Brief Communication

Hemiplegic Cluster

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We report four cases of a new variant of cluster headache associated with hemiparesis. Clinical similarities with hemiplegic migraine suggest that hemiplegic cluster, too, may be a channelopathy. One of our patients had a family history suggestive of an autosomal dominant inheritance.

Key words: cluster headache, hemiparesis, channelopathy

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Cluster headaches are characterized by severe, recurrent, unilateral, periorbital pain lasting 15 to 180 minutes, with associated autonomic symptoms. They may be episodic or chronic and associated with visual and olfactory aura but not hemiparesis.[1] Hemiparesis has never been reported in cluster headache.

We report four cases of cluster headache with hemiparesis.

CASE HISTORIES

Patient 1.—A 47-year-old man presented with a 15-year history of excruciating right retro-orbital and supraorbital region pain; accompanied by ipsilateral tearing, rhinorrhea, nausea, photophobia, and phonophobia. Attacks lasted from 30 minutes to 1 hour, once or twice per day with no more than a 1-week headache-free period without treatment. The pain occurred both at night and during the day. He was successfully treated with a combination of verapamil, divalproex sodium, and lithium carbonate.

One year ago, he began to have spells of right face numbness with right arm and leg weakness. He was unable to hold his arm up during these spells, which occurred weekly and lasted from 4 to 12 hours. These hemiparetic spells started within 5 to 10 minutes of the cluster. He also complained of blurry vision during the headaches. Magnetic resonance imaging (MRI) and magnetic resonance arteriography (MRA) were normal. He had a history of myocardial infarction and diabetes mellitus.

His deceased father had a history of severe unilateral headaches occurring predominantly during the night, which were, at times, associated with an unsteady gait. His brother also suffers from severe headaches with associated unilateral weakness, but, unfortunately, could not be contacted.

Patient 2.—A 45-year-old man had a 7-year history of severe right orbital region pain. Attacks lasted from 20 to 60 minutes and occurred three times a day for 6 to 8 weeks, followed by months of remission. The pain was accompanied by tearing in the right eye, rhinorrhea, nausea, photophobia, and phonophobia. He had episodes of right visual loss accompanied by aphasia and ipsilateral hemiparesis which began 10 to 15 minutes after his headaches began and lasted for up to 24 hours. An MRI and MRA were reported as being normal. He responded to prednisone therapy and is currently on verapamil, topiramate, and divalproex sodium, but continues to have breakthrough headaches.

His father has migraine without aura, and his sister has migraine with aura without hemiparesis.

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Patient 3.—A 32-year-old man developed recurrent severe headaches 5 years prior to evaluation. At first they lasted 1 week, then progressed to 3 weeks, and currently last 5 weeks. The right orbitotemporal region pain lasts up to 2 hours, is sharp, burning, and normally wakes him from sleep at 2 AM. He has had occasional daytime attacks. The headache is associated with right eye lacrimation, conjunctival injection, and rhinorrhea. On one occasion, he lost total vision in his right eye for 30 minutes. Headaches can be provoked by alcohol. He has mild weakness in the left hand with these attacks. His initial neurologic examination showed mild left hemiparesis with normal sensation, reflexes, and normal cranial nerve examination and no Babinski sign. This weakness resolved on a follow-up visit a week later. The patient had relief with oxygen, metoclopramide, and Excedrin. An MRI and MRA were ordered but not done.

There is no family history of headaches or other neurologic disorders.

Patient 4.—A 52-year-old woman with a history of migraine that resolved after surgery for a left middle cerebral artery aneurysm developed episodic cluster headaches following head trauma. Attacks involve the left orbital region, occur up to three times a day, and last from 20 to 40 minutes. Associated with these attacks are a left facial droop, slurred speech, and right hemiparesis that lasts up to 4 1/2 hours. She also experiences right extremity tingling and visual loss in her left eye. A diagnostic workup, including MRI and computed tomography of the head, was negative. She obtains relief with verapamil, melatonin, carbamazepine, and oxygen.

Her mother, sister, and daughter have migraine without hemiparesis.

A summary of these cases is presented in Tables 1 and 2.

