

Trigeminal Neuralgia

Abstract

Trigeminal neuralgia is one of the most severe facial pains that patients can experience . This unpredictable, episodic pain mostly unilateral in the distribution of the trigeminal nerve results in recurrent shooting, pain lasting for seconds to minutes. It is light touch provoked and therefore prevents patients from eating, touching their face and so has a significant impact on quality of life. Patients often consult a dentist because it usually presents like dental pain. Dentists need to avoid irreversible dental treatment. Response to carbamazepine is good but tolerability is poor. Surgical options are available and are generally successful. Patients can gain further information from a patient support group such as Trigeminal Neuralgia Association UK.

Clinical relevance

Although rare, trigeminal neuralgia patients often present to dentists who need to recognise it as a non-dental cause of pain in order to avoid irreversible dental treatment.

Objectives

The reader should understand the importance of recognising trigeminal neuralgia so that irreversible dental treatment is avoided and ensuring medication is prescribed and referral to a GP made urgently.

Definition

Trigeminal neuralgia (TN) is described as a: “sudden, usually unilateral, severe, brief, stabbing, recurrent pain in the distribution of one or more branches of the trigeminal nerve”, which is triggered by light touch activities (1).

Epidemiology

Trigeminal neuralgia is considered to be a rare disease and the estimated prevalence from an old study in the USA put it at 4.1/10,000 (2). More recent studies in the UK (3) and Holland (4) using data from primary care records suggests a higher incidence of 8 to 12.6 per 100,000 per annum. A study in Germany where all the diagnosis were validated by specialists a lifetime prevalence of 0.3% (95% CI 0.1- 0.5%) was estimated (5). Up to 90% of patients develop TN after age 50 with the peak between 60-70 years and there is a slight predominance in women. It can occur in young people and even children. The disease most frequently linked with TN is multiple sclerosis (in around 5-10% of cases). In this group it occurs in a younger age group and there is an increased frequency of bilateral pain. Tumours account for a very small number of cases. Hypertension is a risk factor and strokes more likely (6, 7). Data from a population-based study in Taiwan highlights increased risk of depression, anxiety and sleep disorder after diagnosis of TN (8). There are reports of familial links.

Pathophysiology

TN is a neurological pain. The cause of which is still not completely understood. In many patients, a strongly pulsating blood vessel is found to be pressing on the trigeminal nerve at a point where the cells producing myelin change from the peripheral to central type (9). This causes demyelination and so sets up a cross- circuit between those nerve fibres which relay light touch sensations and those which relay pain signals, the so-called ignition hypothesis (10). The result is intermittent but excruciating and debilitating pain. There is growing

evidence that patients with TN have a number of abnormalities of their nerve functions including abnormal sodium channels, nociceptive inhibitory pathways and possible inflammatory changes but more research needs to be carried out to establish the causes as it could be multifactorial (11, 12) .

Clinical Features

Although it would appear from the diagnostic criteria that the disorder is easy to diagnose, it is being increasingly recognised that this is not the case and more detailed clinical characteristics are now being reported (13,14). It has been generally accepted that in those patients in whom a nerve compression has been identified on Magnetic Resonance Imaging (MRI) the term classical TN is used whereas in those patients where no cause is found it is called idiopathic N. Secondary TN are those in whom a cause is identified e.g. MS, vascular anomalies or tumours (15). The principal features are shown in table 1 alongside the way patients describe their pain (16).

Many patients will first visit a dentist as the pain often presents intra-orally and for that reason patients are convinced that the cause is dental. TN presents abruptly with patients remembering exactly what they were doing during their first attack, called a memorable onset. It is important to establish the timing. It is an episodic pain and drawing diagrams and asking patients to label them can help in differentials.

Figure 1 here

Take a look at the patterns in figure 1. A pattern like number 1 is the most classical type but when the pain episode is severe it can be like number 2 where there is a series of stabs lasting seconds but in quick succession before there is a refractory period when pain cannot be triggered. If the pain in number 2 and the episode last for hours, it is unlikely to be TN. However, there can be an afterpain that is less severe and more burning as shown in number 4. This more prolonged pain has variously been termed concomitant pain or type 2

TN (17). The pain begins at the start of light touch e.g. eating rather than on the rebound as occurs with cracked tooth. Remission periods are common and more likely at the start of the condition. These periods can last for months before the next relapse. However, these periods are totally unpredictable and vary from patient to patient.

