Chronic Paroxysmal Hemicrania Presenting as Toothache

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Chronic paroxysmal hemicrania is an intermittent head-pain problem that is characterized by pain paroxysms lasting about 15 minutes. The attacks usually produce pain in the frontotemporal region and are responsive to indomethacin. A set of symptoms that defines chronic paroxysmal hemicrania is presented, and two cases in which the presenting symptom was toothache are reported. It is emphasized that clinicians should consider chronic paroxysmal hemicrania in the differential diagnosis of orofacial pain.

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Most pain problems perceived in the teeth can be adequately managed by common dental techniques. However, patients may present with pain in the orofacial region that does not arise in the teeth but rather is referred from other organ systems. Such problems require specialized management, not mechanical dental interventions. To formulate a differential diagnosis when a patient presents with orofacial pain, the clinician must be familiar with all possible pain conditions that may be perceived in the orofacial region. Most of these conditions have been previously discussed in the dental literature.[1-3] Chronic paroxysmal hemicrania (CPH), a complex set of symptoms first described by Sjaastad and Dale,[4] may present in the orofacial area but has thus far not been reviewed in the dental literature. This article briefly reviews this syndrome and presents two case reports in which CPH initially presented as maxillary tooth pain.

Clinical Features

Chronic paroxysmal hemicrania is a rare, yet well-characterized,[5] chronic unilateral headache disorder, with specific inclusionary criteria as determined by the International Headache Society.[6] Clinically similar to cluster headache, but with important differences, the main features of CPH are:

1. Unilateral, intense, throbbing periorbital/temporal pain
2. Multiple attacks per day
3. Attacks of short duration
4. Chronic daily pattern of attacks, without remission
5. Female preponderance
6. Associated autonomic symptoms
7. Attacks that are mechanically precipitated by neck movements in some patients
8. Absolute response to indomethacin

Age and Gender

Age of onset of CPH is variable, with Antonaci and Sjaastad[7] finding a range of 11 to 81 years and a mean age of onset of 33.7 years. This is very similar to the age of onset in cluster headache patients.

In an early CPH review,[5] eight of the definite diagnoses and seven of the ten possible diagnoses described were made for women. This was the first remarkable difference noted when comparing the pain problem to that in Ekbom et al's classic cluster headache study,[8] in which 143 patients were male and only 20 were female. As more cases came to light, it became apparent that CPH primarily affects women, although there are definite examples of men with CPH.

The relationship of CPH to the female reproductive cycle has been studied because of this gender difference. In 10 pregnant CPH patients, a trend toward reduction of or freedom from headache was observed, but symptoms resumed immediately after parturition.[7]

Chronic paroxysmal hemicrania has also been known to begin after pregnancy. The administration of birth control pills has been shown to have no influence on the tendency of attacks, while menstruation has been shown to have both positive and negative effects on CPH attacks. There is insufficient evidence of the influence of menopause to draw any conclusions at this time.

Location and Character of the Pain

Typically, CPH patients complain of recurrent daily attacks of intense, throbbing, periorbital and/or temporal pain. These attacks of severe pain are unilateral, always occur on the same side, and run a chronic course without remission. The pain is usually located in the oculotemporal or temporal region, but it may involve the entire hemicranium, including the jaws, and so may be confused with other pain syndromes found in this region (eg, toothache). Patients with CPH have been known to have root canal therapy and even extraction of teeth in an attempt to eliminate what was felt to be the source of the pain.[3] The pain has also been reported to spread down through the neck, to the ipsilateral shoulder and arm.

Frequency of Attacks

In one study,[9] attack frequency in CPH patients has been found to vary between 4 and 38 occurrences over a 24-hour period (mean of 13.6). Another study[7] of 84 CPH patients found the mean number of attacks to be 10.8 ± 5.0 over a 24-hour period. These multiple attacks are a principal characteristic that helps differentiate CPH patients from cluster headache patients, who average only 1 to 3 attacks per day (mean 1.67) during the cluster periods.[9]

The number of pain attacks may be cyclic, with periods of increased and decreased attack frequency. These periods of relative exacerbation and remission blend into each other over weeks and months. Similarly, there is variation in the severity of the pain attacks, with transitions from mild to intense attack periods occurring gradually over a few days. When low-grade pain occurs there may be difficulty in discerning the temporal pattern of the pain. However, unlike cluster headache, clear-cut pain remission phases do not occur in CPH, although up to 42% of patients enter a remission phase in which the pain appears in more episodic clusters, rather than in the regular daily pattern.[7] The pain pattern may resemble that of both cluster and migraine headaches during this phase.

