Chronic Paroxysmal Hemicrania: A Case Report and Review of the Literature

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Chronic paroxysmal hemicrania (CPH) is a rare type of headache that is characterized by daily, multiple, short-lasting attacks of severe pain and associated autonomic symptoms. The pain is strictly unilateral and presents most commonly in the ocular, temporal, maxillary, and frontal areas. The excruciating, throbbing pain of CPH can be misdiagnosed as pain associated with dental pathology, especially when located in the maxillary area. Moreover, pain manifesting in the maxillary and temporal areas can be confused with temporomandibular disorders. CPH patients occasionally seek treatment in dental offices or orofacial pain centers. Accordingly, dentists should be familiar with CPH in order to avoid unnecessary, irreversible dental treatment. A case is presented to highlight many of the features of CPH.
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Dentists are often presented with the challenge of a dental-like pain, which arises from noxious stimulation of a distant anatomic structure. Neuropathic, vascular, or neurovascular pain that is located in the jaws may be confused with toothache.

Neurovascular headaches are characterized by intermittent, severe pain of throbbing quality and thus may mimic toothache, especially when the pain is localized to the lower face. Neurovascular headaches include migraine (with or without aura), cluster headache, and chronic paroxysmal hemicrania (CPH). CPH is a rare type of headache that was first described by Sjaastad and Dale in 1974, and is characterized by multiple, short-lasting, daily attacks of excruciating pain.[1] CPH has been well described in the medical literature; however, it is infrequently reported in the dental literature.[2–4] The dental profession should gain appreciation for this disorder to prevent misdiagnoses and unnecessary dental interventions. Moreover, diagnosing CPH can be particularly gratifying for the clinician, since CPH shows absolute responsiveness to indomethacin, and thus the patient can be quickly rendered pain-free with the appropriate pharmacologic treatment. This article describes a CPH patient who presented for treatment in an orofacial pain center.

Case Report

A 62-year-old woman presented in the orofacial pain center with a 2-year history of severe left-sided facial pain. The past medical history was positive for mitral valve prolapse and asthma. The patient reported that the pain was located in the left suboccipital and maxillary regions and sometimes in the ear, invariably on the left side. The pain was excruciating and lancinating, occurred approximately 20 times per day, lasted for about a half hour, and interrupted the patient's sleep. The pain episodes were associated with lacrimation, nasal congestion, and rhinorrhea on the symptomatic side. Previous diagnoses included trigeminal neuralgia and sinusitis. The patient had undergone left maxillary sinus surgery, which had no effect on the pain. Prior pharmacologic therapy included carbamazepine and prednisone, with no benefit. At the time she presented, she was taking 2,500 mg acetaminophen per day, which offered only partial relief of her head pain. Blood pressure, pulse rate, and body temperature were normal. No abnormalities were observed on clinical examination, including palpation of the masticatory muscles, assessment of temporomandibular joint (TMJ) function, and cervical and postural evaluation. A thorough evaluation of the oral structures did not reveal any dental, periodontal, or mucosal pathology. Neurologic examination and a magnetic resonance imaging (MRI) brain examination were read as normal. The intensity, duration, and frequency of the pain episodes, as well as the associated symptoms and the clinical examination findings met the CPH diagnostic criteria of the International Headache Society Classification (Table 1).[5] Accordingly, the patient was diagnosed with CPH and prescribed indomethacin (75 mg daily). The headaches were completely resolved in 2 days, supporting the diagnosis of CPH (Table 1).

