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Clinical Notes

Cluster-Like Headaches Associated With Internal Carotid Artery Dissection Responsive to Verapamil

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Cluster headache is a disorder of episodic, brief, severe, unilateral pain centered in or around the eye. The pain builds within 15 minutes to excruciating levels, and is described as deep, constant, and boring, piercing, or burning in nature. At least one of the following associated autonomic symptoms must also occur: conjunctival injection, eyelid edema, facial sweating, lacrimation, miosis, nasal congestion, ptosis, or rhinorrhea. A minority of patients have associated nausea, vomiting, photophobia, or phonophobia. During an attack, patients often feel agitated or restless.[1,2,3]

The attack frequency varies from one every other day to 8 a day. The attacks often occur at the same time each day, frequently during sleep. Untreated, the attacks usually last from 30 to 90 minutes, but may last up to 180 minutes. In episodic cluster headache, cluster periods usually last from 1 to 3 months, with remission between cluster periods lasting 6 months to 2 years. Most patients have 1 or 2 cluster periods a year that last 2 to 3 months, with 1 to 2 attacks a day. Chronic cluster headache has either no remission periods or remissions that last less than 14 days.[1,2,3]

To stop an individual headache, oxygen, subcutaneous, or intranasal sumatriptan is commonly used. To stop a cluster cycle, a course of prednisone is often used. To stop a cluster cycle as well as to prevent the next cluster cycle from starting, verapamil is commonly used.[3] One study found that verapamil 120 mg 3 times daily was effective in stopping cluster headache attacks, although most patients required 2 weeks before complete prevention was achieved.[4]

CASE REPORT

The patient is a 55-year-old ambidextrous white man ophthalmologist evaluated for headaches starting 6 months earlier and increasing in frequency, of late occurring 3 times weekly. There was no inciting event reported. He described pain varying from mild to severely disabling around his left orbit that motivated him to pace, and made him want to "pull (his) left eye out of its socket." Associated symptoms included left ptosis, mild lacrimation, and periorbital edema, light and noise sensitivity with particularly bad episodes, and nausea. Headaches lasted 4 to 8 hours, and he had a prodrome of scintillations in his left eye (as opposed to his left visual field). Triggers were dehydration and alcohol, and they were more likely to occur around 1700. Caffeine worked as an abortive, and propranolol 10 mg taken on surgery days made it less likely for him to get a headache on those days.

His past medical history included essential tremor and benign paroxysmal positional vertigo 4-5 years prior.

On interictal examination, his temporal arteries were pulsatile on the left and nonpulsatile on the right. He had a

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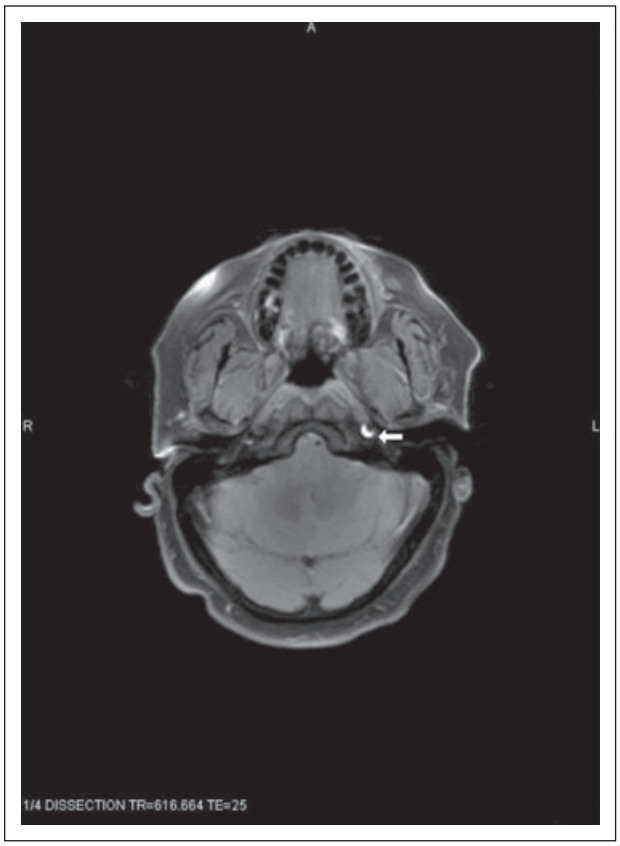

Fig. 1.—MRI image of the distal left cervical carotid artery dissection just prior to the petrous segment. MRI = magnetic resonance imaging.