Duration of Attacks

The pain attacks of CPH generally do not last as long as those of cluster headache. Russell[9] has found the mean duration to be 13.3 minutes with a range of 3 to 46 minutes. By comparison, the same study reported cluster attacks to have a mean duration of 45 minutes. More recently, Antonaci and Sjaastad[7] have reported CPH attacks generally lasting 10 to 30 minutes (mean 20.9 minutes) with a range of 5 to 45 minutes.

Timing of Attacks

The attacks may appear at any particular time, sometimes with clockwork regularity. Russell's study[9] of CPH patients found that attacks seemed to occur mostly in the late afternoon or during the evening, with less than one third of CPH attacks occurring during sleep. It seems therefore that nocturnal pain is not as strong a feature in CPH as in cluster headaches, in which the pain characteristically awakens a patient from sleep.

Associated Symptoms

Autonomic symptoms are similar to, but generally milder than, those found in cluster headache. Such symptoms may include nasal congestion, lacrimation, conjunctival injection, rhinorrhea, ptosis, and eyelid edema on the symptomatic side. Nausea and

vomiting, which accompany many other headache types, are not seen. Sweating, another clinical characteristic seen on the symptomatic side in cluster headache, has been studied in six female CPH patients using an evaporimeter.[10] The results show only two of the six patients to have increased sweating on the symptomatic side, and it was therefore concluded that the sweating pattern seen in cluster headache is not a characteristic of CPH. Interestingly, in patients whose attacks could be precipitated mechanically, marked forehead sweating on the symptomatic side was strongly predictive that a pain attack was about to ensue.

Precipitating Factors

Mechanically precipitated attacks have been described in detail by Sjaastad et al.[11-13] Clinically the same as spontaneous attacks, these mechanical attacks were triggered by either flexion movement of the head and neck or by pressure applied to tender cervical areas. The head flexion-triggered attacks could only be induced if the head itself, and not the entire body, was bent. The pain occurred from 5 seconds to 1 minute after the stimulus, depending on the state of the individual patient. Rotating the head maximally to the symptomatic side could also precipitate such attacks. Following neck flexion in susceptible patients, the autonomic phenomena appeared many seconds ahead of the pain, thus indicating clearly that such phenomena are not due to the pain per se.[14] Alternatively, pressure to certain cervical trigger spots could immediately precipitate attacks of CPH, with the pain and autonomic phenomena appearing together. The mechanisms behind mechanical precipitation of CPH remain unclear, although the sympathetic nervous system is thought to be the primary mediator of the impulses from the neck to the ocular region. Ingestion of alcohol may also trigger CPH, as is the case in cluster headache.

Absolute Effectiveness of Appropriate Doses of Indomethacin

The rapid treatment response to indomethacin forms part of the diagnostic criteria of CPH, allowing indomethacin to be used as a diagnostic test to differentiate CPH from other headaches.

The total response to indomethacin[15] is one of the most impressive factors that identify CPH as a unique entity. The initial two patients studied by Sjaastad and Dale[4] reported acetylsalicylic acid in doses of 6 to 8 g per day as being the only medication that had any benefit prior to use of indomethacin. In both patients, the initial response to indomethacin (75 mg per day) occurred within the first 24 hours. Sometimes the patients benefit at smaller dose levels, and as little as 12.5 mg per day can be effective. The maximum required dose appears to be 250 mg. The effects of indomethacin have been reported to continue for several years after the initiation of treatment without the development of tolerance. Discontinuation of the indomethacin usually causes return of symptoms within 2 days. Jensen et al[16] have reported one patient who, after 3 months of indomethacin treatment, stopped the medication and remained pain free after 6 months.

