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Cluster headache: expansion of the clinical spectrum

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Chapter 5

Cluster-tic syndrome: a cross-sectional study of cluster headache patients

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Abstract

Objective

To determine the prevalence and nature of trigeminal neuralgia in a large group of cluster headache patients.

Background

Cluster-tic syndrome is a rare headache syndrome in which trigeminal neuralgia and cluster headache co-occur. The existence of cluster-tic syndrome as a separate entity is questioned, and figures on prevalence of simultaneous existence of cluster headache and trigeminal neuralgia are not available.

Methods

As part of a nationwide study on headache mechanisms in cluster headache (LUCA), we collected clinical data of 244 cluster headache patients using a semi-structured telephone interview in a cross-sectional design.

Results

In 11 (4.5%) of cluster headache patients, attacks fulfilling International Headache Society criteria for trigeminal neuralgia were also present. In all cases trigeminal neuralgia occurred ipsilateral to cluster headache and in the majority (82%) in the ophthalmic branch. In eight of these eleven patients (73%) the frequency and time-pattern of trigeminal neuralgia seemed to parallel cluster headache and was likely a part of the cluster headache spectrum. In the three remaining patients cluster headache and trigeminal neuralgia were unrelated in time and appeared to occur independently.

Conclusion

Trigeminal neuralgia co-occurred in 11/244 (4.5%) of cluster headache patients. In only 3 (1.2%) patients trigeminal neuralgia seemed to occur independently from cluster headache episodes. Trigeminal neuralgia (-like) attacks in cluster headache patients are most of the time part of the cluster headache spectrum and should then probably not be treated separately. A shared underlying pathophysiological mechanism of cluster headache and trigeminal neuralgia is not supported by this study.

INTRODUCTION

The cluster-tic syndrome is characterized by the co-existence of cluster headache and trigeminal neuralgia and has been described in single case reports and small case series only. (1-12) Cluster headache consists of attacks of severe, strictly unilateral, (supra)orbital, or temporal pain lasting 15-180 minutes, accompanied by facial autonomic symptoms and/or restlessness (table 1). (13-15) Trigeminal neuralgia is characterized by stereotyped, brief (seconds to minutes) attacks of sharp or stabbing pain within the distribution area of one or more branches of the trigeminal nerve, usually the second and third branches which may come spontaneously or after specific triggers (table 1). (13;16)

Cluster-tic syndrome is described very heterogeneously in the literature and it is still questioned whether it is to be seen as a separate syndrome. The term 'cluster tic syndrome' was introduced in 1978 in an abstract (8). From this abstract it is not clear if the author described two different types of attacks in one patient, or that these patients suffered from one type of attack having features of both cluster headache and trigeminal neuralgia. As a consequence the term 'cluster tic' has been used to describe both conditions. Mostly it is used for the co-occurrence of attacks of cluster headache and trigeminal neuralgia within the same patient. Previously we suggested that trigeminal neuralgia and cluster headache only co-occur by chance.(2) Others, however, have stated that this co-occurrence is not coincidental and that attacks of cluster headache and trigeminal neuralgia are caused by the same underlying pathophysiological mechanism (3;4;6;9) or that short-lasting attacks can be part of the cluster headache spectrum and should not receive a separate diagnosis.(10) Lastly, it is asserted that the cluster-tic syndrome is a separate entity consisting of three types of attacks; trigeminal neuralgia attacks, cluster headache attacks and mixed attacks. A single lesion affecting the trigeminal sensory pathway with involvement of both myelinated and unmyelinated fibres, is hypothesised to be the underlying mechanism of cluster-tic.[1] The headache classification of the International Headache Society (ICHD-II) mentions cluster-tic syndrome as a note in the cluster headache section. It defines cluster-tic syndrome as the co-occurrence of trigeminal neuralgia and cluster headache and advises that these patients should receive both diagnoses, because these two types of

attacks each need separate treatments.(13) The objective of our study was to determine the prevalence and nature of trigeminal neuralgia in a large group of cluster headache patients.