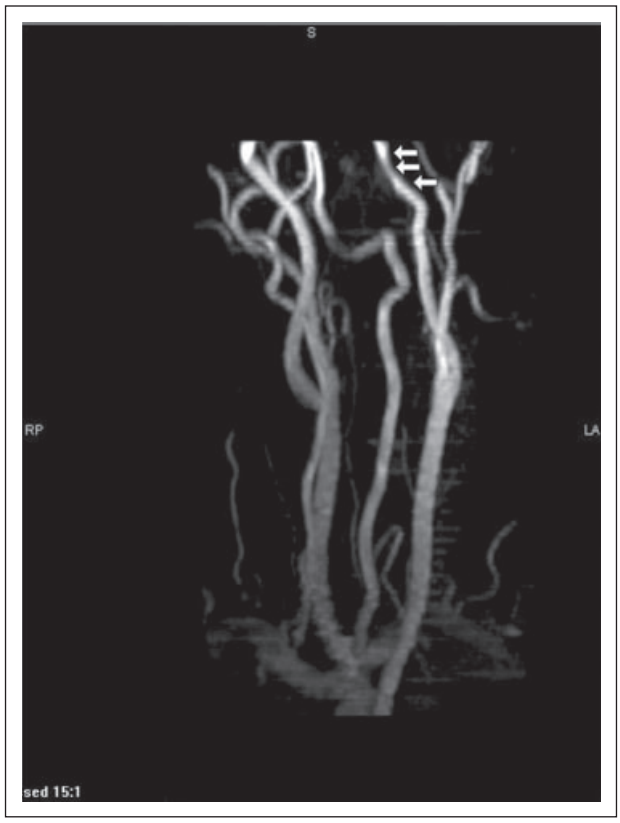

Fig. 2.—MRA image of the distal left cervical carotid artery dissection just prior to the petrous segment. MRA = magnetic resonance angiogram.

bilateral upper extremity essential tremor. There were no autonomic abnormalities whatsoever. There were no carotid artery bruits.

Verapamil extended release (ER) 120 mg po qhs eliminated his headaches immediately, although it interfered with his ability to multitask. He never had an occasion to try the abortive agents he was given.

Magnetic resonance imaging (MRI) of the brain with diffusion and without fat suppression 13 days after his initial evaluation revealed a distal left cervical carotid artery dissection just prior to the petrous segment, with 50% luminal narrowing (Fig. 1). No other abnormalities were seen. He was hospitalized where CT angiogram (CTA) and magnetic resonance angiogram (MRA) showed the same abnormality (Fig. 2).

He was anticoagulated on warfarin with a target international normalized ratio (INR) of 1.5-2.5. He was also diagnosed with hypertension and started on propranolol 10 mg twice daily (BID). The verapamil was stopped without recurrence of his headaches.

COMMENTS

This patient presented with a clinical picture resembling cluster headache, with episodic stabbing pain around his eye, associated agitation, and autonomic signs including ptosis, lacrimation, and periorbital edema. Several features were atypical. The headaches started in his 50s, were preceded by a scintillating aura, were associated with nausea, and lasted 4-8 hours.

Despite these atypical features, this patient's headaches fell well within the spectrum of cluster-like headaches, and it could even be argued that they should have met the diagnostic criteria for cluster headaches. Cluster headache generally begins in the late 20s, but can begin at any age.[2,5] Auras and gastrointestinal symptoms are more characteristic of migraines,[6] although aura was reported in 2%, 6%, 14%, and 23% of cluster headache patients in several series.[7-10] Krymchantowski[11] reviewed descriptions of aura associated with cluster headache, hemicrania continua, and even chronic paroxysmal hemicrania. One series reported nausea and vomiting in 27.8% of cluster headache patients,[10] and

another reported nausea in 43.5% and vomiting in 17.4% of male cluster headache patients.[12] Van Vliet et al identified nausea, photophobia, and phonophobia as factors associated with a delay in the diagnosis of cluster headache, and advocated that the presence of aura, nausea, or vomiting should not rule out a diagnosis of cluster headache.[13] Van Vliet found that patients not meeting the International Headache Society criteria for cluster headache (IHS-CH) solely because of their headaches lasting longer than 3 hours had a similar response rate to verapamil (54%) as did patients fully meeting the IHS-CH (61%), and recommended that the upper limit of 3 hours be increased in future diagnostic criteria.[14] Actually, the IHS recognized that a duration longer than 3 hours is possible is some attacks.[15] Published series of patients with cluster headaches with migraines features has been reviewed elsewhere,[16] and the diagnosis of "cluster-migraine" as a distinctive entity has also been discussed.[17]