Studies comparing various other anti-inflammatory medications found that none were any more effective than acetylsalicylic acid or as effective as indomethacin.

Laboratory Findings

The following significant findings were made via laboratory investigation. The interested reader is referred to Sjaastad[17] for a more complete discussion of CPH, including the various tests and studies thus far carried out on CPH patients.

Corneal Indentation Pulse (CIP) Amplitudes

The CIP amplitudes of CPH patients were found to be at the upper range of normal between attacks; however, the CIP amplitudes were significantly increased on the symptomatic side during attacks.[18] Marked increases in CIP amplitudes basically reflect an increase in pulsatile blood volume. Fluorescein appearance time was studied to determine if there was a change in intraocular blood flow. Almost identical fluorescein appearance time was seen in both eyes, suggesting that the amplitude change is due to local changes in ocular circulation and not to a generalized vasodilation. This is further supported by the lack of changes in internal carotid artery blood flow, blood pressure, and CSF pressure during an attack.

Intraocular Pressure

Increased intraocular pressure of 4 to 6 mm Hg has also been reported in CPH patients; this may be due to the acute vasodilation that results from the increased volume which occurs in the ocular vascular bed during pain attacks.

Pupillometry

Patients with CPH tend to have a relatively small pupil on the symptomatic side, but pupillometric studies have not shown that a specific sympathetic deficit is present. By contrast, patients suffering from cluster headache often present with an associated Horner's syndrome.

Blood Tests

Many tests were performed, but all were found to be within normal limits. No significant alterations in any of the blood coagulation factors were found in patients with CPH.

Urinary Histamine Excretion

Histamine has been closely associated with pathogenesis of cluster headache and therefore was studied in the CPH patients. No good correlation between the degree of histamine excretion and the severity of the attacks could be observed.

Proposed Mechanisms

Since the establishment of this relatively new headache entity, many physiologic parameters have been studied in CPH patients to better understand and evaluate the mechanisms that could be responsible. Particularly the work of Ottar Sjaastad, these studies have led to speculation that CPH symptoms are mediated either by autonomic impulses or vascular factors. The latter could be associated with either occlusion of arterial flow in the carotid or vertebral arteries, which may occur during head rotation or flexion, or vasoactive substances released from cerebral (or neck) blood vessels.

It has thus been theorized that mediation of CPH symptoms is via the blood vessels and/or autonomic impulses. Based on the response to the anti-inflammatory medication indomethacin, it has been suggested that the source of the pain in CPH is an active neurogenic inflammatory process involving prostaglandins and vasoactive algesic substances, such as bradykinin and histamine. However, this would not account for the changes seen in the CIP amplitudes, the regular pattern of CPH attacks, or the lack of response to other anti-inflammatory medications. The fact that CPH attacks can be precipitated with mechanical manipulation, without any refractory time between the manipulation and the onset of the autonomic signs, does not support the hypothesis that there is a blood-borne substance released from the ipsilateral carotid artery. The unilaterality of CPH is also difficult to explain by this proposed mechanism.

Cerebral angiography studies have failed to elucidate any consistent finding that may produce traction on the blood vessels and so stimulate release of vasoactive substances that can mediate pain. Nor was any evidence found of external compression of either the internal or common carotid arteries, effectively disproving the hypothesis that reduced cerebral blood flow subsequent to arterial compression is the cause of the headache.

A conflicting hypothesis suggests that changes in cerebral blood flow patterns related to the opening of arteriovenous anastomoses may result in pain. This hypothesis is based on the finding that reduction in cerebral blood flow is known to occur with administration of indomethacin.[19] By exclusion, it seems the most likely cause for precipitation of attacks is via the autonomic nervous system. The sympathetic system is most likely involved, as the parasympathetics to the end organs are hardly affected when the head is flexed. Sjaastad[17] has concluded that in CPH it was most likely that pain and autonomic phenomena are triggered in parallel.

Case 1

A 53-year-old white woman presented with the complaint of an intermittent sharp pain that was localized in the left maxillary and temporal regions. The pain was described as occurring several times a day and was often associated with tearing in the ipsilateral eye and sweating.

