

# Acute Confusional Migraine in an Adolescent: Response to Intravenous Valproate

## abstract

Acute confusional migraine (ACM) is a dramatic, rare manifestation of migraine described mostly for children and adolescents. There are few data on the treatment of an ACM attack. Prochlorperazine has been suggested as an effective drug. The authors of some reports have suggested that valproic acid may play a role in the prevention of ACM and as treatment for acute migraine headache in the adult population. However, this medication has not been reported as first-line, acute therapy for ACM. We report here the case of a 12-year-old girl who presented with an ACM attack that resolved rapidly after intravenous administration of valproic acid. *Pediatrics* 2010;125:e956–e959

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### KEY WORDS

confusional migraine, treatment, valproate

### ABBREVIATIONS

ACM—acute confusional migraine

VPA—valproic acid

EEG—electroencephalogram

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Acute confusional migraine (ACM) is 1 of several migraine equivalents recognized in pediatric patients.<sup>1</sup> The treatment of childhood migraine episodes (ie, acute headache attacks) is still controversial because of the little evidence available in the literature regarding safety and efficacy of migraine medications in this population. There have been even fewer reports in the literature regarding the treatment of ACM. Valproic acid (VPA) is well established as a preventive therapy and as acute treatment in adults.<sup>2-4</sup> In children, VPA seems to be an effective prophylactic agent for migraine attacks.<sup>5</sup> It was also reported to prevent recurrent ACM attacks in a 10-year-old girl.<sup>6</sup> We describe here the case of a teen-aged girl whose symptoms resolved after intravenous administration of VPA during an ACM attack.

## CASE REPORT

A 12-year-old girl presented to the emergency department with acute-onset confusion. Approximately 1 hour before arriving to the emergency department she complained of bilateral blurriness of her lower visual field, frontal headaches, and paresthesiae of her left arm and face. Within minutes, she was found by her mother in a confusional state, unable to comprehend simple commands. Her speech was slurred. The patient was brought by her parents to the emergency department.

On arrival, she had no fever or evidence of an acute intercurrent disease. There was no history of trauma. Five days before her admission she received diphtheria and tetanus toxoid vaccine (booster). She had no personal history of headaches. A few weeks earlier, the patient complained of abdominal pain and was diagnosed with lactose intolerance by a breath hydrogen test. Her mother had a his-

tory of migraine attacks, often with transient visual disturbances.

On physical examination, the girl was awake but confused. Her body temperature was 36°C, respiratory rate was 16 breaths per minute, blood pressure was 124/74 mm Hg, and heart rate was 130 beats per minute. She had no meningeal signs or signs of trauma. The general physical examination was normal. She was confused and irritable. Her speech was unclear, and she could not understand simple commands or perform simple tasks. Visual field examination appeared normal to confrontation, except for a questionable defect in the upper quadrants. Results of funduscopy were normal. Within the limits of an uncooperative examination there were no motor, sensory, or coordination deficits noted. Deep tendon reflex examination was normal.

Results of a full blood count with differential and testing of serum glucose, serum urea nitrogen, and aminotransferase levels and prothrombin and thrombin time were normal. Results of a urine toxin screen and urine  $\beta$  human chorionic gonadotropin test were negative. An electroencephalogram (EEG), performed 2 hours after confusion onset, showed diffused slowing in the form of high-amplitude  $\delta$  activity, more prominent on the left hemisphere. The possibility of an epileptic event (complex partial seizure) was considered, and intravenous midazolam (4 mg) was administered, followed by the appearance of diffuse fast ( $\beta$ ) activity, more obvious over the right hemisphere, also suggestive of left hemisphere dysfunction. However, sleep EEG patterns were symmetric. No clinical improvement occurred.

At this time, the differential diagnosis included ACM, acute subdural hematoma, intracranial lesion, toxic exposure, postictal confusion, and meningoen- cephalitis. A computed tomography scan was performed 3 hours after the onset

of confusion under a dose of 2.5 mg/kg propofol and 2 mg of midazolam intravenously and revealed no abnormality. Lumbar puncture showed normal glucose and protein levels and no white cells. At this stage, the child partially awoke and was still confused. ACM was considered the most likely diagnosis. Intravenous valproate was administered at a loading dose of 20 mg/kg 3 hours and 45 minutes after the onset of confusion. She also received 2 doses of intravenous acyclovir (10 mg/kg per dose) pending cerebrospinal fluid analysis to rule out herpes encephalitis.

