RESIDENT & FELLOW SECTION

Clinical Reasoning: A Teenager With Right-Sided Headache and Periorbital Changes

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Abstract

While migraine is the most common headache disorder in children and adolescents presenting to a neurologist, other primary headache disorders are important to recognize. Trigeminal autonomic cephalalgias represent a rare group of primary headache disorders with different characteristics, workup, and management. In this study, we present an adolescent with 1 common and 1 unique headache phenotype, followed by a guided discussion of the differential diagnoses, workup, treatments, and a brief summary of further management considerations.

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Section 1

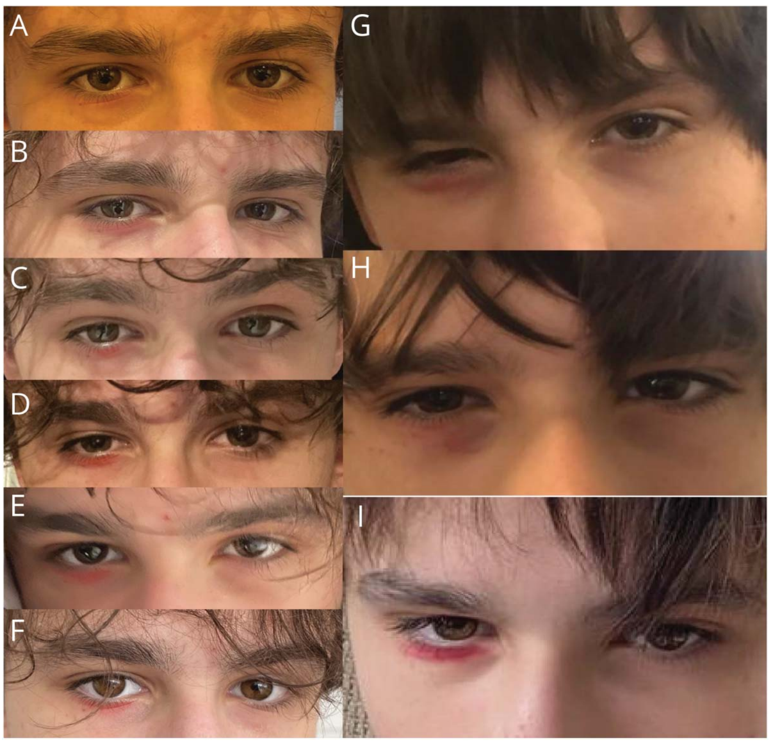
A 15-year-old right-handed adolescent boy presented with headaches since age 12 years. Headache 1 is described as rapid-onset severe right-sided supraorbital/frontotemporal sharp or stabbing pain typically starting in the morning or evening, rated as 6–9/10 in severity. Each spike lasted approximately 1 hour, followed by a briefer improvement with background pain, described as "there" before recurrence in a saw tooth pattern for a total of 2–3 days. Each initial attack began with ipsilateral eyelid edema, which transitioned after a few hours into inferior palpebral erythema through the end of the last attack. There was no conjunctival injection, tearing, ptosis, miosis, sweating, congestion, or rhinorrhea (Figure). Severe pain episodes were associated with photophobia, phonophobia, and nausea but not restlessness or agitation. Each active course occurred on average 3 times per month or as frequently as 4 times in 2 weeks in the fall and winter, less commonly in the spring and summer. There were no identified triggers, and medications containing ibuprofen, naproxen, and aspirin were ineffective.

Headache 2 is described as moderate to severe pressure around/behind the eyes lasting an average of 6 hours occurring 1–2 times/week, with associated photophobia and phonophobia without nausea, vomiting, or preceding aura. They were neither nocturnal nor triggered by Valsalva maneuvers. These headaches decrease his activity, and activity made these headaches worse. There were no obvious triggers, but attacks were responsive to over-the-counter medications. Pediatric Migraine Disability Scale score was 18. Medical history was negative, but there was a family history of migraine and reported trigeminal neuralgia in maternal grandmother. A detailed neurologic examination was normal, including sharp fundoscopic disks.