The severity can be so high patients cannot eat, swallow their saliva and become dehydrated and lose weight.

It is important to elicit the sharp, stabbing, shooting, electrical character of the pain by asking "How does it feel?" and encouraging patients to use metaphors. We have done this using images (18). Sleep often brings relief except when going through a very severe bout. Some patients may report intermittent autonomic features on the painful side only at times of pain such as red eye, runny eye, drooping of the eyelid, redness of the cheek or nasal changes. These autonomic features may, however suggest another diagnosis such as SUNA , short unilateral neuralgiform pain with autonomic features. Very rarely do they report other types of chronic pain. Unequal use of the mouth can lead to pain in the muscles of mastication.

On careful examination some patients may have subtle sensory changes. Touching a trigger point can elicit an attack of pain and this can be diagnostic. Intra oral examination can show decreased oral hygiene on the side of the pain.

Patients with TN experience considerable activity limitation and the limitation is particularly pronounced with activities that involve the face (e.g. eating, talking, touching the face, being intimate). Weight loss can be substantial as a result. Social isolation is common as patients cannot eat at social events. Fear is very pronounced as they can never predict when they will get their next attack of pain. Over 50% of the patients take a significant amount of time off work. The disability experienced by the patients is associated with high levels of anxiety (>50%) and over 40% are depressed with 75% showing evidence of catastrophizing (19). Information from Trigeminal Neuralgia Association (TNA UK) and the

national press eight people are known to have committed suicide as a result of TN since 1996.

Table 1 Features of classical trigeminal neuralgia as described by clinicians and patients

Differential Diagnosis

It is difficult to make the initial diagnosis as the patient will not have been experiencing the pain for a long time and no remission periods are reported. Patients will report a lack of response to paracetamol and NSIADs. It is certainly much more likely to be a dental cause especially when patients have a heavily restored dentition. However, the dentist must be guided by the history, use examination and imaging when making the diagnosis. A trial of carbamazepine can often be diagnostic as in the initial phases of the condition it can result in complete pain relief. TN can be the first presenting episode for multiple sclerosis and its presentation is the same as for classical TN although patients are more likely to have bilateral episodes of pain. Glossopharyngeal neuralgia is extremely rare and can be difficult to differentiate from TN. The pain is felt either in the throat on swallowing or in the ear. If the pain is centred over the temple region, of longer duration and the patient is over 50. C reactive protein and an ESR must be done to rule out temporal arteritis. Other neuralgic pains such as post herpetic neuralgia will be associated with a history of previous herpes zoster and the pain is continuous. Trigeminal neuropathic pain will be linked to a traumatic event be it dental or facial trauma.

Our UK study shows that it takes on average four years for a patient to receive the correct treatment plan and 83 % would have been seen by at least one other specialist, one third by two or more specialists before a suitable management plan is made (19). As the trigeminal nerve also supplies the teeth, 70% of patients will have consulted a dentist and 8% will have had treatment some of which was unnecessary and even harmful. Who the patient consults first will often determine the secondary referral and as shown in figure 2 this often leads to

inappropriate care and a need for further referral. It is important to identify who has an interest in this condition in your district. Patients are prepared to travel long distances to get appropriate care.

Figure 2 here

Investigations

It is important to rule out any dental causes so local imaging is required before other investigations are done. Specialists will do MRIs to determine if there is a secondary cause.