METHODS

Dutch cluster headache patients of 18 years or older were recruited via a headache website as part of a large nationwide research project that aims at the study of headache mechanisms in primary headache disorders, of which LUCA (Leiden University Medical Centre Cluster headache Neuro Analysis programme) is the cluster headache part. It is also partly a follow-up of the RUSSH (Rare Unilateral Severe and Short-lasting Headaches) study that started in 1998. The RUSSH study database contains data on 3472 self-reported patients with cluster headache and other unilateral, short lasting headaches, and these patients were invited by regular mail to participate in the present study.(17) In LUCA, subjects were asked to fill out an extended questionnaire on cluster headache, including the International Headache Society (ICHD-II) criteria.(13)

For the LUCA study, we conducted a semi-structured telephone interview to confirm the cluster headache diagnosis.(18) We asked additional specific questions on trigeminal neuralgia if patients had reported to experience very short attacks of unilateral, facial pain next to cluster headache attacks. These questions were about the nature of the pain, frequency, duration, involved trigeminal division and triggers. For both conditions, cluster headache and trigeminal neuralgia, criteria of the ICHD-II were used (table 1).(13)

A tentative diagnosis of "cluster headache" and "trigeminal neuralgia" was first made by the interviewer (CC) and then confirmed, in consultation with one of the study physicians (LAW and CMW) or neurologist (JH).

All participants who met the ICHD-II criteria for both cluster headache and trigeminal neuralgia were telephonically approached for a second interview by the interviewer (CC). In this interview questions were asked to further elucidate the symptoms of trigeminal neuralgia, the relation with cluster headache treatment, and temporal relation to cluster headache attacks.

Table 1. Diagnostic criteria for Trigeminal Neuralgia and Cluster headache from the International Headache Society (13)

Trigeminal neuralgia
A. Paroxysmal attacks of pain lasting from a fraction of a second to 2 minutes, affecting one or more divisions of the trigeminal nerve and fulfilling criteria B and C
B. Pain has at least one of the following characteristics:
1. intense, sharp, superficial or stabbing
2. precipitated from trigger areas or by trigger factors
C. Attacks are stereotyped in the individual patient
D. There is no clinically evident neurological deficit
E. Not attributed to another disorder
Cluster headache
A. At least 5 attacks fulfilling criteria B–D
B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes if untreated
C. Headache is accompanied by at least one of the following:
1. ipsilateral conjunctival injection and/or lacrimation
2. ipsilateral nasal congestion and/or rhinorrhoea
3. ipsilateral eyelid oedema
4. ipsilateral forehead and facial sweating
5. ipsilateral miosis and/or ptosis
6. a sense of restlessness or agitation
D. Attacks have a frequency from one every other day to 8 per day
E. Not attributed to another disorder

Baseline characteristics of participants who were successfully interviewed and participants who were not reached were compared using χ^2 tests for categorical data and student's t-tests for continuous variables. Alpha was set to 0.05.

Approval for this study was obtained by the local medical ethical committee of the Leiden University Medical Centre. All participants provided written informed consent.

RESULTS

From April till July 2010, a total of 437 subjects filled out the LUCA questionnaire. A total of 291 subjects were finally contacted for a telephone interview and included in the study and 244 patients received a final cluster headache diagnosis based on the ICHD-II criteria. Baseline characteristics of 291 included patients were compared to 146 excluded patients. Interviewed subjects were

significantly older (P=0.018), but absolute differences were small (47.3 vs. 44.5 years). There were no significant differences with respect to gender, episodic or chronic cluster headache, proportions of patients using anti-cluster headache medication (prophylactic and acute), or the proportion of patients with a physician diagnosis of cluster headache. Eleven subjects (4.5%) of these 244 cluster headache patients also met ICHD-II criteria for trigeminal neuralgia (table 2).

Trigeminal neuralgia occurred ipsilateral to cluster headache in all 11 patients. Six patients (55%) reported that the onset of cluster headache had preceded the onset of trigeminal neuralgia, sometimes by several years; one patient reported trigeminal neuralgia before the onset of cluster headache and the remaining patients (n=4) did not remember which symptoms had come first. Eight patients (73%) reported that trigeminal neuralgia frequency followed the annual rhythmicity of cluster headache; the other three patients (27%) stated that both types of attacks occurred independently. The distribution of trigeminal neuralgia was as follows: seven (63%) patients reported symptoms exclusively in the ophthalmic branch; two patients (18%) had symptoms in the ophthalmic and maxillary branches; in two patients (18%) only the maxillary branch was affected. None of the patients reported symptoms in the mandibular branch. Trigeminal neuralgia attack frequency varied from ten times a day to five or ten times a year. Efficacy of verapamil on trigeminal neuralgia and cluster headache was reported by four patients (36%), the remaining patients reported no efficacy of cluster headache treatment on the trigeminal neuralgia attacks. No patients had received specific trigeminal neuralgia medication. Seven of eleven patients reported that they had undergone a cerebral magnetic resonance imaging (MRI) scan for their headaches, of whom five reported that there were no abnormalities and two patients did not remember. Four patients stated they had never had a cerebral MRI scan.

