

CLINICAL CORRESPONDENCE

Cluster headache after dental extraction: implications for the pathogenesis of cluster headache?

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Introduction

Cluster headache (CH) is a disorder of unilateral attacks of severe periorbital, supraorbital or temporal pain, lasting 15–180 min (1). In general, attacks are accompanied by autonomic symptoms, i.e. ipsilateral miosis, lacrimation, conjunctival injection, nasal congestion and rhinorrhea. The episodic form of CH, found in about 80% of all CH patients, is characterized by its distinct temporal pattern. One to 8 headache attacks per day occur during bouts lasting 2 weeks to 3 months, followed by remission for months or years. Along with migraine and other rare hemicranias, CH is regarded as a primary headache disorder. More than 250 years after the first known description of CH by van Swieten (2), the pathophysiology of this disorder is still controversial. Recent brain imaging studies demonstrated the activation of the ipsilateral hypothalamus during a CH attack (3). Moreover, morphological enlargement of the hypothalamus found in CH sufferers suggests an inborn predisposition for the development of CH (4).

In this report, we present two patients who developed ipsilateral CH shortly after the extraction of an ipsilateral molar tooth. We review the literature on CH associated with head trauma or structural brain lesions and discuss the implications of these cases for the pathogenesis of CH.

Case reports

Patient 1

In a 48-year-old man, the left upper third molar tooth was extracted in August 1995 because it was impacted and future complications were expected by his dentist. Before the extraction, the patient had always been free of headache or dental pain. The extraction was not followed by infection or peripheral nerve lesion. Two weeks later, strictly left-sided, severe headache attacks of

predominantly retroorbital and infraorbital localization occurred, previously unknown to the patient. The headache attacks were associated with injection and, less frequently, lacrimation of the left eye, as well as congestion of the left nasal concha. In general, 1–3 headache attacks per day occurred without remissions longer than 1 week. The duration of individual headache attacks was approximately 1 h but could exceed more than 6 h, especially during times of high attack frequency. Headache attacks occurred more often during the night, but also during daytime while working as a crane driver.

Symptomatic headache was suspected, but further diagnostic efforts including computed tomography did not reveal any underlying lesion. Finally, the patient was admitted to our headache outpatient clinic where chronic CH was diagnosed, i.e. diagnosis 3.1.3 of the International Headache Society (IHS) (1).

Neurological examination, electroencephalogram (EEG) and cranial magnetic resonance imaging (MRI) were normal. The patient was a heavy smoker since adolescence. He had suffered from 2 myocardial infarctions in the last 5 years. The family history was negative regarding CH or migraine.

The inhalation of oxygen terminated the CH attacks and the prophylactic treatment with verapamil reduced their frequency. No CH attack occurred during a cortisone treatment starting with 100 mg prednisolone per day and tapering down to 5 mg per day. CH attacks recurred, however, 3 days after stopping prednisolone therapy. A prophylactic treatment combining verapamil and lithium carbonate led to a long-lasting reduction in the frequency of CH attacks.

Patient 2

A 47-year-old woman had an extraction of her first right lower molar tooth in June 1999 due to dental caries. Two weeks later she developed strictly right-sided, severe

headache attacks of periorbital localization, previously unknown to the patient. The headache attacks were accompanied by lacrimation and rhinorrhea. The attacks occurred mostly during the night or in the morning and lasted between 30 min and 1 h. The frequency of the attacks varied from one attack within a few days up to 3 attacks per day. Remissions lasted no longer than 1 week. A further dental examination led to an endodontic treatment of the root of the right lower canine tooth in September 1999. Since the headache attacks did not resolve, the patient was admitted to our headache outpatient clinic. We diagnosed chronic CH, i.e. diagnosis 3.1.3 of the IHS (1).

The neurological examination was normal with the exception of slight pain on pressure at the right infraorbital foramen. The EEG and the cranial MRI did not reveal any abnormalities. Before the start of CH in 1999, the patient suffered from infrequent migraine attacks with mainly occipital headache and with visual aura, i.e. diagnosis 1.2 of the IHS (1).

CH attacks stopped 1 week after the beginning of prophylactic treatment with 240 mg verapamil. In November 2000 CH attacks returned with a frequency of 1–2 attacks per week. Verapamil was then increased to 320 mg per day. This led to a reduction of attack frequency and duration. The patient tried to pause verapamil several times since the start of the therapy. Three to seven days after termination of the therapy with verapamil, CH attacks recurred. Due to the rapid success of the prophylactic medication, the patient did not make use of oxygen inhalation for the acute treatment.

