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Headache With Right Upper Extremity Weakness and Dysphasia in an Adolescent

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A l0-year-old boy was brought to the emergency department (ED) for evaluation of headache, garbled speech, and right upper extremity weakness. One half hour prior to arrival the family had been at a shopping mall when the boy had suddenly grabbed his head, cried out that he had a terrible headache, and sank to the floor without striking his head. There was a questionable momentary loss of consciousness, but no motor activity or urinary incontinence. Immediately afterwards the parents noted that the boy was not using his right arm. He had two episodes of forceful, projectile vomiting. Parents noted that they could not understand his speech. The parents immediately transported him to the hospital.

The patient had no past medical history except for a heart murmur echocardiographically proven to be due to a bicuspid aortic valve. There was no history of trauma, headaches, or drug use. There was no significant family history.

On initial ED evaluation the patient appeared alert and in moderate distress, holding his forehead in his left hand. Vital signs were blood pressure 116/76, pulse 120, respiratory rate 18, oral temperature 97.6° C, and his skin was cool and dry. On physical examination there was no sign of trauma, pupils were equal and reactive to light, fundi had sharp disk margins, and the neck was supple and nontender. Cardiac examination revealed a I/VI systolic ejection

murmur, and the lungs were clear. The abdomen was soft, and there were no lesions on the skin. On neurologic examination, cranial nerves II -XII were intact. Motor examination showed 5/5 strength in all muscles on the left side and the right leg, but there was 0/5 strength in all the muscles groups in the right upper extremity. Deep tendon reflexes were +2 and symmetrical; toes were downgoing. Sensation was intact (localized and withdrew from pin prick) There were no meningeal signs.

The patient could understand and carry out three-step commands, however he had difficulty with naming and repetition.

The patient was placed in a semiprone position with his head elevated at 45 degrees, and airway management equipment was readied at the bedside. He was placed on oxygen and an ECG monitor showed normal sinus rhythm. An 18-gauge intravenous line of 5% dextrose in 0.45% normal saline was placed in the left antecubital vein; when the intravenous line was started, blood was obtained for a bedside glucose determination, which registered 80 mg / dL. Blood was sent for a complete blood count, electrolytes, calcium, magnesium, BUN, creatinine, glucose, and PT, PTT. Urine was sent for a toxicology screen looking specifically for phencyclidine, cocaine, and amphetamines. Arrangements were made for a stat head computed topography (CT) scan. The patient remained stable over the first hour in the emergency department except for one more episode of vomiting. His expressive dysphasia persisted. The arm weakness began to resolve and by the time he was sent for the CT scan his strength had improved to 3/5. All of the laboratory tests returned within normal limits except for the toxicology screen and sedimentation rate which were still pending.

Critical Questions

1. The initial ED differential diagnosis of this patient's presentation includes all of the following except:
a. Hemorrhagic stroke
b. Embolic stroke
c. Migraine headache
d. Complex partial seizure

2. One of the most common focal neurologic findings reported in SAH is:
a. Dilated unilateral pupil
b. Unilateral facial drop
c. Deviated tongue
d. Dysphagia

3. Speech is usually controlled by which side of the brain:
a. Right
b. Left

4. Patients presenting within one hour of symptom onset with a suspected SAH who have a negative head CT and normal CSF analysis are best managed:
a. Head CT with contrast
b. Emergency cerebral angiogram
c. Discharge with follow-up
d. Repeat LP at 12 hours

Differential Diagnosis

Acute headache with focal neurologic compromise in an otherwise healthy adolescent poses an interesting differential diagnosis that must be systematically and expeditiously investigated. Etiologic categories include hemorrhagic, embolic, thrombotic, vasospastic, and neoplastic intracranial events. Infectious, metabolic, and ictal causes are less likely in this case due to the patients age and sudden onset. Aphasia and hemiplegia indicated a lesion in the left frontal region, involving both the motor cortex and Broca's area. However, in general a lesion involving both Broca's and the upper extremity should also involve the face (explaining the non-fluent speech problem and difficulty with word formation described in a Broca's aphasia)

In the hemorrhagic category, a subarachnoid hemorrhage (SAH) was considered a likely possibility. Subarachnoid hemorrhage is classically characterized by a severe and sudden onset of headache, neck stiffness, mental status change, and bloody cerebral spinal fluid. However, focal neurologic deficits are not characteristic of SAH, but can occur when blood ruptures into the brain or when there is a subsequent cerebral infarction. Approximately 30% of aneurysms involve the posterior communicating artery which courses next to the third cranial nerve; when the aneurysm compresses the parasympathetic fibers coursing on the outside of the third nerve, a dilated ipsilateral pupil may result. Subdural and epidural hemorrhages are usually progressive in character and associated with a history of trauma. They were considered unlikely in this patient.