DISCUSSION

We investigated the prevalence of trigeminal neuralgia in a cluster headache population by means of an interview in which patients responded to a website or to an invitation after participation in our previous cluster headache study. Eleven of 244 cluster headache patients (4.5%) also had trigeminal neuralgia

attacks according to the ICHD-II criteria (13), a number that exceeds the estimated prevalence of trigeminal neuralgia in the general population (1-2/1,000).(19) A striking difference between the trigeminal neuralgia we found in cluster headache patients and trigeminal neuralgia in the general population is that trigeminal neuralgia attacks in cluster headache patients often occurred in the first branch of the trigeminal nerve, whereas in the general population the first branch is least affected. Besides, the trigeminal neuralgia patients in this study hardly ever reported typical trigeminal neuralgia triggers (touching, chewing, swallowing, etc). Nevertheless, according to the current ICHD-II criteria, the patients in our study should be classified as having 'cluster-tic' syndrome. Eight of our patients reported these trigeminal neuralgia attacks to be closely related to the occurrence of cluster headache. An alternative ICHD-II diagnosis that could be considered in these patients is primary stabbing headache, especially in patients experiencing these stabs in the first branch of the trigeminal nerve, lasting up to a few seconds and having no triggers (patients 4,5,6,10). Primary stabbing headache is a head pain occurring in single or series of stabs exclusively or predominantly felt in the distribution of the first branch. These stabs last for up to a few seconds and recur with irregular frequency ranging from one to many times per day and have been described to co-occur with cluster headache. Most of the time treatment is not needed. (20) Another explanation for the trigeminal neuralgia attacks in our patients could be that these attacks are an altered expression of cluster headache attacks due to partially effective prophylactic medications, whereby ophthalmic branch stabbing pains are a sign of a cluster headache attack without the full complement of symptoms. Moreover, jabs of pain occurring interictally have been described in cluster headache patients.(21) This would also advocate treating these single stabs and cluster headache as one entity. One patient in our study (nr. 1 in Table 2) reported that trigeminal neuralgia attacks were accompanied by lacrimation, so Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT) could be an alternative diagnosis in this case, however, lacrimation has also been described in trigeminal neuralgia.(22;23) In only three of our patients, trigeminal neuralgia occurred independently from cluster headache attacks and periods, but also these patients had atypical attacks: neuralgia was located in the ophthalmic branch (patient 10 and 11) and ophthalmic and maxillary branch (patient 2) and no triggers were reported.

Table 2. Description of trigeminal neuralgia in cluster headache patients

Patient M/F (ECH/ CCH)	Age (year)	Pain location	Ipsilateral/ contralateral to CH	Duration	Frequency	Triggers	Accompanying Signs	Relation to CH Periodicity	Relation to CH treatment
1 F (ECH)	75	V2 Cheek, upper jaw	Ipsilateral	30 sec.	3-4/m during half an hour	Speaking	Lacrimation	CH manifested first TN attacks occur before a CH period initiates	TN attacks decrease after proper CH treatment with verapamil
2 M (ECH)	54	V1-V2 Behind eye, upper jaw	Ipsilateral	1 sec.	5-6/y	None	None	CH manifested first TN attacks occur outside a CH period	Effect of CH treatment is unknown on TN frequency
3 F (ECH)	39	V2 Upper jaw, cheekbone	Ipsilateral	1-5 sec.	2/m	Touching Cold	None	CH manifested first TN attacks increase when CH attacks increase TN attacks also occur independent of CH attacks	CH treatment had no influence on TN frequency
4 M (ECH)	51	V1 Temporal bone	Ipsilateral	1 sec.	2/m	None	Twitching eye	TN attacks increase when CH attacks increase TN attacks occur within a CH period and prior to a CH attack	CH treatment had no influence on TN frequency
5 M (CCH)	42	V1 Temporal, going inwards	Ipsilateral	5-6 sec.	10/d	None	Seeing a purple stain in eye	TN attacks occur before and after CH attacks TN also randomly occurs without CH attacks TN attacks increase when CH attacks increase	CH treatment had no influence on TN frequency
6 F (CCH)	57	V1 Forehead	Ipsilateral	1 sec.	3-4/w	None	None	CH manifested first TN attacks increase when CH attacks increase TN attacks occur also independent of CH	TN attacks decrease after proper CH treatment with verapamil