Within 30 minutes of receiving the intravenous VPA, the girl recovered fully, showing no further signs of confusion. She remained asymptomatic and was discharged within 24 hours without any further treatment. At a follow-up visit 1 month later she remained asymptomatic. Results of a repeat EEG 3 months after the event was normal. Her family reported no further attacks or headache episodes when contacted by telephone 18 months after the ACM episode.

## DISCUSSION

Migraine is common in the pediatric population. Its incidence ranges from 3% to 11% during childhood to 8% to 23% during adolescence. Before puberty, there is a mild male predominance, shifting to female predominance after adolescence.<sup>7</sup> ACM is 1 of 5 migraine equivalents that have been recognized in children. The other migraine equivalents are benign paroxysmal torticollis, benign paroxysmal vertigo, abdominal migraine, cyclic vomiting, and acephalgic migraine.<sup>1</sup> ACM is a rare manifestation of migraine that occurs in 0.04% of pediatric migraine series. The male/female ratio is 3:1 to 11:2. Most patients are in the 5- to 16-year age group. The majority (77%–100%) of them have a family

history of migraine, and 20% to 53% have a personal history of migraine.<sup>1,8</sup>

ACM presents as a sudden confusional state, usually accompanied by agitation, visual symptoms, dysarthria, and memory disturbance. In most cases, headache precedes or follows the attack. The attack lasts 30 minutes to 24 hours. Head trauma has been recognized as a strong predisposing factor.<sup>8,9</sup> Physical examination is normal in virtually all cases. Encephalitis, meningitis, metabolic changes, brain lesions, toxic exposure, and seizures are important differential diagnoses.<sup>8,10</sup> Given the frequent association between migraine and occipital epilepsy, it is possible that some cases of ACM actually represent ictal (epileptic) confusion.<sup>11</sup> Therefore, ACM remains a diagnosis of exclusion.

The typical EEG pattern of ACM is diffuse slowing in the  $\delta$  range, with no evidence of epileptiform activity. Within 1 to 3 days, the EEG returns to normal.<sup>12</sup> Magnetic resonance angiography in the case of a 10-year-old girl showed narrowing of the left middle and posterior cerebral artery during the ACM attack.<sup>6</sup> Moreover, a 7-year-old boy showed decreased cerebral blood flow in the left posterior splenium region on computed tomography with *N*-isopropyl[<sup>123</sup>I]-*p*-iodoamphetamine (IMP-SPECT) performed during the attack.<sup>15</sup> It is interesting to note that our patient's EEG

revealed more severe involvement of the left hemisphere.

The treatment of acute migraine headaches in pediatrics is controversial because there have not been many controlled trials performed in this population. Among agents that have shown efficacy and safety in controlled trials are nonsteroidal anti-inflammatory drugs, acetaminophen, triptans, and dopamine antagonists.<sup>7,14</sup>

VPA is commonly prescribed for epilepsy. It is also used for mood disorders, chronic migraine, and neuropathic pain.<sup>15</sup> Its mechanism of action has not been completely established. Among the suggested effects are increased  $\gamma$ -aminobutyric acid levels, sodium and calcium channel blocking, and a central catecholaminergic effect. VPA has also been shown to be effective in the treatment of acute migraine headaches in the adult population.<sup>3,4</sup> Moreover, VPA has effectively reduced migrainous pain and reversed EEG migrainous pattern in glyceryl trinitrate-induced migraine attacks.<sup>16</sup>

There have been few reports in the literature regarding the treatment of ACM. Indeed, only 2 case reports concerning pediatric patients have been published. A 10-year-old girl with recurrent ACM responded to VPA as preventive treatment of further attacks.<sup>6</sup> The other report pertained to cases of 2 patients with ACM that re-

sponded to prochlorperazine.<sup>17</sup> VPA has also been shown to be effective in an adult patient with cyclic vomiting, which supports its use for migraine equivalents.<sup>18</sup>

We report here the case of a 12-year-old girl with a first episode of ACM that was responsive to VPA during the acute confusional phase. Her EEG findings indicated acute encephalopathy, concurring to previously reports. It should be noted that her left hemisphere appeared to be more affected, in concordance with former individual case reports showing evidence of left circulation involvement.<sup>6,13</sup> After the administration of VPA, our patient's symptoms resolved quickly and did not recur. A repeat EEG a few weeks after the attack was normal. She has not experienced further attacks or migraine headaches during the 18 months after the event.

In the pediatric population, VPA has only been shown in previous research to be effective for migraine prevention, whereas trials in adults have addressed both its prophylactic properties and its efficacy in acute migraine headaches. There are scarce reports regarding the pharmacologic treatment of ACM. Our patient responded quickly to intravenous VPA, with prompt resolution of the confusion. Hence, the role of VPA in ACM should be explored further.

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