

Observational Studies

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Is this really trigeminal neuralgia? Diagnostic re-evaluation of patients referred for neurosurgery

<https://doi.org/10.1515/sjpain-2021-0045>

Received March 2, 2021; accepted June 14, 2021;
published online August 2, 2021

Abstract

Objectives: Patients with facial pain are sometimes referred for neurosurgical treatment with a poorly documented diagnosis of trigeminal neuralgia. In such cases, neurosurgery will usually not be helpful. We conducted a re-evaluation of the diagnosis in patients referred for neurosurgical treatment of presumed trigeminal neuralgia. Our objective was to find out why and how often misdiagnosis occurred.

Methods: A retrospective study was done in consecutive first-time patients referred for trigeminal neuralgia to our outpatient clinic in 2019. We used five ICHD-3-based clinical criteria to verify or exclude the diagnosis. In patients where trigeminal neuralgia was excluded, we established a diagnosis for their facial pain based upon medical history and a physical examination by a neurosurgeon – often supplemented with examination by an oral surgeon.

Results: Thirty-eight patients were referred for presumed trigeminal neuralgia. Only 17 of them fulfilled the five criteria and were diagnosed with trigeminal neuralgia. In 20 of the remaining 21 patients trigeminal neuralgia could be clearly excluded, while one of the patients had a periodontitis closely mimicking trigeminal neuralgia. In 14 of the 21 patients we diagnosed temporomandibular dysfunction or dental conditions. MRI scans had detected low-grade neurovascular contacts in 13 of the 21 patients, a finding that was clearly overestimated by the referring neurologists in seven patients.

Conclusions: Overdiagnosis of trigeminal neuralgia was common in patients referred for neurosurgery, mostly due to insufficient clinical evaluation combined with an overestimation of MRI-detected NVCs. The clinical diagnosis

should be critically re-evaluated before recommending neurosurgery to patients referred for presumed trigeminal neuralgia.

Keywords: diagnostic criteria; facial pain; multidisciplinary; neurosurgery; overdiagnosis; trigeminal neuralgia.

Introduction

Trigeminal neuralgia (TN) is a characteristic and disabling facial pain condition. The diagnosis is purely clinical, based on five typical and recognizable diagnostic criteria, and often straightforward [1–5]. But sometimes the pain syndrome can be less clear-cut. Then the number of differential diagnoses is legion – even in a tertiary referral clinic.

With a prevalence of around 0.1% and an incidence around 4–5 per 100,000 per year, TN is rarely encountered in general neurology and very rarely in general medical or dental practice [6, 7].

Therefore, misdiagnosis, meaning underdiagnosis or overdiagnosis, can be expected and is not unusual. A thorough diagnostic workup of referred patients is essential in order to select the right patients for neurosurgical treatment, i.e. those with the best chances to benefit from surgery.

In our neurosurgical outpatient clinic, where TN patients are referred if medical therapy fails, we frequently observe misdiagnosed cases. Referring neurologists sometimes seem to put more emphasis in their diagnostic workup on neurovascular contact (NVC) detected on MRI than on the pain characteristics and the clinical examination.

Therefore, we have critically re-evaluated the diagnosis in first-time patients referred for surgical treatment of TN. Our objective was to find out how often and why misdiagnosis occurred in the actual setting – in order to improve our diagnostic evaluation, and select the appropriate treatment accordingly.

Materials and methods

In 2019, we enrolled consecutive first-time patients referred for presumed trigeminal neuralgia – and seen in our outpatient clinic by one

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neurosurgeon with a special interest in facial pain. Their diagnosis was re-evaluated using five well-defined criteria, and in selected cases an oral surgeon was consulted. If necessary, the physical examination was supplemented with dental X-rays or cone beam computer tomography (CBCT). Patient records, and in some cases follow-up data, were retrieved and examined retrospectively.

Diagnostic criteria in trigeminal neuralgia

Trigeminal neuralgia is a pain syndrome characterized by five clinical criteria, see Table 1 [1, 3].

Revised ICHD-criteria from 2018 and IASP-criteria from 2016 include MRI-findings to establish the diagnosis “Classical TN”. A joint committee between the International Association for the Study of Pain and the International Headache Society has classified trigeminal neuralgia into “classical” with severe neurovascular contact, “secondary”, and “idiopathic”, and has developed revised diagnostic criteria that are included in the ICHD-3 [4].