Review of the literature

Although CH is regarded as a primary headache disorder, there are several case reports in the literature suspecting symptomatic or secondary CH or CH-like headache. Some case studies describe CH patients with ipsilateral arteriovenous (AV) malformations (5, 6). In one patient, strictly right-sided CH changed to the left side after embolization of an AV malformation mainly supplied by the left anterior cerebral artery (7). Moreover, dissections of the internal carotid (8) or vertebral artery (9), aneurysms of the vertebral artery (10) or of the intracranial arteries (11) and a pseudoaneurysm of the cavernous sinus (12) were found in patients with CH.

Some patients with CH revealed intracranial neoplasms, e.g. an adenoma of the pituitary gland (13) or cerebral (14, 15) and upper cervical meningiomas (16). In a few cases, subdural haematoma (17), aspergillus infection (18), herpes zoster ophthalmicus (19), or nasopharyngeal carcinoma encircling the internal carotid artery (20) were found in CH sufferers. There are at

least 4 reports covering 6 male patients who developed ipsilateral CH after the enucleation of an eye (21–24). The latency between enucleation and CH onset ranged between 3 weeks (21) and 18 years (23). In some patients, symptomatic CH was diagnosed since CH resolved immediately after the successful treatment of brain tumours (13–15), an AV malformation (5, 6), a vertebral artery aneurysm (10), or an impacted wisdom tooth (25).

The limited value of some of these case studies must be kept in mind. Some reports do not meet the IHS criteria for the diagnosis of CH either because of the long duration of attacks (26) or the absence of typical autonomic symptoms (27, 28). In others, the temporal relationship between CH and structural lesions is not known (e.g. patient no. 1 in Greve and Mai, 11) or the time between trauma and development of CH is very long (e.g. 18 years in Prusinski *et al.*, 23).

Discussion

In this report, we describe the development of ipsilateral chronic CH shortly after the extraction of a molar tooth in two patients. Both patients fulfil the IHS diagnostic criteria of CH (1). In both patients, aged 48 and 47 years, respectively, the onset of CH is remarkably late in life. According to a large epidemiological study, the average age for the onset of episodic CH is 29 years and for chronic CH unremitting from onset is 37 years (29). It is well known that many patients with CH are misdiagnosed as having symptomatic headache due to dental disease. This often leads to unnecessary and ineffective dental therapies, in some cases even to the extraction of several teeth (30). In our patients, short-lasting unilateral headache attacks were definitely unknown before the tooth extraction and were clearly not the reason for the extraction.

All case reports, including the one presented here, face the difficult question whether there is a true causal relation between or a mere coincidence of CH and the structural lesion. The epidemiology of CH and of dental extractions seems to suggest a mere coincidence: The prevalence of CH is less than 1 per 1.000, the incidence around 1 per 10.000 per year (31, 32). The annual number of dental extractions, in contrast, is considerably higher (33). In the patients presented in this report, and in the patient with CH after enucleation of the ipsilateral eye, previously published by our group (21), we nevertheless suggest the diagnosis of 'secondary' CH because of the following characteristics: (a) The headache disorder exactly meets the IHS criteria for CH (b) the headache attacks are responsive to standard acute and prophylactic treatment of CH (c) CH attacks are ipsilateral to the

structural lesion and (d) a close temporal relation between the development of the structural lesion and the onset of CH exists.

The clinical presentation of patients with secondary CH seems to be very similar to those suffering from primary CH. This is true with respect to the frequency and duration of attacks, the autonomic symptoms, the male/female ratio and, particularly, the prompt effectiveness of acute and prophylactic treatment. However, a decisive difference between secondary and primary CH seems to exist. The majority of patients with secondary CH, including the ones presented here, have chronic CH (10, 11 (1 patient), 12, 13, 15, 19, 24 (2 patients), 34 (4 patients) as opposed to episodic CH (6, 9, 11 (1 patient) 21–23, 24 (1 patient), 25). In patients with primary CH, 82% have episodic and 11% chronic CH (29).