Table 1 Section 3.2 of the International Headache Society Classification[5]

3.2 Chronic paroxysmal hemicrania
Diagnostic criteria
A. At least 50 attacks fulfilling B-E
B. Attacks of severe unilateral orbital, supraorbital, and/or temporal pain always on the same side lasting 2 to 45 minutes.
C. Attack frequency above 5 a day for more than half of the time (periods with lower frequency may occur)
D. Pain is associated with at least one of the following signs/symptoms on the pain side:
1. Conjunctival injection
2. Lacrimation
3. Nasal congestion
4. Rhinorrhea
5. Ptosis
6. Eyelid edema
E. Absolute effectiveness of indomethacin (150 mg/day or less)
F. At least one of the following:
1. History, physical and neurologic examinations do not suggest one of the disorders listed in groups 5–11
2. History and/or physical and/or neurologic examinations do suggest such disorder, but it is ruled out by appropriate investigations
3. Such disorder is present, but chronic paroxysmal hemicrania does not occur for the first time in close temporal relation to the disorder

Discussion

Chronic paroxysmal hemicrania is an uncommon headache syndrome that is included in the International Headache Society classification (Table 1).[5] It affects 7 per 10,000 individuals, and has a higher prevalence among females (female to male ratio of 2.36:1).[6] The mean age of onset is 34 years, ranging from 6 to 81 years.[7]

Clinical Features

Chronic paroxysmal hemicrania is characterized by strictly unilateral (hence the term "hemicrania") attacks of severe and short-lasting (hence the term "paroxysmal") pain that recur multiple times per day and show a dramatic response to indomethacin. The pain presents most commonly in the ocular, temporal, maxillary, and frontal regions.[6] It is less often localized in the nuchal, retro-orbital, and occipital areas.[6] Chronic paroxysmal hemicrania manifesting as otalgia accompanied by a sensation of external ear obstruction has been reported.[8] The pain is described as excruciating and has a throbbing, stabbing, or boring quality.[9,10] The frequency of pain attacks ranges from 1 to 40 per day with a median frequency of approximately 5 to 10.[9] Attacks occur around the clock and interrupt the patient's sleep.[11] Persistent soreness in the affected area between the attacks is not uncommon.[6,11] The duration of painful episodes ranges between 2 to 120 minutes with a mean of approximately 20 minutes.[6] Head flexion or rotation can precipitate the paroxysms in approximately 10% of patients, while alcohol does so in about 7%.[6]

Ipsilateral lacrimation and rhinorrhea, conjunctival injection, and nasal congestion constitute the most common coexisting signs and symptoms.[6] Other reported associated signs and symptoms include ptosis, miosis, swelling of the eyelid, overheatedness, sweating, photophobia, phonophobia,

nausea, and sensitivity of the skin on the symptomatic side.[10,11] Even though the pain is strictly unilateral, the ocular and autonomic phenomena can be bilateral, although more prominent on the affected side.[10]

Pathophysiology

The etiology of CPH is still unknown; however, several putative pathophysiological mechanisms have been proposed.

Autonomic symptoms and signs are closely associated with the pain episodes, suggesting that autonomic activation may play a role in the pathogenesis of CPH. Notably, both sympathetic (increased sweating, increased intraocular pressure) and parasympathetic (lacrimation, nasal secretion, and miosis) phenomena occur in CPH.[12] Moreover, heart rhythm disturbances, such as multiple extrasystoles and bradycardia have been reported, leading to the hypothesis that a dysfunction in the central control of the autonomic nervous system characterizes CPH attacks.[10,13] However, block of autonomic function, either by atropine administration systemically or by stellate ganglion blockade, does not alleviate the pain, indicating that autonomic disturbances do not account for CPH.[12]

Dysfunction of the hypothalamic limbic pathways has been suggested to account for the clocklike regularity of the pain episodes, while a centrally triggered neurogenic inflammation has been thought to account for the occasional bilateral manifestation of the autonomic phenomena.[10,14] Relatedly, levels of calcitonin gene-related peptide and vasoactive intestinal peptide have been shown to be elevated in the cranial circulation during attacks.[15] Neurogenic inflammation produced by local pathologic conditions is also thought to play a role, since removal of a maxillary cyst arrested the pain in 1 CPH patient.[2,16]

Genetic factors do not seem to play a role in CPH; no familial occurrence is reported.[6] Hormonal factors, on the other hand, may affect CPH. The pain attacks ceased throughout the pregnancy period in 90% of the cases, while in some patients the onset of the disorder occurred following delivery.[6]

Differential Diagnosis

Table 2 summarizes important points for the differential diagnosis of CPH.