These five criteria, extracted from the ICHD-3 classification, are all necessary to diagnose trigeminal neuralgia [1, 3–5, 9, 15], Table 1.

The acronym PUTIN, or PUTIN’s rule of five, sums up the five criteria and can serve as a memory aid, see Figure 1.

Results

Among 102 patients consulting for facial pain, thirty-eight were first-time referrals from neurologists (36 patients), from one neurosurgeon (one patient) and one oral surgeon (one patient) – all for surgical treatment of presumed trigeminal neuralgia. All of these 38 patients had been examined by one or several dentists before consulting their neurologist.

The 64 other patients were seen for routine follow-up, for recurrent pain after neurosurgical treatment, or for other types of facial pain.

Trigeminal neuralgia patients (n=17)

Our diagnoses, using PUTIN’s rule of five in the 38 first-time referrals, were TN in 17 of the 38. The neuralgia was secondary to long-standing disseminated sclerosis in 3 of 17 patients. MRI showed a pontine plaque at the ipsilateral

Table 1: The five ICHD-3-based clinical criteria used to establish the TN diagnosis.

Five clinical criteria P-U-T-I-N	ICHD-3 terminology [3]	Comments
Paroxysmic attacks of severe stabbing pain	...Recurrent paroxysms of... ...Lasting from a fraction of a second to 2 minSevere intensityElectric shock-like, shooting, stabbing or sharp in quality	Lasting usually for seconds, may last for 2 min, but the 2 min limit is not validated [8].
Unilateral pain, in trigeminal territory only	...Unilateral facial pain in the distribution of one or more divisions of the trigeminal nerve, with no radiation beyond,	Bilateral TN is rare, and in those rare cases pain attacks are not simultaneous.
Triggered by innocuous facial or intra-oral stimuli	Precipitated by innocuous stimuli within the affected trigeminal distribution	Triggering of pain paroxysms by stimuli applied to intra- or extra-oral trigger zones are considered by many to be an essential part of the clinical picture [9–11].
Intermittent pain; short or ultrashort breaks between attacks, longer breaks (months) between painful periods	Between paroxysms, most patients are asymptomatic Two phenotypes: ...Purely paroxysmal TN or ... TN with concomitant continuous or near-continuous pain between attacks	Probably nearly half of the patients with otherwise typical TN will have some <u>concomitant pain</u> (lasting >2 min) – more or less continuous, sometimes triggered and sometimes severe – between the painful paroxysms [8, 10, 12]. But the intense paroxysms still are the main complaint [13].
Normal physical examination between pain attacks	Other than the triggering phenomenon, most patients with TN fail to show sensory abnormalities within the trigeminal distribution unless advanced methods are employed Not better accounted for by another ICHD-3 diagnosis	Some of the patients with otherwise typical TN may have subtle <u>sensory deficits</u> in the trigeminal area [5, 14].



- Paroxysmic
- Unilateral
- Triggered
- Intermittent
- Normal

(Permission granted. Photo by Alexei Nikolsky/AFP/NTB)

Figure 1: PUTIN's rule of five.

trigeminal root entry in one of the three, multiple supratentorial lesions in the second, and was negative in the third patient.

In the 14 patients with primary TN, MRI revealed an NVC grade 2 or 3 in 4, while the others had grade 1 NVC or no NVC.

Thirteen of them were treated surgically with MVD or percutaneous glycerol injection. The remaining four patients chose to continue with their medication, just wait and see, after they had been informed about the surgical options.

Other diagnoses, not trigeminal neuralgia (n=21)

Twenty-one of the 38 referred patients did not fulfill the clinical criteria for the TN diagnosis.

In 4 of the 21, the referring neurologists had expressed doubt about the diagnosis, but suggested that MVD could be an option since the MRI scan had shown a trigeminal NVC.

The 21 were on average 49 years old (20–89 years), they had facial pain with a mean duration of 3.5 years (0.25–14 years), and 16 of them were female.

Pain was bilateral in 5, and unilateral in 16, left-sided in 9. None of the patients had only V1 (first branch of trigeminal nerve) pain. V2 pain only was registered in six patients, V3 in 3, and in 7 patients several trigeminal areas were affected. MRI scanning had shown an NVC in 13 of 20 examined patients - grade 2 in one patient, grade 1 in the remaining 12 patients. Antiepileptic drugs had provided pain relief in 5 of 16 patients.