History

The pain attacks were initially felt as pain in the upper premolar area, prompting the patient to visit her dentist. The dentist proceeded to perform root canal treatment on the premolar, which did not substantially reduce the pain. The patient then consulted numerous physicians, including internal medicine and neurologic specialists, and was eventually diagnosed as suffering from migraine. Trials using a number of migraine prophylactic medications, including propranolol and amitriptyline, were attempted without any benefit. The patient reported that her pain had been most successfully reduced by the use of 6 to 12 aspirin per day. The pain could be triggered by the patient extending her head up and back, as would occur when the patient reached to get a teacup from a cupboard

located above her head. The pain had also been noted to be worse during cold weather.

Examination

The medical history revealed a family history of migraine, and the patient reported a previous history of some intermittent migrainous symptoms. The review of systems was within normal limits. Psychosocial questioning revealed a happily married woman with two children and no major stressors or financial problems. The Minnesota Multiphasic Personality Inventory (MMPI) was administered and the scales were found to be unelevated. The dental, stomatognathic, myofascial, cervical spine, and cranial nerve examinations were all within normal limits.

Impressions

The intermittent chronic nature of the attacks, occurring several times a day with associated autonomic features and triggerable by certain head movements, led to a preliminary diagnosis of CPH. The fact that only aspirin had been helpful was also suggestive of CPH. The patient was started on a trial of 25 mg of indomethacin three times per day. The patient called 48 hours later to advise that she was pain free. The initial controlling dose was found to be 125 mg per day, but she is now being maintained on 25 mg without any side effects. The patient has found that the longest she can stay off the indomethacin is 7 days before her symptoms will return.

Case 2

A 67-year-old, retired white man presented with the complaint of intermittent daily attacks of pain that was localized to the maxillary molar area. The pain was described as feeling as if a dentist were drilling the tooth without using local anesthesia. The attacks generally lasted 10 to 20 minutes, occurred regularly in the afternoon and then during the night, and occasionally woke him from sleep.

History

These pain attacks had been present over a 3-year period and no triggers had been identified that would precipitate the attacks. There were no associated autonomic symptoms with the pain. When asked if anything aggravated the pain, the patient reported that stress could be a factor. Aspirin was the only alleviating factor described by the patient and was also reported to help stave off an attack. The patient had initially thought the pain was of dental origin and so had consulted a dentist, who failed to find any dental pathology. A physician thought that trigeminal neuralgia was a possibility and prescribed Dilantin (100 mg three times a day), but this failed to produce any relief from the attacks. The patient was referred to a neurosurgeon, who thought trigeminal neuralgia was an unlikely diagnosis, and was then referred on to an otolaryngologist. The ensuing examination, together with sinus radiography, proved negative for pathology, and it was suggested to the patient that perhaps a temporomandibular joint (TMJ) problem was present. The patient then consulted a second dentist, who felt the problem was unlikely to be related to TMJ, and was referred to the Cedars-Sinai Anesthesia Pain Center.

Examination

The medical history and review of systems were all within normal limits. Dental, stomatognathic, myofascial, cervical spine, and cranial nerve screening examinations were negative or within normal limits. Psychosocial questioning was negative for possible depression and did not reveal a need for psychometric evaluation.

Impressions

Assessment of the chronic nature of the attacks, combined with the unilaterality, regularity, duration, and lack of remission periods or triggers, led to a preliminary diagnosis of CPH. It was therefore thought that indomethacin trial may be helpful, and the patient was started on 75 mg indomethacin SR per day, which was increased to 75 mg twice per day after 4 days. One week later the patient reported total relief from the attacks. One month later he was still free of pain and was being maintained on 75 mg indomethacin SR per day.