Recently, the hypothalamus was found to play a central role in the pathophysiology of CH. Functional brain imaging revealed activation of the ipsilateral hypothalamic grey matter during a CH attack (3). Moreover, the hypothalamus is morphologically enlarged in patients with CH pointing at a possible predisposition for the development of CH (4). The association between head trauma or structural brain disease and CH suggest that additional environmental cofactors are important for the onset of CH. This notion is strengthened by large epidemiological studies demonstrating a high incidence of previous head trauma in patients with CH (29–36). Of 374 males with CH, 13% had suffered from a head injury with loss of consciousness and 24% without loss of consciousness (29). Due to the long duration between preceding head trauma and CH onset (10 years on average), the trauma cannot merely be regarded as a trigger of CH but rather as a cofactor in CH's pathogenesis.

While there is considerable clinical evidence for an association between brain or head lesions and the development of CH, the crucial question is still undetermined: How could a head injury or a structural brain disease contribute to the development of CH? Most patients described in the literature had a lesion of richly innervated tissues, i.e. vessels, meninges, eyes, or teeth. As far as we know, there is no reported case of secondary CH due to glioma. The two patients presented here started with CH after the extraction of a molar tooth which is richly innervated by unmyelinated C fibres (37). These C fibres project to the trigeminal subnucleus caudalis of the brainstem. Experimental tooth pulp denervation is known to result in a hyperactivity and in expanded receptive fields of neurones in the trigeminal nuclei (38). Reorganizational changes start within minutes or days after deafferentation of teeth (39) or of limbs (40). However, phantom limb pain, a common complication of limb amputation and phantom tooth

pain do not necessarily begin immediately after amputation or tooth extraction (41, 42). The delayed onset of phantom pain suggests that, in many patients, reorganizational changes need to evolve until they have perceptual consequences. Similar mechanisms might be involved in the development of CH in our patients and could explain why CH started with a latency of 2 weeks after dental extraction. It might be possible that the ongoing reorganization of spinal and brain stem networks induced by the irritation or deafferentation of C fibres contributed to hypothalamic reorganization, a structure regarded as the anatomical basis of CH's pathophysiology.

References

1. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia* 1988; 8 Suppl 7:1–92.
2. Isler H. Episodic cluster headache from a textbook of 1745: van Swieten's classic description. *Cephalalgia* 1993; 13:172–4.
3. May A, Bahra A, Büchel C, Frackowiak RSJ, Goadsby PJ. Hypothalamic activation in cluster headache attacks. *Lancet* 1998; 352:275–8.
4. May A, Ashburner J, Büchel C, McGonigle DJ, Friston KJ, Frackowiak RS et al. Correlation between structural and functional changes in an idiopathic headache syndrome. *Nat Med* 1999; 5:836–8.
5. Mani S, Deeter J. Arteriovenous malformation of the brain presenting as a cluster headache – a case report. *Headache* 1982; 22:184–5.
6. Muñoz C, Tejedor-Díez E, Frank A, Barreiro P. Cluster headache syndrome associated with middle cerebral artery arteriovenous malformation. *Cephalalgia* 1996; 16:202–5.
7. Gawel MJ, Willinsky RA, Krajewski A. Reversal of cluster headache side following treatment of arteriovenous malformation. *Headache* 1989; 29:453–4.
8. Rosebraugh CJ, Griebel DJ, DiPette DJ. A case report of carotid artery dissection presenting as cluster headache. *Am J Med* 1997; 102:418–9.
9. Cremer PD, Halmagyi GM, Goadsby PJ. Secondary cluster headache responsive to sumatriptan. *J Neurol Neurosurg Psychiatry* 1995; 59:633–4.
10. West P, Todman D. Chronic cluster headache associated with a vertebral artery aneurysm. *Headache* 1991; 31:210–2.
11. Greve E, Mai J. Cluster headache-like headaches: a symptomatic feature? A report of three patients with intracranial pathologic findings. *Cephalalgia* 1988; 8:79–82.
12. Koenigsberg AD, Solomon GD, Kosmorsky G. Pseudoaneurysm within the cavernous sinus presenting as cluster headache. *Headache* 1994; 34:111–3.
13. Tfelt-Hansen P, Paulson OB, Krabbe A. Invasive adenoma of the pituitary gland and chronic migrainous neuralgia. A rare coincidence or a causal relationship? *Cephalalgia* 1982; 2:25–8.
14. Hannerz J. A case of parasellar meningioma mimicking cluster headache. *Cephalalgia* 1989; 9:265–9.