Embolic etiologies in an adolescent can arise from cardiac valve disease, dysrhythmia, and from intravenous drug use. This patient's bicuspid aortic valve was not considered a likely source of emboli since there had been no preceding procedures predisposing him to bacteremia. ECG monitoring showed no dysrhythmias and there were no signs of intravenous drug use.

Thrombosis can arise from sludging and is seen in patients with sickle cell disease or myelodysplasias. This patient was Caucasian and had a normal CBC, thus making thrombosis unlikely. Neoplastic disease usually presents with gradual onset of symptoms, but sudden neurologic defects could occur if the vascular supply became compromised or if there was hemorrhage into a preexisting tumor.

In the metabolic category, both hypoglycemia and hypokalemia can cause focal neurologic deficits, however, both were eliminated as possibilities with the return of normal laboratory tests.

Localized vasospasm or inflammation were considerations. When migraines are considered, there is usually an individual or family history of similar episodes. When collagen vascular disease is considered, other manifestations of disease are usually present.

Drugs, such as cocaine and amphetamines, and adulterants, such as quinine, can induce vasospasm and can be investigated using urine and serum toxicology screening.

Meningitis and encephalitis do not usually cause focal deficits unless there is abscess formation. These diagnoses were unlikely since this patient had dramatically abrupt onset of symptoms with neither a fever nor a stiff neck.

The last consideration was that this patient could be postictal with a Todd's paralysis, which can follow a seizure. The paralysis can last up to one week. This diagnosis was unlikely since there was no history of seizures, and there was no evidence of seizure activity with this episode.

Clinical Course

The child returned from CT after 40 minutes. The right hemiplegia was completely resolved, the aphasia was significantly less, and he could now express words clearly though still with some difficulty. He continued to indicate that he had a severe left-sided headache by holding his forehead. He had had two episodes of retching while in CT.

The CT scan (which was done with and without contrast) was within normal limits with no evidence of subarachnoid blood, swelling, hydrocephalus, or space-occupying masses. A urine drug of abuse screen was negative for cocaine, amphetamines, PCP, and narcotics. The child was given an intravenous injection of meperidine (Demerol) 25 mg and promethazine (Phenergan) 12.5 mg to help with the headache and vomiting.

A lumbar puncture was performed. Opening pressure was 120, and the fluid was clear and sent for cell count, chemistries, and Gram stain.

Three and one-half hours after arrival, the patient was lying comfortably in bed. All neurologic deficits were resolved. The headache persisted, but was tolerable. The child was alert, cooperative, and able to answer all questions with fluent speech. All CSF studies were normal and the toxicology screen returned showing no evidence of drug use.

The patient was admitted to the pediatric ward, the headache resolved overnight, and he had a completely normal examination in the morning. An electroencephalogram was done and showed no abnormalities. A diagnosis of hemiplegic migraine was made, and the patient was discharged with follow-up by the pediatric neurologist. Three months later he experienced a similar episode that also resolved over several hours.

Discussion

This patient's initial presentation was alarmingly suggestive of a cerebrovascular catastrophe. The rapid recovery of neurologic deficit in the context of resolving headache and the negative work-up pointed to a diagnosis of hemiplegic migraine. The diagnosis was made even more certain when the presentation recurred three months later.

Migraine without aura (once referred to as common migraine) and migraine with an aura (once called classic migraine) are the two major groups of migraine. (1) The headache in

migraine without an aura is moderate to severe in intensity, throbbing, and unilateral, though it can generalize bilaterally. It can be associated with nausea, vomiting, anorexia, photophobia, phonophobia, yawning, drowsiness, and difficulty concentrating. The diagnosis requires five previous attacks. Though there is no specific aura, there may be a nonspecific prodrome that precedes the headache by hours or days.

The headache in migraine with an aura is preceded by visual, sensory, and/or motor symptoms. Diagnosis requires at least two attacks having at least three of the following four characteristics: fully reversible focal cerebral, cortical, or brainstem dysfunction, at least one aura symptom, no aura symptom lasting more than 60 minutes, headache follows aura with a free interval of less than 60 minutes.

Complicated migraine does not easily fit into the International Headache Society's classification of migraines but in general is a term used to describe neurologic defects that persist after resolution of migraine headache. (2) This would include migraines that have an aura lasting more than one hour, hemiplegic migraines, ophthalmoplegic migraines, and migrainous infarction.