The mechanism by which a dissecting internal carotid artery (ICA) aneurysm can cause cluster-like headaches is not known. In our patient, it is possible that periodic elevations in the patient's blood pressure caused stepwise progression of the dissection, producing the pain as well as the Horner's syndrome every time the dissection extended. The patient's immediate response to verapamil as well as lack of recurrence when he was switched to propranolol for his newly diagnosed hypertension is consistent with this hypothesis. The patient's headaches were more likely to occur around 1700, and a circadian periodicity of blood pressure fluctuation has been well described, with a mid morning as well as a late afternoon peak.[18,19] Were this hypothesis valid, however, one would also expect his headaches to occur more frequently in the mid morning with the first peak in blood pressure. Alternatively, it is possible that ischemia distal to the dissection resulted in periodic reflex vasodilatation of the downstream arterial system including the ophthalmic artery. Dilation of the ophthalmic artery as well as narrowing of the carotid siphon during cluster headaches has been documented.[20,21]

Cluster headaches secondary to dissecting carotid artery aneurysms have been reported in eleven previous cases (Table 1). In 2 cases, verapamil in conjunction with another medication (aspirin in one, anticoagulation in another) stopped the attacks within 2 weeks.[22,23] In 2 others, steroids in conjunction with anticoagulation stopped the attacks over 2 weeks.[24,25] This case is therefore the third reported case in which verapamil stopped cluster or cluster-like headache attacks in spite of the serious underlying pathology of a dissecting carotid aneurysm. This case is unique because verapamil was the only preventive given, it was given at a relatively low total daily dose, and yet it still worked so quickly that the patient never had the occasion to try any of the headache abortive medications he was given. Similarly, previously reported patients responded partially to cluster headache abortive, including nasal sumatriptan,[22] oxygen and nonsteriodal antiinflammatory drugs (NSAIDs),[26] and acetaminophen with codeine.[27]

The larger underlying question is whether response to headache medication excludes serious underlying pathology. Jagoda et al observed that the only published data regarding response to pain medications as an indicator of underlying headache etiology is in the form of case reports, and cited 7 cases of headaches which responded to analgesics but were subsequently found to have with serious underlying causes (2 intracerebral hemorrhages, 2 viral meningitides, 1 subarachnoid hemorrhage, 1 meningeal carcinomatosis, 1 carbon monoxide poisoning).[28] The ensuing Emergency Medicine level C recommendation was that pain response to therapy should not be used as the sole diagnostic indicator of the underlying etiology of an acute headache. Our case report, as well as the above previously reported cases of carotid dissection that responded to headache medication, supports this recommendation.

This case is also unique because the headaches started 6 months prior to his initial presentation; the next longest time reported from onset to medical evaluation was 6 weeks.[23]

Of note, in 5 cases, the carotid dissection was not seen on carotid ultrasound.[24-26,29] In our case, the diagnosis was made on the basis of an MRI of the brain without fat saturation. In 2 cases, MRI interpretations did not reveal the dissection.[24,25] However, one MRI was subsequently reinterpreted by a neuroradiologist, who identified a slight hyperintense semilunar shape at the beginning of the petrous left ICA, and recommended an MRI with fat saturation study, which subsequently confirmed the diagnosis.[25] It was not stated whether the MRI for the other patient was carried out with fat saturation.[24] In addition, in all cases in which an MRI fat saturation study was specifically mentioned, the diagnoses were made on MRI.[23,25,29] Studies that identified the lesion in all cases included MRA,[22,24,30] CTA,[23,24] and angiogram.[24,27]

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Table 1.—Cluster Headaches Associated With Dissecting Carotid Artery Aneurysms