Questions for Consideration:

1. What is the initial approach for this teen with headaches?
2. Is imaging indicated?

Figure Periorbital Edema and Inferior Palpebral Erythema



(A–F) Single attack on indomethacin; (A) first attack onset; (B) 30 minutes from onset; (C) 90 minutes from onset; (D) 120 minutes from onset; (E) 17 hours from onset; (F) 18 hours from onset. (G and H) Single attack off indomethacin. (I) Notable inferior palpebral erythema.

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Section 2

The first step in evaluating children with headache is to rule out a secondary headache disorder. The following characteristics commonly referred to as "red flags" should warrant further workup in children. A common mnemonic used is $SNOOP_4Y$: Systemic signs/symptoms, Neurologic signs/symptoms, sudden Onset, Onset in sleep/early morning, Positional exacerbation, Precipitated by Valsalva, Parents (lack of family history), Progressive symptoms, and Young age.[1] Whereas migraine without red flags does not necessitate imaging, other headache types do.

The patient in the vignette presented with 2 distinct headache phenotypes. Headache 2 meets criteria for migraine without aura[2] and alone would not warrant imaging in the absence of red flags.[3] The rapid-onset relatively brief stabbing/sharp attacks of headache 1 do not meet criteria for migraine and may be manifestations of more nefarious etiologies such as neoplastic, vascular, and infectious diseases. Therefore, secondary causes must be ruled out with neuroimaging; MRI brain and MR angiography were normal.

Questions for Consideration:

1. How do we classify headache 1?
2. How do we differentiate between migraine and headache 1?

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Section 3

Headache 1 falls within the category of trigeminal autonomic cephalalgia (TAC), which are generally characterized by unilateral orbital, supraorbital, and/or temporal pain with ipsilateral autonomic features and/or agitation.[2] Whereas onset of migraine attacks are typically gradual or in a crescendo-decrescendo pattern with duration greater than 2 hours in youth, onset of TAC attacks are rapid and most are under 180 minutes. Similarly, migraine is frequently bilateral in adolescents, whereas TACs are unilateral. Another diagnostic clue is a sense of restlessness. Most children (and adults) with migraine report headache severity worsened by activity or avoid routine activities during attacks, as is included in the criteria. By contrast, patients with TACs may become restless during attacks and may not stop moving. Cluster headache (CH) is associated with agitation occasionally so severe as to elicit suicidal ideation in 55% and suicide attempt in 2% of adults in one study.[4] Fortunately, this sense of restlessness is less common in the pediatric group,[5] including this patient.

TAC includes 4 distinct primary headache disorders varying primarily in duration and frequency, as listed in the Table: hemicrania continua (HC), CH, paroxysmal hemicrania (PH), and short-lasting unilateral neuralgiform headache attacks including those with conjunctival injection and tearing and those including 1 or other cranial autonomic symptoms.[2] This patient's attack duration of greater than 30 minutes is most consistent with CH, though the frequency >8/day is more consistent with PH. However, the frequency and duration of TAC attacks in children are not always consistent with adult criteria.[5] One helpful distinction is that HC and PH criteria also include absolute prevention with therapeutic doses of indomethacin, though there have been observations that this may not be as absolute for children and adolescents. See eFigure 1 (links.lww.com/WNL/C446) for a diagnostic algorithm of TACs.

Indomethacin trial to 75 mg thrice daily for 2 weeks improved the duration and severity of attacks but did not resolve them. Because the response to indomethacin was not absolute in this patient, CH would be the most appropriate diagnosis. Indomethacin has been reported to be effective in CH, especially in children and adolescents.[6] In addition, while obtaining a more detailed family history, it was revealed that grandmother's attacks were associated with ipsilateral ptosis, likely representing a TAC rather than trigeminal neuralgia as previously believed. Positive family histories have been reported in CH[7] and other TACs.[8]

Ecchymosis and erythema have rarely been reported in adults with migraine and CH,[9] and V1 distribution erythema has been described in a child with probable CH,[10] though erythema localized to the lower eyelid seen here is unique. Autonomic symptoms are not uncommon in migraine, and some are more

Table Diagnostic Criteria for Trigeminal Autonomic Cephalalgias Based on the International Classification of Headache Disorders 3rd Edition (ICHD-3)[2]