Discussion

Chronic paroxysmal hemicrania is a rare head pain syndrome, but one that should be considered in the differential diagnosis of throbbing or boring pain in the maxillary region. This is particularly so where there is a chronic daily pattern of multiple pain attacks of short duration. Dental pathology should be ruled out first, and the use of local anes-

Table 1 Organ System Classification of Headache Problems That Present as Toothache[3]

Organ system	Diagnosis	Presence	Quality
Intracranial	Infarct	Continuous	Steady, dull
	Tumor	Intermittent	Steady, dull
Extracranial	Sinusitis	Continuous	Dull
Musculoskeletal	Myofascial pain	Continuous	Dull, aching
Neurovascular	Migraine	Intermittent	Throbbing
	Cluster	Intermittent	Throbbing
	Chronic paroxysmal hemicrania	Intermittent	Throbbing
Neurogenic	Trigeminal neuralgia	Intermittent	Sharp, shooting
	Pretrigeminal neuralgia	Continuous	Dull, aching
Sympathetic nervous system	Atypical odontalgia	Continuous	Dull, burning
Psychogenic	Psychogenic pain	Variable	Variable

thetic blocks may be required to ascertain that the pain is not pulpal in origin. The presence of intermittent throbbing pains that are not dental in origin is generally suggestive of a neurovascular disorder (Table 1). Sinus, myofascial, and TMJ problems are also far more common than CPH and should be ruled out by the appropriate diagnostic procedures.

The chronic, unremitting nature of the attacks, which are often associated with autonomic signs such as lacrimation, nasal stuffiness, conjunctival injection, and rhinorrhea, should alert the clinician to the possibility of CPH. An indomethacin trial is the best test for establishing the diagnosis of CPH, with a lack of response effectively ruling out CPH. Sjaastad[17] has utilized indomethacin trial to rule out CPH whenever headache attack frequency exceeds 4 occurrences in a 24-hour period. It should be noted that cerebrovascular disease and other intracranial pathology may cause headache with similar features to CPH, and neuroimaging is recommended wherever CPH-type symptoms are present.[20]

The indomethacin effect, although absolute, is dose dependent, and the dose should be titrated for each patient. For an indomethacin trial start the patient with 75 mg per day and increase by 25 mg every 3 days, up to a maximum of 250 mg. If no effect is noted within a few days, a CPH diagnosis can be virtually excluded. The indomethacin should be taken with food to reduce the possibility of gastric side effects. For those patients in whom gastric side effects are significant, the use of either the sustained release preparation or suppositories may be helpful. However, these preparations result in lower blood levels, and higher doses may be required for equivalent effects to be achieved. If a positive effect occurs, the dosage can be varied up (to a maximum 250 mg per day) or down to find a maintenance dose that keeps the patient headache free. The cyclic nature of CPH should be kept in mind, recognizing that the patient may enter a period of exacerbation that requires dosage readjustment. Tolerance does not seem to occur, indeed it has been reported that the amount of drug required may even decrease over time.[21]

Conclusion

Little is known about the nature of this uncommon facial pain condition, other than it is controlled by indomethacin. At this stage the basis for the absolute effect of this medication is unknown. Any proposed mechanism presented at this time to explain CPH is also speculative.

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Resumen

Hemicráneo Paroxístico Crónico Presentado como una Odontalgia

El hemicráneo paroxístico crónico es un problema de cefalea intermitente caracterizado por paroxismos de dolor de 15 minutos de duración, aproximadamente. Los ataques están localizados usualmente en la región frontotemporal y responden al uso de la indometacina. Se presenta un grupo de síntomas que definen el hemicráneo paroxístico crónico; también se reportan dos casos en los cuales se presentó la odontalgia como síntoma. Se enfatiza el hecho de que los clínicos deberían considerar el hemicráneo paroxístico crónico en el diagnóstico diferencial del dolor orofacial.

Zusammenfassung

Zahnschmerzen als Symptom von chronischer paroxysmaler Hemikranie

Chronische paroxysmale Hemikranie (CPH) ist ein schubweise verlaufender Typ von Kopfschmerzen, der durch ca. 15 Minuten andauernde Schmerzattacken im frontotemporalen Bereich charakterisiert. Typischerweise spricht die CPH auf Indomethacin-Therapie an. Dieser Artikel umfasst eine Literaturdurchsicht über die Symptome der CPH und berichtet über zwei Fälle, bei denen Zahnschmerzen im Bereich der Oberkieferprämolaren und -molaren das Hauptsymptom waren. Die Autoren weisen darauf hin, dass die CPH in die Differentialdiagnose orofacialer Schmerzen miteinbezogen werden muss.