15. Taub E, Argoff CE, Winterkorn JMS, Milhorat TH. Resolution of chronic cluster headache after resection of a tentorial meningioma: case report. *Neurosurgery* 1995; 37:319–22.
16. Kuritzky A. Cluster headache-like pain caused by an upper cervical meningioma. *Cephalalgia* 1984; 4:185–6.
17. Formisano R, Angelini A, De Vuono G, Calisse P, Fiacco F, Catarci T. Cluster-like headache and head injury: case report. *Ital J Neurol Sci* 1990; 11:303–5.
18. Heidegger S, Mattfeldt T, Rieber A, Wikstroem M, Kern P, Kern W et al. Orbito-sphenoidal *Aspergillus* infection mimicking cluster headache: a case report. *Cephalalgia* 1997; 17:676–9.
19. Sacquegna T, D'Alessandro R, Cortelli P, De Carolis P, Baldrati A. Cluster headache after herpes zoster ophthalmicus. *Arch Neurol* 1982; 39:384.
20. Appelbaum J, Noronha A. Pericarotid cluster headache. *J Neurol* 1989; 236:430–1.
21. Evers S, Sörös P, Brilla R, Gerding H, Husstedt IW. Cluster headache after orbital exenteration. *Cephalalgia* 1997; 17:680–2.
22. McKinney AS. Cluster headache developing following ipsilateral orbital exenteration. *Headache* 1983; 23:305–6.
23. Prusinski A, Liberski PP, Szulc-Kuberska J. Cluster headache in a patient without an ipsilateral eye. *Headache* 1985; 25:134–5.
24. Rogado AZ, Graham JR. Through a glass darkly. *Headache* 1979; 19:58–62.
25. Romoli M, Cudia G. Cluster headache due to an impacted superior wisdom tooth: case report. *Headache* 1988; 28:135–6.
26. Herzberg L, Lenman JAR, Victoratos G, Fletcher F. Cluster headaches associated with vascular malformations. *J Neurol Neurosurg Psychiatry* 1975; 38:648–9.
27. Hindfelt B, Olivecrona H. Cerebral arteriovenous malformation and cluster-like headache. *Headache* 1991; 31:514–7.
28. Testa D, Frediani F, Bussone G. Cluster headache-like syndrome due to arteriovenous malformation. *Headache* 1988; 28:36–8.
29. Manzoni GC. Cluster headache and lifestyle: remarks on a population of 374 male patients. *Cephalalgia* 1999; 19:88–94.
30. Bittar G, Graff-Radford SB. A retrospective study of patients with cluster headaches. *Oral Surg Oral Med Oral Pathol* 1992; 73:519–25.
31. Krogh Rasmussen B. Epidemiology of cluster headache. In: Olesen J, Goadsby PJ, editors. *Cluster Headache and Related Conditions* Oxford: Oxford University Press, 1999:23–6.
32. Swanson JW, Yanagihara T, Stang PE, O'Fallon WM, Beard CM, Melton LJ et al. Incidence of cluster headaches: a population-based study in Olmsted County. *Minnesota Neurology* 1994; 44:433–7.
33. Angelillo IF, Nobile CG, Pavia M. Survey of reasons for extraction of permanent teeth in Italy. *Community Dent Oral Epidemiol* 1996; 24:336–40.
34. Reik L. Cluster headache after head injury. *Headache* 1987; 27:509–10.
35. Italian Cooperative Study Group on the Epidemiology of Cluster Headache. Case-control study on the epidemiology of cluster headache. I. Etiological factors and associated conditions. *Neuroepidemiology* 1995; 14:123–7.
36. Manzoni GC, Terzano MG, Bono G, Micieli G, Martucci N, Nappi G. Cluster headache – clinical findings in 180 patients. *Cephalalgia* 1983; 3:21–30.
37. Närhi M. The neurophysiology of the teeth. *Dent Clin North Am* 1990; 34:439–48.
38. Sessle BJ. The neurobiology of facial and dental pain: present knowledge, future directions. *J Dent Res* 1987; 66:962–81.
39. Kwan CL, Hu JW, Sessle BJ. Effects of tooth pulp deafferentation on brainstem neurons of the rat trigeminal subnucleus oralis. *Somatosens Mot Res* 1993; 10:115–31.
40. Calford MB, Tweedale R. Immediate and chronic changes in responses of somatosensory cortex in adult flying-fox after digit amputation. *Nature* 1988; 332:446–8.
41. Ramachandran VS, Hirstein W. The perception of phantom limbs. *Brain* 1998; 121:1603–30.
42. Marbach JJ. Is phantom tooth pain a deafferentation (neuropathic) syndrome? Part I. Evidence derived from pathophysiology and treatment. *Oral Surg Oral Med Oral Pathol* 1993; 75:95–105.