	Hemicrania continua	Cluster headache	Paroxysmal hemicrania	Short-lasting unilateral neuralgiform headache attacks[a]
Number of attacks	At least 1 continuous attack	At least 5	At least 20	At least 20
Pain severity (and quality)	At least moderate exacerbations	Severe or very severe	Severe	Moderate to severe (stabs)
Duration	>3 mo	15–180 min	2–30 min	1–600 s
Frequency	Continuous	Every other d up to 8/d	>5/d	At least daily
One of the following associated symptoms ipsilateral to the headache		Conjunctival injection and/or lacrimation		
		Nasal congestion and/or rhinorrhea		
		Eyelid edema		
		Forehead and facial sweating		
		Miosis and/or ptosis		
OR:	Restlessness or agitation or aggravation of pain by movement	Restlessness or agitation		
Therapeutic response	Absolute response to therapeutic doses of indomethacin		Absolute response to therapeutic doses of indomethacin	

Not better accounted for by another ICHD-3 diagnosis.
[a] Subcategories include the following: short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT), which requires both conjunctival injection *and* lacrimation ipsilateral to the headache; and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA), which can have either conjunctival injection *or* lacrimation, but not both.

frequently unilateral, though are generally milder than in CH.[11] Tearing particularly is unilateral in 15.8% and bilateral in 10.7% of patients with migraine in one study, though eyelid edema and eye redness are more frequently bilateral.[12] Because autonomic changes can be unilateral in migraine, this should not be considered in isolation when differentiating between migraine and TACs. Underlying mechanisms of palpebral erythema are likely similar to other autonomic symptoms including release of vasoactive intestinal peptide, which is elevated in all CH and only migraine attacks with accompanying autonomic symptoms.[11,13]

Co-occurrence of TAC and migraine in both the patient and his grandmother has been reported in 16.7% of patients with CH in one study[14] and in 15.6% in another with a higher rate of comorbidity in those with chronic CH vs episodic CH.[15] Central sensitization or biologic correlation could account for this finding. Involvement of overlapping hypothalamic and brainstem nuclei and calcitonin gene–related peptide and pituitary adenylate cyclase–activating peptide elevation in migraine and CH indicate a potential underlying pathophysiologic mechanism.[13] Similarly, a large genome-wide association study identified 4 susceptibility loci for CH, one of which has been associated with migraine.[e1]

Question for Consideration:

1. Which management strategies should be considered?

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Section 4

Management of these distinct primary headache disorders differ: preventive medications such as amitriptyline, topiramate, or valproate may be offered to children and adolescents with migraine in which the attacks occur greater than 1–2 times/week or with a significant degree of disability.[e2] In addition, healthy habits and cognitive behavioral therapy (CBT) should be discussed.[e3] By contrast, treatment for TACs may depend on the specific subtype. Indomethacin is a reasonable first-line therapy because it could be both therapeutic and diagnostic, as reviewed earlier. In addition, because the absolute distinction is not as clear for children and adolescents, a trial of indomethacin may be advantageous, even when the diagnosis suggests an indomethacin nonresponsive headache. After discussing risks and benefits of all 3 aforementioned preventive medications for migraine, valproate titrated to 750 mg twice daily with education on healthy habits and CBT improved frequency to 2 migraine attacks per month.

For his TAC, indomethacin trial was recommended at the onset of next attacks as follows: 25 mg TID for 5 days up to 2 weeks if effective; if ineffective, increase to 50 mg TID for 5 days up to 2 weeks if effective; if ineffective, increase to 75 mg TID for 5 days up to 2 weeks with gastric protection but to no avail. High-flow oxygen was recommended at the onset of next attack to aid in diagnosis because this therapy is ineffective in all but CH but was only attempted once toward the end of an attack, so efficacy could not be established. Sumatriptan (20 mg) nasal spray and gammaCore device, a noninvasive vagus nerve stimulator, were prescribed. GammaCore (three 2-minute stimulations) was effective in alleviating an attack after which sumatriptan brought full relief. He continues to use gammaCore (two 2-minute stimulations) nightly as partial prevention, and valproate was weaned off after migraine improved. A discussion of therapies for CH and other TACs is available in eAppendix 1 (links.lww.com/WNL/C446).

While TACs are rare in children, CH begins before age 21 years in 35% of individuals in one large national survey, and delay to diagnosis is greater in youth.[4] It is therefore important to recognize clinical characteristics, initial workup, and management to prevent prolonged high grade of disability and socioeconomic burden.[e4]

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