed that the patient experienced monthly headaches which were unilateral, throbbing, and partially relieved by acetaminophen. His mother and older sister had frequent severe headaches, though neither experienced aura. The patient had not experienced aura symptoms with his previous headaches or episodes of abdominal pain.

He did experience motion sickness and frequent abdominal pain and vomiting as a young child. He did not get ice cream headache.

Review of the patient’s records revealed that the diagnosis of Crohn disease was purely clinical—he had never had biopsy-proven pathology. He had never experienced bloody or mucous-covered stools, extraintestinal manifestations of Crohn disease, or highly elevated inflammatory makers. His abdominal pain came on more with stress and with nitrite-containing foods, both known migraine triggers. Often the episodes of abdominal pain lasted only 1–2 hours.

A repeat endoscopy and intestinal biopsies were negative for evidence of Crohn disease, raising significant doubts about this diagnosis. His gastrointestinal symptoms were considered to most likely be due to abdominal migraines.

MIGRAINE WITH AURA IN CHILDREN Migraine is common in children. The prevalence is 3% in children aged 3-7 years, 4%–11% in those 7–11 years, and 8%–23% in teenagers. One quarter of patients with migraine experience aura. Auras are thought to be based on cortical spreading depression; a wave of depolarization followed by hyperpolarization spreads across the cortex, precipitating neurologic dysfunction. Prognostically, 50%–60% of adolescents with migraine with aura are still symptomatic at 5- to 7-year follow-up.

In migraine with typical aura, visual, sensory, or dysphasic symptoms develop over 5–20 minutes, and resolve within 60 minutes. Headache typically occurs with the aura, or follows within 60 minutes. The headache may be ipsilateral or contralateral to the aura symptoms, usually contralateral. Visual auras are most common, followed by sensory, then language. Motor aura is least common and is a defining feature of hemiplegic migraine.

This patient’s hemisensory tingling was most likely a typical aura, even though it came on quickly. The slow, spreading quality of migraine aura is often helpful in distinguishing it from ischemic deficits, which tend to be maximal at onset. Neurologic deficits from aura usually resolve within 20–60 minutes, though this is also often the case in transient ischemic attacks. In migraine aura, positive symptoms such as tingling are often followed minutes later by negative symptoms, as they were in this case when the tingling gave way to diminished sensation. A migratory pattern, or so-called Jacksonian march, can also be seen in seizure.

Migraine with prolonged aura. Aura in migraine is considered prolonged if it lasts more than 1 hour but less than 7 days, with longer aura termed persistent aura. Most patients experience prolonged aura in only a minority of attacks, often experiencing typical length aura with other attacks.

Adult patients with migraine with aura are at greater stroke risk than controls, although the absolute risk remains small, estimated in one study at 12.4 ischemic strokes per 10,000 women per year. It is not known whether prolonged aura carries a greater risk for vascular events than typical aura.

Hemiplegic migraine. Hemiplegic migraine can be familial or sporadic. The familial form may be due to mutations in voltage-gated channels CACNA1A and SCN1A or the Na+/K+ pump ATP1A2 gene. The etiology of the sporadic form, which this patient had, is less clear, although some patients have mutations in the same genes.

The motor aura of hemiplegic migraine is unique. There is no biphasic symptom progression, specifically no jerking before the onset of weakness. While most attacks come on over minutes, 7% of patients experience onset of weakness in under 1 minute, as this patient did. The weakness is twice as likely to affect the arm as the leg. Duration can be hours to days, though most still resolve within an hour. Most patients also experience typical aura symptoms during an attack, usually sensory, as this patient did. The hemiplegia is almost always accompanied by head pain, unlike other auras (e.g., visual), which can occur without headache. The pathophysiology of motor aura is now being explored with mouse models as the genes have been identified. Some have hypothesized that the aura in hemiplegic migraine is from vasospasm, not cortical spreading depression. However, there is no evidence for this or for increased stroke risk over other migraines with aura.

Abdominal migraine. Abdominal migraine is one of several childhood migraine equivalents. These syndromes are thought to be developmental manifestations of genes that in adulthood will be expressed as migraine headache. An example of this potential is that benign torticollis of childhood can be linked to the familial hemiplegic migraine gene CACNA1A. Children with migraine equivalents make up an estimated 10% of all migraineurs referred to pediatric
neurology clinics. Three migraine equivalent syndromes are recognized in International Classification of Headache Disorders–II: cyclical vomiting, abdominal migraine, and benign paroxysmal vertigo of childhood. Several others are proposed: benign paroxysmal torticollis of infancy, acephalgic migraine, and acute confusional migraine.