Migraine equivalents are a controversial subject and are debated as to whether they even exist. They refer to recurrent reversible symptoms that are produced by migraine but have no associated headache. The diagnosis is one of exclusion.

Pathophysiology: Overall, it is now thought that migraine begins centrally and affects blood vessels secondarily through the trigeminal vascular system. (3) The vascular theory for migraine proposes that the neurologic symptoms associated with migraine are the result of constriction of the intracranial blood vessels while the headache is the result of vasodilatation of the extracranial vessels which release vasoactive polypeptides that lower the pain threshold. Though once widely accepted, blood flow studies have not fully confirmed this mechanism, and physiologically induced cephalic vasodilation does not induce an attack nor do potent vasoconstrictors such as phenylephrine abort an attack. However, it has been documented that during an aura there is vasoconstriction with hypoperfusion. Migaine without an aura is not usually associated with a change in regional cerebral blood flow.

The neural hypothesis of migraine states that symptoms are due to abnormal function of the cerebral cortex and not to spasm of major cerebral arteries. This is supported by cerebral blood flow studies which show that cerebral cortical hypoperfusion occurs focally and spreads slowly over the cortex in a distribution independent of blood flow from the cerebral arteries.

There is increasing evidence that migraine headache is mediated through serotonin (5-HT) though it is unclear if it is due to inadequate synthesis of 5-HT, excessive breakdown, or abnormal 5-HT receptor function. (3) There are four main 5-HT receptors, $5\text{-HT}_{1\text{-}4}$, and four subtypes of 5-HT_1, 1A-1E. 5-HT_1 is inhibitory and modulates neurotransmitter release presynaptically, 5-HT_2 is an excitatory postsynaptic receptor (prophylactic agents

such as methysergide, amitriptyline, calcium channel blockers are 5-HT_2 receptor antagonists). 5-HT_1 receptors are located on peptide containing trigeminovascular axons within the dura mater and are not present on extracranial vascular tissue innervated by the trigeminal nerve, and stimulation of these receptors result in vasoconstriction. Agonists to these receptors (DHE and sumatriptan) abort migraine attacks and relieve acute symptoms. Reserpine , which depletes CNS 5-HT precipitates headache which is then reversed if 5-HT agonists are given.

The unified or neurovascular hypothesis for migraine pathogenesis proposes that migraine headache is due to both vasodilation and to the extravasation of neuropeptides. Trigger factors activate 5-HT and norepinephrine containing neurons in the locus ceruleus and dorsal raphe nuclei in the brain stem activating pain-provoking and neuroinflamatory mediators in the cerebral cortex. These mediators activate nociceptors on trigeminovascular afferent terminals within the meninges, which in turn stimulate neurons in the brain stem, thalamus, cerebral cortex to create awareness of pain. Activation of the sensory perivascular terminals then release into the vessel wall substance P, neurokinin A, and calcitonin gene-related products to cause a sterile inflammatory process which sensitizes nerve endings and sustains the pain long after the initial trigger has disappeared. 5-HT_1 agonists selectively block the development of neurogenic inflammations within the dura mater following trigeminal antidromic stimulation. These agonists also result in vasoconstriction thus blocking the pain related to vasodilatation. Interestingly, sleep is associated with decrease firing of 5-HT containing neurons in the raphe, and it is observed that sleep frequently aborts headache in many patients.

Hemiplegic Migraine: Hemiplegic migraine is a syndrome characterized by headache and visual sensory, aphasic, and / or motor symptoms. (4) Most patients, as the one presented, have at least two symptoms during attacks. Familial hemiplegic migraine (FHM) is an autosomal dominant inherited subtype of migraine with aura in which transient hemiparesis is followed by a migraine headache though the neurologic deficit may outlast the headache. (5) It is due to a gene mutation within the neuronal calcium channel. (Yu) The aura is generally prolonged and fulfill the criteria of the International Headache Society for prolonged aura. (6) Familial hemiplegic migraine is divided into pure familial hemiplegic migraine which affects 80 % of families, and familial hemiplegic migraine with permanent cerebellar signs which affects 20 percent of families. (7)

Magnetic resonance angiograms have demonstrated both vasospasm and vasodilatation in patients with acute hemiplegic migraine. (8) The headaches are usually throbbing and begin at the same time as the motor deficits. They are unilateral 70% of the time and generalized in 30 % of cases. When the headache is unilateral it is located contralateral to the motor deficits 67% of the time. The motor deficits can be partial or complete, and it is very rare to have facial weakness. Parasthesias or sensory deficits are often associated with hemiplegic migraines and can precede the motor deficits. (4)

Disturbances in speech are common, especially when the right side of the body is involved. Disturbances range from mild slurring to expressive and receptive dysphasias.