Cluster Headache. Cluster headache (CH) is a type of neurovascular headache that can sometimes be difficult to distinguish from CPH. Cluster headache is also characterized by multiple, daily attacks of unilateral, excruciating headache that are associated with autonomic phenomena.[5] However, the CH attacks are longer-lasting, occur less frequently, and tend to occur mainly at night. Moreover, CH is characterized by a prominent male preponderance (female to male ratio 1:6) and does not exhibit the absolute response to indomethacin that characterizes CPH.

Dental Pulpal Pain. Chronic paroxysmal hemicrania exhibits several common features with pain associated with dental pathology. The short duration of the CPH pain attacks, the recurrence, the excruciating intensity that awakens the patient from sleep, and the pulsatile quality of the CPH pain can be confused with dental pulpal pain, especially when the maxillary region is involved. Localization of the CPH pain in the maxilla is not uncommon.[6] Thus, CPH patients may occasionally be misdiagnosed and undergo unnecessary, irreversible dental treatments (eg, fillings, crowns, endodontic therapy, extractions, apical surgery). Benoliel and Sharav reported on 7 CPH cases, 4 of which had been confused with pain of dental origin.[2] One of these patients had undergone extraction, and another patient had a root canal treatment. Delcanho and Graff-Radford[3] reported on a CPH patient who underwent root canal treatment, and Moncada and Graff-Radford[4] described a patient who had experienced complete mouth reconstruction. Diagnostic anesthetic blocks are of paramount importance in helping to differentiate pain of dental origin from heterotopic pains, and should be used routinely in the dental practice when jaw pain is encountered in the absence of obvious dental pathology.[17]

Temporomandibular Disorders. Chronic paroxysmal hemicrania may also be misdiagnosed as pain associated with temporomandibular disorders (TMD). A patient with CPH underwent tomograms of the TMJ.[2] Delcanho and Graff-Radford reported on a patient who had undergone arthrograms of the TMJ and had been recommended condyloplasty of the TMJ.[3] The presentation of CPH pain in the temporal and maxillary regions may contribute to the misdiagnosis. Also, manifestation of pain in the ear, as in the present case, can add to the confusion, since ear pain is often associated with TMD. Moreover, CPH patients may exhibit ipsilateral masticatory muscle tenderness.[2] The above may underlie the relatively frequent referral of CPH patients to orofacial pain clinics.[18] However, CPH is a quite distinct entity from TMD, and a detailed history of the patient's pain complaint should help the clinician to easily distinguish between them.[19]

Table 2 Differential Diagnosis of CPH

	CPH	CH	DPP	TMD	TN	Secondary CPH
Prevalence	Rare	0.40% to 0.09%	Very common	5% to 10%	0.015%	Very rare
Age of onset	30 to 40	30 to 40	After teeth eruption	5 to 60	50 to 60	Variable; depends on specific underlying disease
Female:Male ratio	2.36:1	1:6	1:1	2.5:1	3:2	Variable; depend on specific underlying disease
Localization	Oculotemporal, frontal, maxillary	Oculotemporal, frontal	Mouth, jaws cheek, ear	Jaws, temple, TMJ, ear	V2/V3 > V1	Oculotemporal, frontal, maxillary
Pain intensity	Excruciating	Excruciating	Moderate-excruciating	Mild-moderate (severe exacerbations may occur)	Excruciating	Excruciating
Pain quality	Throbbing, stabbing, boring	Throbbing, stabbing, boring	Throbbing, sharp	Dull, aching	Lancinating, stabbing	Throbbing, stabbing, boring
Pain frequency	Intermittent; 5 to 40/day	Intermittent; 1 to 8/day	Intermittent; variable	Intermittent or constant	Intermittent; variable	Intermittent; 5 to 40/day
Pain duration	2 to 120 min	15 to 180 min	Min-hours	Variable	Seconds	2 to 120 min
Associated signs	Autonomic	Autonomic	Dental caries	Limited mouth opening, TMJ sounds, deviation of jaw on opening, ear stuffiness	Facial tic	Autonomic
Precipitating factors	Alcohol, head movement	Alcohol, nitroglycerine	Heat and cold stimuli	Talking, chewing, yawning	Touch, vibration, wind	Variable; eg, bending over, coughing, straining
Interrupts sleep	Yes	Yes	Yes	No	No	Yes/No
Treatment	Prophylactic: indomethacin	Prophylactic: Verapamil, lithium, steroids; Abortive: O2, sumatriptan	Tooth restoration, endodontics	Behavioral therapy, physical therapy, splint, NSAIDs, stress reduction	Carbamazepine, baclofen, phenytoin, neurosurgery	Treatment of the underlying disease