7 M (ECH)	53	V1-V2 Upper jaw, temporal	Ipsilateral	1 sec.	2-3/d	None	None	CH manifested first TN attacks occur usually within a CH period TN attacks increase when CH attacks increase and vice versa	TN attacks decrease after proper CH treatment with verapamil
8 M (ECH)	29	V1 Temporal	Ipsilateral	2 min.	5-10/y	None	None	TN attacks occur usually within a CH period and prior to a CH attack, but also randomly TN attacks decrease when CH attacks decrease	CH treatment had no influence on TN frequency
9 F (ECH)	27	V1 Temporal	Ipsilateral	4-5 sec.	4/d	Light, sound touching	None	TN manifested first TN attacks increase when CH attacks increase TN attacks occur usually within a CH period	TN attacks decrease after proper treatment with verapamil
10 F (ECH)	31	V1 Temporal, eye	Ipsilateral	2-3 sec.	1-2/m	None	None	CH manifested first TN attacks occur independent of CH	Effect of CH treatment on TN frequency unknown
11M (ECH)	52	V1 From eye to jaw with temporal as punctum maximum	ipsilateral	2-4 min. (2min more often)	5-10/d	None	None	TN attacks occur independent of CH	CH treatment had no influence on TN frequency

TN = trigeminal neuralgia
CH = cluster headache
ECH = episodic cluster headache, CCH = chronic cluster headache
M = male, F = female
d = day, w = week, m = month, yr = year
sec = seconds, min = minutes
V1= ophthalmic branch, V2= mandibular branch, V3= maxillary branch

It has been suggested that in cluster-tic syndrome, trigeminal neuralgia should be treated separately from cluster headache.(13) In part of our patients, however, trigeminal neuralgia responded to cluster headache treatment. None of the patients in this study received specific trigeminal neuralgia medication. Of course, in case of a patients with cluster headache and trigeminal neuralgia in which trigeminal neuralgia does not improve to cluster headache medication, trigeminal neuralgia treatment could be considered. In the literature some cluster-tic patients in whom trigeminal neuralgia or cluster headache medication was not effective, received surgical treatments (often decompression of the trigeminal nerve), and these were described to be often effective for both cluster headache and trigeminal neuralgia attacks.[1;5;10] However, attacks of cluster headache could eventually reappear after initial relief of both cluster headache and trigeminal neuralgia after trigeminal nerve decompression.(1;10) Also 'secondary' cluster-tic has been described; in three patients the cluster tic syndrome resolved after treatment of a prolactinoma, pituitary adenoma, or epidermoid in the sella turcica.(24-26) In two other patients, the suggested underlying cause was a basilar artery ectasia and a dural carotid-cavernous fistula.(27;28) In another patient the cluster tic syndrome appeared to be related to multiple sclerosis.(29) In our study none of the patients reported structural abnormalities, but this should be interpreted with caution, as it is a questionnaire study, and not all patients underwent an MRI investigation.

Despite the possibility of recall bias affecting the description of the headache attacks, especially in patients with prolonged pain-free periods, the increased prevalence of trigeminal neuralgia in the LUCA study suggests some kind of relation between cluster headache and these trigeminal neuralgia-like symptoms. Previous publications on approximately 40 cases with co-occurring cluster headache and trigeminal symptoms have been described in the literature since 1978(1-12;24;30) and reported the atypical nature of trigeminal neuralgia in many of these.(1,4,6,9,10,11) Consistent with these findings, most of our patients also reported atypical symptoms; they experienced a low trigeminal neuralgia attack frequency, the attacks were predominantly affecting the first branch of the trigeminal nerve and typical triggers for trigeminal neuralgia were reported seldom. In addition, frequency and intensity of trigeminal neuralgia attacks paralleled cluster headache attacks and patients reported

a positive effect of cluster headache treatment on intensity and frequency of trigeminal neuralgia.

In conclusion, trigeminal neuralgia co-occurred in 11/244 (4.5%) of cluster headache patients, meaning that these patients suffered from two headache syndromes according to the ICHD-II criteria: cluster headache and trigeminal neuralgia. In only 3 (1.2%) patients trigeminal neuralgia seemed to occur independently from cluster headache episodes. According to our opinion, in most of our patients, the attacks were part of the cluster headache spectrum. Our results suggest that cluster headache and trigeminal neuralgia, occurring independently in time and distribution of pain, and therefore needing separate treatment, seems to be very rare. Trigeminal neuralgia (-like) attacks in cluster headache patients are often part of the cluster headache spectrum. A shared underlying pathophysiological mechanism of cluster headache and trigeminal neuralgia appears not plausible in our opinion.

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Potential conflicts of interests

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