Abdominal migraine presents in school-aged children as periumbilical or midline dull abdominal pain that lasts 1 to 72 hours. There may be associated anorexia, nausea, vomiting, or pallor. There is usually a family history of migraine, and about 70% of children also have typical migraines, although it may be several years before these emerge.

**TREATMENT OF MIGRAINE WITH AURA IN CHILDREN**

### Treatments

**Prophylaxis.** The decision of when prophylaxis is indicated can only be made in conjunction with the family or caregivers. Even relatively infrequent migraines may merit daily treatment if they are frightening to the child, or likely to trigger repeated unnecessary imaging studies, such as in hemiplegic migraine. In fact, the US Headache Consortium recommends prophylactic therapy for those whose migraines are accompanied by hemiplegia or prolonged aura. Preventive migraine therapies in children and adolescents were recently reviewed; this discussion focuses specifically on treatment of migraine with aura.

There is no proven treatment for migraine with aura. In a survey of adult headache specialists, 55% thought verapamil was most effective, while 18% preferred valproate. Flunarizine is widely used in the United Kingdom and particularly effective in children with hemiplegic migraine. Verapamil may also be effective for hemiplegic migraine. Lamotrigine for aura in general, and divalproex for persistent aura. One open-label study with ketamine suggests that the development of suitable agents with actions at excitatory glutamate receptors may be one way forward. Many headache specialists avoid beta-blockers in patients with prolonged aura out of concern that they may limit compensatory vasodilation, although this is more a theoretical concern.

The best prophylactic therapy for migraine with aura remains to be established, and on the individual level often requires trial and error. Calcium-channel blockers are a reasonable first choice. Given the often cyclical nature of migraine, the duration of prophylactic therapy need not be interminable. One approach is to treat for the duration of the school year and wean over the summer.

### Acute therapies

With present knowledge, acute aura itself is not treatable. Treatment should therefore focus on the head pain. Acetaminophen and nonsteroidal anti-inflammatory drugs are first-line agents. Almotriptan is approved by the Food and Drug Administration for acute migraine therapy in adolescents. Several other triptans have been studied in adolescents and children and used off-label, notably nasal spray sumatriptan. In case reports, IV verapamil seems effective for acute hemiplegic migraine. Triptans are contraindicated in hemiplegic migraine because it was wrongly considered when they were developed that vasospasm was an important part of migraine aura, and there are thus insufficient systematic data upon which to base any other recommendation.

**CASE CONCLUSION** On follow-up 7 weeks later, the patient reported no further episodes of abdominal pain or headache. Given the current infrequency of his symptoms, he and his parents did not desire prophylaxis. The decision was made to treat acute episodes with naproxen. If his migraines become more frequent, he will start verapamil.

**DISCLOSURE**

Dr. Gelfand serves on the Resident & Fellow Editorial Team for Neurology®. Dr. Fullerton serves on the DSMB for Berlin Heart; serves on the editorial board of Pediatric Neurology; receives research support from the NIH (NINDS R01 NS062820 A2 [contact PI] and NINDS K02 NS053883 [PI]) and the American Heart Association; and has provided expert testimony in legal proceedings regarding children with stroke. Dr. Goadsby has served as a consultant for or served on a scientific advisory board for Advanced Bionics, Allergan, Inc., Almirall, Amgen, ATI, AstraZeneca, Belgian Research Council, Boehringer Ingelheim, Bristol-Myers Squibb, Boston Scientific, CoLucid Pharmaceuticals, Cotherex Medical, Inc., Eli Lilly & Company, Fidelity Foundation, GlaxoSmithKline, Johnson & Johnson, Kalypsys Inc., Medtronic, Inc., MAP Pharmaceuticals, Inc., Migraine Research Foundation, Migraine Trust, Minster Pharmaceuticals, Johnson, Kalypsys Inc., Medtronic, Inc., MAP Pharmaceuticals, Inc., Migraine Research Foundation, Migraine Trust, Minster Pharmaceuticals plc, Medical Research Council-UK, Merck & Co., Inc., the NIH/NINDS (consultant), Netherlands Research Council, Neuralieve, NeurAson Inc., NeuroTherapeutics Pharma, Organisation for Understanding Cluster Headache–UK and US, and Pfizer Inc.; serves on the editorial board of Cephalalgia; receives royalties from the publication of Mechanism and Management of Headache, 7th ed. (Elsevier, 2005); and has received research support from GlaxoSmithKline, Neuralieve, Merck & Co., Inc., Johnson & Johnson, and MAP Pharmaceuticals, Inc.

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**REFERENCES**

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