CPH = chronic paroxysmal hemicrania; CH = cluster headache; DPP = dental pulpal pain; TMD = temporomandibular disorders; TN = trigeminal neuralgia; TMJ = temporomandibular joint; V = trigeminal nerve divisions; O2 = oxygen; NSAIDs = nonsteroidal anti-inflammatory drugs.

CPH pain has a throbbing quality and is excruciating, while TMD are characterized usually by dull pain of mild or moderate intensity.

Trigeminal Neuralgia. The excruciating intensity of CPH pain and its intermittent temporal pattern may lead to the misdiagnosis of trigeminal neuralgia (TN), especially when the pain has lancinating character, as in the present case. However, trigeminal neuralgia is characterized by shorter pain attacks that can be triggered by innocuous stimulation and are not associated with autonomic phenomena. Another important feature of TN that can effectively distinguish it from CPH is that TN typically does not interrupt the patient's sleep. Finally, carbamazepine is effective in TN, while indomethacin has no effect.

Secondary CPH. The secondary causes of CPH should also be included in the differential diagnosis. Cases of CPH associated with arteriovenous malformation, cerebral infarction, cavernous sinus meningioma, ruptured aneurysm, collagen vascular disorder, as well as benign and malignant brain tumors have been reported.[16,20–22] Accordingly, neurologic and MRI examinations should be performed in all CPH patients to rule out organic headache.[9,10]

Management

The response to indomethacin prophylactic treatment is absolute. Accordingly, a drug trial is advocated when the frequency of headache episodes is higher than 4 per day.[23] The recommended dose is 75 mg per day for 3 days, followed, if necessary, by 150 mg per day for another 3 days.[24] The usual effective dose ranges between 50 and 125 mg per day, but a high dose of 200 to 250 mg per day may be necessary to abort pain during a deterioration.[25] The pain usually disappears within 48 hours with a range of a few hours to 5 days.[6] On discontinuation, symptoms reappear within 12 hours to a few days.[11] Signs of tolerance to the indomethacin have

not been observed; in contrast, the effective indomethacin dose may decrease with time.[6,11]

Common adverse effects include dyspepsia, anorexia, nausea, and abdominal pain. To prevent gastrointestinal adverse effects, gastroprotective agents, such as histamine-2 or proton pump blockers, can be prescribed.[9] Intolerable adverse effects may necessitate the selection of an alternative drug. Salicylates may also ameliorate the symptoms, while naproxen, prednisone, ergotamine, butazolidine, diclofenac, ketoprofen, and verapamil have been reported to offer partial relief in some patients.[6,26] The reason why equipotent cyclooxygenase inhibitors are less effective than indomethacin and the mechanism underlying the dramatic response to indomethacin are currently unknown.[10]

Conclusions

It is not uncommon for CPH patients to consult a large number of doctors, and receive a variety of misdiagnoses and a plethora of failed treatments until they are correctly diagnosed.[11] Dentists as well as orofacial pain specialists should be familiar with this headache syndrome since patients occasionally seek treatment in orofacial pain centers.[18]

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