How was TN excluded in the 21 patients? (Table 2)

- Absent or atypical pain paroxysms in all 21 patients
- Absent or atypical trigger mechanisms in 20 patients
A typical trigger was found in only one patient (Case history), but his pain paroxysms lasted for several minutes and he had a tender molar. Three patients reported atypical triggers: increased pain many minutes/hours after psychological stress or exposure to cold wind. The remaining 17 patients had no trigger mechanisms.
- Time course of pain: Long-lasting (hours) exacerbations or continuous pain only, in 20 patients
- Clinical examination abnormal: painful teeth and/or muscles and/or restricted mouth opening in 11 patients.
- Simultaneous bilateral pain in 5, outside trigeminal area in 2 of them
- Dental X-rays or CBCT: abnormal in two patients (periodontitis)

In 20 patients, 2–5 of the five criteria were not met, and the diagnosis TN was definitely excluded. For instance, in all the 10 patients with a normal clinical examination, we found that 2–4 of the other four TN criteria were absent.

In one of the patients all of the five criteria were missing. She had been suffering from chronic maxillary pain, sometimes bilateral, for one year and was diagnosed with a typical TMD by the oral surgeon.

Only one of the 21 patients had a history closely mimicking TN; the patient referred in the case history. Findings in the physical examination were confirmed by the oral surgeon and the computed tomography (CT) scan showed periodontitis.

Case history – tooth pain or TN?

One patient (male, 57 years) had suffered from intermittent, severe, paroxysmic pain in the left maxillary region for 3 months, pain intensity graded as 8/10 on the Numeric Rating Scale (NRS 0–10), lasting for several minutes, elicited by touching a left upper molar, effectively relieved by a small dose of carbamazepine. No sensory deficits were detected clinically.

He had been seen by two different dentists who both stated that his pain was not of dental origin. The MRI scan showed a tortuous vertebral artery compressing cranial nerves 7 and 8, but not affecting the trigeminal nerves.

After a few weeks carbamazepine was withdrawn due to a severe allergic reaction. The pain recurred, and he was referred by a neurosurgeon for TN treatment.

Table 2: Pain characteristics in 21 patients where typical TN was excluded.

The five criteria		Deviations from criteria
Paroxysytic pain <2 min	0/21	<u>Continuous</u> pain in 12 <u>Intermittent</u> in 9, but lasting >2 min
Unilateral pain in territory	14/21	<u>Simultaneous bilateral</u> pain in 5 <u>Outside trigeminal territory</u> in 4
Triggers, typical	1/21	Pain triggered by chewing on a tender molar in one patient, who was diagnosed with periodontitis = typical trigger. Atypical triggers with <u>delayed pain</u> in three patients, <u>after</u> physical or psychological stress or cold wind.
Intermittent pain	9/21	But with paroxysms/exacerbations lasting for several minutes in two patients, for hours in 7.
Normal clinical examination (subtle sensory deficit not counted)	10/21	<u>Abnormal findings</u> in the remaining 11 patients: – Tender masticatory muscles 9 – Painful percussion of teeth 5 – Restricted mouth opening 4

The table shows how often each of the five criteria were present in the 21 patients. None of the patients had pain paroxysms lasting less than 2 min, only one patient had a trigger phenomenon that resembled triggering in TN.

The diagnosis was understandable since it was based on the medical history alone. But on physical examination the oral surgeon found local tenderness of the maxilla and an upper molar, tooth 26, and a cone beam CT scan showed signs of apical periodontitis. The patient became pain-free after endodontic treatment. It is noteworthy that two dentists had missed the diagnosis.

Revised diagnoses in 21 patients after excluding TN

TMD was diagnosed in seven patients, and was associated with rheumatoid arthritis in one of them.

Five of the patients had odontalgia atypica, OA, meaning persistent pain after dental surgery. OA is tooth pain or pain in a site where a tooth has been extracted, but without clinical and radiological evidence of pathology [16, 17]. It is estimated to occur in 4–5% of patients after dental surgery [17].

Other dental causes were identified in two patients: periodontitis and insufficient endodontic treatment.