COMMENTS

These four patients had headaches (severe, unilateral, orbital, supraorbital, and/or temporal pain associated with autonomic symptoms, lasting up to 2 hours and with a frequency of one to three attacks a day) that fulfilled the International Headache Society criteria for cluster headache. They also had accompanying transient hemiparesis lasting less than 24 hours in three patients, in the fourth the duration was uncertain. This was ipsilateral to the pain in two, contralateral in one, and crossed in the fourth. Hemiparesis occurred multiple times in three patients and once in one patient. Three had visual symptoms and one, aphasia. Two patients had no risk factors for cerebrovascular disease, one had a history of diabetes mellitus and myocardial infarction, and the fourth had a history of cerebral aneurysm. One patient had a family history suggestive of a dominantly inherited

Table 1.—Headache Characteristics*

Patient	Side of HA	Duration of HA, min	Autonomic Symptoms	Chronic or Episodic	No. of Attacks per Day	Migraine Symptoms	Medication
1	Right	30-60	Tearing Rhinorrhea	Chronic	1-2	Nausea Photophobia Phonophobia	Verapamil Divalproex sodium
2	Right	20-60	Tearing Rhinorrhea	Episodic	3	Nausea Photophobia Phonophobia	Topiramate Divalproex sodium Verapamil
3	Right	Up to 120	Tearing Conjunctival injection	Episodic	1-2	—	Verapamil Oxygen
4	Left	20-40	Tearing Rhinorrhea Eyelid droop	Chronic	1-3	Photophobia Phonophobia	Verapamil Oxygen Melatonin Carbamazepine

*HA indicates headache.

Table 2.—Neurologic Symptoms*

Patient	Side of Motor Symptoms	Duration, h	Time of Onset	Total No. of Attacks	Visual Loss	Other	Evaluation
1	Ipsilateral	4-12	5 min after onset	6	Negative	Numbness in face	MRI, MRA, exam normal
2	Ipsilateral	Up to 24	15 min after onset	6	Ipsilateral	Aphasia	MRI, MRA, exam normal
3	Contralateral	Uncertain	Uncertain	1	Ipsilateral	None	Left hemiparesis on exam
4	Ipsilateral facial and contralateral arm, leg	Up to 4.5	At peak of headache	Multiple	Ipsilateral	Dysarthria	Head CT, exam normal

disorder. Patient 3 was examined and we documented a mild hemiparesis during a cluster cycle; the other cases were from retrospective chart reviews.

These cases defy simple neuroanatomical explanations, with the pain and eye symptoms ipsilateral to the hemiparesis on two occasions, contralateral in one, and crossed in the last. This may represent dissociation between neural and vascular events that occurred during hemiplegic cluster. In hemiplegic migraine, the hemiparetic attacks are usually preceded by a headache and may last from less than 1 hour to days or weeks. Hemiplegic migraine with visual obscuration and hemiplegia ipsilateral to the headache has been described.[2] Our patients had two unusual cluster headache features: hemiplegia and visual symptoms (vision loss/blurry vision). Hörven et al[3] noted visual symptoms in patients with cluster headache. He attributed these to a marked increase in corneal indentation pulse amplitudes measured by dynamic tonometry in the affected eye. This may be a reflection of increased resistance (vasoconstriction) to the blood flow in the eye.

These symptoms are more than just a casual association and may be a new cluster headache variant. They are remarkably similar to familial hemiplegic migraine. The rate of hemiparetic attacks is similar to what Bradshaw and Parsons[4] described in patients with hemiplegic migraine where 17% had a single hemiplegic episode, 37% had between two and six episodes, and the remainder had more than seven attacks. Three of our patients had multiple attacks of hemiparesis. Recently, some cases of familial hemiplegic migraine have been found to be due to a calcium channelopathy with a mutation in the brain-specific P/Q-type calcium channel alpha 1A subunit gene (*CACNA1A*) on chromosome 19p13.[5,6] This same gene may be involved in common forms of migraine, with and without aura.[7] The symptomatology and suggestive family history in one patient imply that hemiplegic cluster, too, may be a channelopathy. Interestingly, verapamil, an L-calcium channel blocker, is used in high doses in cluster headache treatment (in excess of that used to treat arterial hypertension), and may interact with one or more of the voltage-dependent calcium channels.[8] Genetic studies may help us find the cause of hemiplegic cluster disorder.

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