When receptive dysphasias are present the patients often appear acutely confusional or even psychotic. Amnesia for the events can occur when the hemiplegic migraine resolves.

Hemiplegic migraines usually start before the patient is 25 years old. There is a 3:1 female to male predominance. Patients or family frequently have a history of migraines, and the hemiplegic migraines usually occur interspersed between episodes of classic migraine. (4) In 72% of attacks, the limb symptoms last fewer than three hours, however rarely the hemiplegia can last for days, and there have even been reports of cerebral infarction with permanent deficits. (9, 10) Vomiting is rarely seen in these patients.

Treatment

Serotonin receptor modulators are first line drugs in the management of acute migraine attacks: (11, 12) Narcotics are second line drugs, at best, recommended after nonsteroidal anti-inflammatory agents. (12) Sumatriptan and DHE have not been tested extensively in children less than 12. In one study, adolescents 12-18 were treated with a 90% success rate with IV DHE and metoclopramide.(13) Dosing for DHE is age dependent, see table. The anti-emetic of choice in children is promethazine since it does not have the risk of dystonia that is associated with metoclopramide or prochlorperazine.

Because familial hemiplegic migraines are due to a genetic mutation affecting calcium channels, calcium channel blockers have been tried in management and case reports suggests their efficacy. (14, 15, 16) In one case study, a 28 year old woman who had migraines since age 11 developed a hemiparesis and eyelid ptosis symptoms at age 27; during one severe attack, symptoms failed to respond to nonsteroidals, propanolol, and sumatriptan but rapidly resolved after verapamil, 5 mg intravenously over two minutes. (14)

Conclusion

There is surprisingly little written in the literature about hemiplegic migraines. First-time presentation is alarming for both the patient and the treating physician and mandates a thorough work-up. As discussed, the differential diagnosis includes many life-threatening conditions that must be excluded before a final diagnosis can be made. However, a careful history that discovers similar previous events are reassuring and may impact the aggressiveness of the work-up.

Final Diagnosis

Hemiplegic migraine

TREATMENT ESSENTIALS

Migraine

- Assess patients for dehydration and hydrate as indicated.
- Anti-emetics and im/iv drugs in patients with nausea or vomiting, except when using sumatriptan which has anti-emetic properties.
- Assess for pregnancy and avoid ergots and sumatriptan if positive.
- Ergots and sumatriptan are contraindicated in patients with coronary artery disease, hypertension, hepatic or renal impairment, or patients with new neurologic deficits.
- In general, narcotics are avoided in treating migraine

Acute Migraine

Naproxen sodium	275 mg	PO	2-3 tabs at onset, repeat 1-2 tabs in 2 hours if needed
Ibuprofen	200 mg	PO	1-4 tabs
Ketorolac	60 mg	IM	
Isometheptene	65 mg	PO	2 capsules at onset then 1 capsule q1 hour up to 6
Acetaminophen	325 mg		
Dichloralphenazone	100 mg		
Aspirin	330 mg	PO	1-2 tabs q 4 hours up to 6 tabs in 24 hours
Caffeine	40 mg		
Butalbital	50 mg		
Prochlorperazine	25 mg	PO/PR	
	5-10 mg	IM/IV	
Metoclopramide	10 mg	PO/IM/IV	
Chlorpromazine	1 mg/kg	IM	
	.5 mg/kg	IV	
Ergotamine	1 mg	PO/SL	1-4 mg at onset followed by 1-2 mg q 1/2 hour up to a max of 5 mg in 24 hours
Ergotamine	2 mg	PR	1/2-1 suppository at onset followed by 1/2 suppository 1/2 hour p to a max of 5 mg in 24 hours
DHE	0.5-1 mg	IV/IM	repeat q 1 hour for total max of 3 doses in 24 hours
Sumatriptan	6 mg	subcut	can repeat once in 12 hours
Prednisone	80 mg	PO	rapid taper over 1 week
Dexamethasone	20 mg	PO	rapid taper
Lidocaine	1 mg/kg	IV	

Discharge patients after improvement, with medications in case of headache relapse.

Notify primary care physician of patient's ED visit.

Instruct patient on indications to return to ED and for follow-up with primary care physician.