Report	Demographics Past medical history (if given) Duration of headache at presentation	Tests and results	Atypical features	Response to medication
Hardmeier 2007[22]	38M 3 weeks	Neurosonography and MRA head/neck – left distal extracranial DAICA	Ear pain persisted after the initial attack ended	Nasal sumatriptan – partial relief Aspirin 100 mg daily + verapamil 240 mg daily – attacks resolved in 2 weeks, but moderate continuous pain persisted in the left lower face
Rigamonti 2007 (1)[24]	50M HTN, MI, high cholesterol 1 month	EcoDoppler of extracranial vessels – negative. MRI – lacunar CVAs CTA and angiogram – DAICA at the extra-intracranial passage	2 days prior to presentation he had an attack lasting 12 hours, with residual ptosis afterwards lasting at least 48 hours	Antiaggregant therapy – no further attacks
Rigamonti 2007 (2)[24]	49M 2 weeks	EcoDoppler – negative MRI brain + MRA head/neck – DAICA at the extra-intracranial passage, confirmed on angiogram	2 days prior to presentation he developed persistent ipsilateral ptosis between attacks	Anticoagulation plus steroids – headaches subsided over 2 weeks; steroids then stopped without recurrence of pain
Razvi 2006[23]	44M 6 weeks	CTH – normal CTA and MRI w/fat-sat – extracranial DAICA	Headache attacks lasted 1 to 6 hours Residual partial ptosis between headache attacks	Anticoagulation+verapamil – attacks resolved in 2 weeks
Hannerz 2005[30]	58M 8 days to first medical care 19 days to hospital admission and diagnosis	MRI, MRA – extracranial DAICA with complete occlusion Diffusion and PWI – several areas of restricted diffusion in the right hemisphere, estimated 7-10 days old	Bilateral nasal congestion, Ipsilateral 2/10 pain between attacks "... more pronounced Horner's syndrome on the right side than usually found in cluster headache patients after an attack."	Heparin and warfarin for 3 days – attacks stopped, were replaced with 2-4/10 ipsilateral hemicrania, worse with exercise
Frigerio 2003[29]	50F Migraines and left ICAD 1 year prior with the same symptoms presenting contralaterally 3 weeks	Carotid dopplers – normal MRI w/fat sat – high cervical DAICA	Pulsating pain 1 week after onset, there started slight ipsilateral headache between cluster attacks that increased over time such that finally the attacks presented like exacerbations of a persistent dull pressure like pain O/E *during pain-free interval* – ipsilateral ptosis, meiosis, and *frontal anhydosis*	Heparin then warfarin – symptoms improved and stopped after 10 days

Mainardi 2002[25]	41F 1 month	ecoDoppler – normal MRI brain – initially interpreted as normal; subsequently reread by a neuroradiologist who identified a slight hyperintense semilunar shape at the beginning of the petrous left ICA MRI w/fat saturation – intracranial DAICA	Sudden onset of initial headache pain centered around left jaw, lasted 6 hours, associated with left ptosis and left hemipharynx pain with swallowing which persisted after the initial headache resolved and was replaced with a modest diffuse compression headache, lasted 20 days	Steroids and anticoagulation – pt had a single isolated headache 1 day later but then they stopped
Aymerich 2000[26]	48M Smoker 10 days	CTH+/–C was normal ecoDoppler and transcranial Doppler – normal MRI brain – extracranial DAICA	Continuous headache for 2 days prior to presentation	Oxygen and NSAIDs improved but did not eliminate the pain
Rosebraugh 1997[27]	34M 2 weeks	CTH – incidental venous pool. MRI brain – extracranial DAICA with occlusion. Confimed with cerebral angiogram	Visual scintillations	Acetaminophen with codeine partially relieved the pain Anticoagulated, recanalization was documented but headaches did not improve
Biousse 1994[31]	Review of 65 patients with non traumatic extracranial carotid dissection; in 2 cases the pain mimicked cluster headache	Unknown	Unknown	Unknown

CTA = CT angiogram; CTH = CT head; CVA = stroke; DAICA = dissecting aneurysm of the internal carotid artery; HTN = hypertension; ICAD = internal carotid artery dissection; MI = myocardial infarction; MRA = magnetic resonance angiogram; PWI = perfusion weighted imaging.

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