Management

The wide range of treatments, both medical and surgical, currently in use for TN is ample proof that there is no simple answer on how the condition should be managed (20). The level of evidence for current treatments is extremely poor due to a lack of high quality studies (21). A variety of outcome measures for treatment are used which makes comparisons between treatments virtually impossible. A 50% reduction in pain is considered an effective outcome for medical management but patients expect a 100% pain relief from surgical procedures which can be obtained in some patients . It is important that clinicians managing these patients use internationally approved guidelines and have as far as possible evidence based care pathways. An overall care pathway as used at UCLH NHS Foundation Trust is shown in Figure 3. This is similar to that used by the headache neurologists in Denmark. It is important that there is a multidisciplinary team . (22)

Figure 3 here

Pharmacological

No analgesics including opioids provide adequate pain relief and the mainstay remain anti-epileptic drugs. The first line drug is carbamazepine and it needs to be started at a low dose e.g. 100mg two or three times a day and gradually increased up to 800mg daily . Slow

escalation helps to reduce side effects. It will have an effect in 24 hours. Oxcarbazepine is another alternative which has fewer side effects and fewer drug interactions. Other drugs that can be prescribed by the GP include lamotrigine, baclofen, gabapentin and pregabalin. All will result in significant cognitive side effects such as memory problems, drowsiness whereas more peripheral side effects include nausea and weight gain, . It is useful to encourage patients to keep a diary when the pain becomes more severe or when changing drugs. The diary can also be used to determine if a remission period has occurred.

Surgical

When the side effects of medication become intolerable or the drugs themselves cease to be effective, various surgical procedures can be tried, but here there are widely different techniques used and outcomes are varied and result in complications which can affect quality of life.

Some of these surgical procedures are deliberately destructive to the trigeminal nerve and can lead to loss of sensation in the face. The only one that is non-destructive, microvascular decompression (repositioning an offending blood vessel which maybe pressing on the nerve) is a major neurosurgical procedure with potential for significant complications. It has recently been suggested that only those patients who have both compression of the trigeminal nerve in the root entry zone as well as anatomical changes (thinning of the nerve or distortion of the nerve) should be subjected to a microvascular decompression. Microvascular decompression offers the longest pain relief period (70% of patients remain pain free and still off drugs after 10 years) but this treatment may not always be appropriate due to a patients' age or physical condition. The other procedures are mainly done at the Gasserian ganglion level, radiofrequency thermocoagulation, glycerol rhizotomy or balloon compression. Stereotactic radiosurgery aims to irradiate the trigeminal nerve in the posterior fossa and its effects are delayed. All these procedures can result in varying levels of sensory loss and on average result in four years of pain freedom.

Acute attacks

Many patients will get flare ups which can be so severe that they attend accident and emergency units. Often, they are given opioids which do little to relieve their pain. To date the evidence for managing these is of low quality. However, it is noted that local anaesthetics injected into trigger areas can be helpful as shown by a study that added ropivacaine injections to the use of gabapentin. The two main sites would be infraorbital nerve and inferior dental nerve blocks. A lidocaine injection followed by a marcaine injection to prolong the effect can be helpful. This can be done daily till the increased dose of medication has had time to take effect.

Other

It is important to take a biopsychosocial approach and a course of cognitive behaviour management can be helpful. Through a patient support group TNA UK patient can meet fellow sufferers and also have access to high quality information [www.tna.org](http://www.tna.org.uk) uk. They also hold meetings that are attended by patients and healthcare professionals (23) The Brain and Spine Foundation publish a useful booklet on facial pain which provides details of TN and other related conditions and can be downloaded from <https://www.brainandspine.org.uk/>.