Migraine in Children

If oral medications fail, consider IM DHE plus promethazine:

DHE	6-9 years old	0.1-0.15 mg	IM
	9-12 years old	0.2 mg	IM
	12-16 years old	0.25-0.5 mg	IM
Promethazine	6-9 years old	.25 mg/kg up to a max of 25 mg	
	> 9 years old	.25 mg/kg up to a max of 50 mg	

Status Migrainosus

Admit to hospital

DHE 1 mg iv after metoclopramide 10 mg iv every 8 hours for two days.

Prednisone 80 mg/day or dexamethasone 20 mg/day in short tapering dosing.

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Annotated Bibliography

Welch K, Levine S. Migraine-related stroke in the context of the international headache society classification of head pain. Arch Neurol 1990; 47:458-462

This article reviews the pathophysiology of stroke related migraine and presents a series of cases that demonstrate various related predisposing conditions. Sections of the article include "coexisting stroke and migraine", "stroke with clinical features of migraine", "migraine induced stroke", "migraine without stroke risk factors", "migraine with stroke risk factors" . Two of the 12 cases presented are pediatric cases.

Welborn C. Pediatric migraine. Emerg Med Clin No Am 1997; 15: 625-636

This is an excellent overview of migraine headaches in children. It reviews the limited literature available in treatment of pediatric migraine and provides a useful table of treatment options.

Thomsen L, Eriksen M, Roemer S, et al. A population based study of familial hemiplegic migraine suggests revised diagnostic criteria. Brain 2002; 12:1379-1391.

This is the only systematic search for familial cases of migraine in the literature. More than 27,000 case records from headache clinics in Denmark were screened and 147 patients were identified. The study provides an excellent demographic profile of this rare disease

Rapoport A (ed). Severe headache: Focus on migraine. Neuology 1994; 44 (suppl 3):1-32

This supplement to the journal, Neurology, is devoted to issues in migraine written by experts with significant expertise in the area. Dalessio wrote a article that provides an excellent overview of diagnostic criteria for headache using the International Headache Society classification and provides an excellent approach to historical and physical findings that direct clinical decision making. Other articles in the issue discuss pharmacologic treatment, chronic headache, and management of recurrent headache.

Bradshaw P, Parsons M. Hemiplegic migraine, a clinical study. Q J Med 1965; 34; 65-86.

This is one of the largest series of patients with hemiplegic migraine reviewing the clinical presentation of 75 patients with predominantly or exclusively unilateral limb symptoms. The paper distinguishes familial hemiplegic patients from non-familial. 42 patients were studied with angiography and based on the findings and clinical course this article concluded by recommending that young patients without risk factors for vascular disease can be managed with supportive care and without diagnostic interventions (of course, this study was performed before easy access to head CT).

Critical Questions

1. **The initial ED differential diagnosis of this patient's presentation includes all of the following except:**
   a. Hemorrhagic stroke
   b. Embolic stroke
   c. Migraine headache
   d. Complex partial seizure

2. **One of the most common focal neurologic findings reported in SAH is:**
   a. Dilated unilateral pupil
   b. Unilateral facial drop
   c. Deviated tongue
   d. Dysphagia

3. **Speech is usually controlled by which side of the brain:**
   a. Right
   b. Left

4. **Patients presenting within one hour of symptom onset with a suspected SAH who have a negative head CT and normal CSF analysis are best managed:**
   a. Head CT with contrast
   b. Emergency cerebral angiogram
   c. Discharge with follow-up
   d. Repeat LP at 12 hours

Answers

1. d. Complex partial seizures should result in global dysfunction and not focal deficits as in this case. A hemorrhagic or embolic stroke were possible and an evaluation was indicated. A subarachnoid hemorrhage was actually unlikely since SAH will rarely give the focal findings this patient presented with.

2. a. Subarachnoid hemorrhage that results from an aneurysm on the posterior communicating aneurysm will result in a dilated unilateral pupil. This finding results from compression of the parasympathetic nerve fibers that course on the outside of the third nerve. Significant compression can result in a third nerve palsy which would include a ptosis and gaze that is "down and out" resulting from unopposed fourth and sixth cranial nerve function.

3. b. 80 % of people have their primary speech center on the left side of the brain.

4. d. It can take up to twelve hours after a small hemorrhage for blood to settle down to the CSF in the lower spine and for xanothochromia to appear. Consequently, when there is a high index of suspicion and the LP is performed early, waiting for twelve hours after onset of headache is a reasonable approach to managing the patient. CT with contrast would not help to detect acute blood. An angiogram has inherent risks and is negative in up to 20% of patients with SAH; consequently, a conservative approach with supportive care and repeat LP is prudent.