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References

1. Merskey H, Bogduk N. Classification of chronic pain. Descriptors of chronic pain syndromes and definitions of pain terms. 2nd ed. Seattle: IASP Press; 1994 1994.
2. Katusic S, Beard CM, Bergstralh E, Kurland LT. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945-1984. *Ann Neurol.* 1990;27(1):89-95.
3. Hall GC, Carroll D, Parry D, McQuay HJ. Epidemiology and treatment of neuropathic pain: The UK primary care perspective. *Pain.* 2006;122(1-2):156-62.
4. Koopman JS, Dieleman JP, Huygen FJ, de MM, Martin CG, Sturkenboom MC. Incidence of facial pain in the general population. *Pain.* 2009;147(1-3):122-7.
5. Mueller D, Obermann M, Yoon MS, Poitz F, Hansen N, Slomke MA, et al. Prevalence of trigeminal neuralgia and persistent idiopathic facial pain: a population-based study. *Cephalalgia.* 2011;31(15):1542-8.
6. Pan SL, Chen LS, Yen MF, Chiu YH, Chen HH. Increased risk of stroke after trigeminal neuralgia--a population-based follow-up study. *Cephalalgia.* 2011;31(8):937-42.
7. Pan SL, Yen MF, Chiu YH, Chen LS, Chen HH. Increased risk of trigeminal neuralgia after hypertension: A population-based study. *Neurology.* 2011;77(17):1605-10.
8. Wu TH, Hu LY, Lu T, Chen PM, Chen HJ, Shen CC, et al. Risk of psychiatric disorders following trigeminal neuralgia: a nationwide population-based retrospective cohort study. *J Headache Pain.* 2015;16:64.
9. Maarbjerg S, Wolfram F, Gozalov A, Olesen J, Bendtsen L. Association between neurovascular contact and clinical characteristics in classical trigeminal neuralgia: A prospective clinical study using 3.0 Tesla MRI. *Cephalalgia.* 2015.

10. Devor M, Amir R, Rappaport ZH. Pathophysiology of trigeminal neuralgia: the ignition hypothesis. *Clin J Pain*. 2002;18(1):4-13.
11. Moisset X, Villain N, Ducreux D, Serrie A, Cunin G, Valade D, et al. Functional brain imaging of trigeminal neuralgia. *Eur J Pain*. 2011;15(2):124-31.
12. Hung PS, Chen DQ, Davis KD, Zhong J, Hodaie M. Predicting pain relief: Use of pre-surgical trigeminal nerve diffusion metrics in trigeminal neuralgia. *Neuroimage Clin*. 2017;15:710-8.
13. Maarbjerg S, Gozalov A, Olesen J, Bendtsen L. Trigeminal neuralgia--a prospective systematic study of clinical characteristics in 158 patients. *Headache*. 2014;54(10):1574-82.
14. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38(1):1-211.
15. Cruccu G, Finnerup NB, Jensen TS, Scholz J, Sindou M, Svensson P, et al. Trigeminal neuralgia: New classification and diagnostic grading for practice and research. *Neurology*. 2016;87:1-9.
16. Zakrzewska JM. *Insights : facts and stories behind trigeminal neuralgia*. Gainesville: Trigeminal neuralgia association; 2006 2006.
17. Maarbjerg S, Gozalov A, Olesen J, Bendtsen L. Concomitant persistent pain in classical trigeminal neuralgia--evidence for different subtypes. *Headache*. 2014;54(7):1173-83.
18. Zakrzewska JM, Padfield D. The patient's journey through trigeminal neuralgia. *Pain Clinical Update*. 2014;22(1):1-7.
19. Zakrzewska JM, Wu J, Mon-Williams M, Phillips N, Pavitt SH. Evaluating the impact of trigeminal neuralgia. *Pain*. 2017;158(6):1166-74.
20. Zakrzewska JM, Linskey ME. Trigeminal neuralgia. *BMJ*. 2014;348:g474.
21. Cruccu G, Gronseth G, Alksne J, Argoff C, Brainin M, Burchiel K, et al. AAN-EFNS guidelines on trigeminal neuralgia management. *Eur J Neurol*. 2008;15(10):1013-28.

22. Heinskou T, Maarbjerg S, RoCHAT P, Wolfram F, Jensen RH, Bendtsen L. Trigeminal neuralgia--a coherent cross-specialty management program. *J Headache Pain*. 2015;16:66.
23. Zakrzewska JM, Jorns TP, Spatz A. Patient led conferences--who attends, are their expectations met and do they vary in three different countries? *Eur J Pain*. 2009;13(5):486-91.

Figure captions

Figure 1 Timing of attacks

Footnote Severity across time

Figure 2. Pathways of referral for patients with trigeminal neuralgia

Figure 3 Care pathway for trigeminal neuralgia used at UCLH NHS Foundation

Trust UK

Footnote MS multiple sclerosis PROMS patient related outcome measures

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