Two patients were diagnosed later by neurologists, with persistent idiopathic facial pain, PIFP, according to the ICHD-3 criteria [13, 18].

Fibromyalgia was diagnosed later, also by neurologists, in two patients during neurological follow-up.

In one patient tension headache was the major complaint.

Cervical myelitis, transitory, at C1 level, was discovered on MRI in a patient with unilateral facial pain, later

bilateral. She also had slight transitory motor disturbances in both hands. The MRI findings were normalized after a few months, and her pain became more chronic and atypical. Medullary affection at the upper cervical level has been reported as a possible explanation of facial pain [19].

What happened later in the non-TN patients?

Medication, physiotherapy or chiropractor treatment, dental splint, dental treatment and spontaneous improvement has had some effect in most patients, but five of the patients, in the TMD or OA category, have been difficult to treat and still have significant pain after one year.

Discussion

Over diagnosis of TN

The main finding in this study is overdiagnosis of TN in a significant proportion of patients referred for neurosurgery. We applied five strict and well documented diagnostic criteria from the ICHD-3 classification, and excluded TN in 21 of 38 patients [3]. Previously TN overdiagnosis has been documented in general practice, but, to our knowledge, it has not been explicitly reported in neurosurgical patients even if “misdiagnosis” of TN is recognized as a problem [2, 20].

Underdiagnosis of TN resulting in dental over-treatment, delayed diagnosis and erroneous medication is well documented [21–23].

Overdiagnosis is also an important quality problem putting the patient at risk for useless medical and operative treatment.

Why was TN overdiagnosed by the referring neurologists?

We found that some of our colleagues let MRI replace the old-fashioned and time-consuming clinical judgment. They have simply put too much emphasis on MRI findings and used any sign of an NVC as a diagnostic criterion. In one patient with facial myalgias, for instance, high quality MRI was done three times, in search of an NVC, but with negative results again and again. Another patient, with continuous facial pain and after a low-grade NVC had been detected, was informed that the MRI had “confirmed the diagnosis of TN”. And a third patient with chronic pain felt relieved when she learnt from her neurologist that MRI had shown “an operable cause of her pain”. As specialists, we must state clearly that NVCs can be detected on MRI scans in close to 90% of healthy individuals and should not be used as a diagnostic criterion for TN [24].

Eller et al. have argued that facial pain can be classified on the basis of the medical history alone, and that “even the most inexperienced neurosurgeon can make an accurate diagnosis” with their classification scheme [25]. They may be right in some straightforward cases, but such a classification system will undoubtedly lead to quite a few cases of dental pain being misdiagnosed as TN [2, 14, 26].

Therefore, we agree with those who insist that patients referred for facial pain resembling TN always deserve both a thorough medical history and a physical examination [3, 5, 8, 14, 27].

Diagnoses in non-TN cases

The large proportion (14/21) of TMD and odontological diagnoses is not unexpected since TMD and dental problems are the commonest causes of chronic facial pain in the general population [26].

It is worth noting that periodontitis was the closest TN imitator in this small series. This is in agreement with Casey’s remark that dental pain may be quite similar to TN in the lower branches [14]. The diagnosis of an underlying cracked tooth or periodontitis can be difficult, even for

dentists. It can be helpful to remember that provoking factors in tooth pain are slightly different from the TN triggers: cold or hot liquids, sweet stimuli, percussion or pressure on the teeth [26].

Multidisciplinary approach

Rare conditions resulting in facial pain, like cervical myelitis, may occur, and we know that the number of differential diagnoses is considerable [27–29].

Therefore, we and our patients need a multidisciplinary approach. Both medical history and physical examination are necessary to establish a diagnosis when TN has been excluded. Oral surgeons are consulted in many cases, and in some cases neurologists, ENT surgeons, ophthalmologists, maxillary surgeons, psychiatrists or specialists in pain treatment. And imaging is done as indicated.

Since 2018, neurosurgeons and oral surgeons at Oslo University Hospital have collaborated to evaluate patients with facial pain together in our out-patient clinic. Last year a neurologist joined our team. We hope to provide faster and more precise diagnosis and follow-up plans in the future for this suffering group of patients, some of whom commute endlessly between specialists.

Limitations and strengths of the study

This is small retrospective study of highly selected patients, very different from the general population. The diagnostic criteria are well-defined and strict, but not all are validated (e.g. duration of pain paroxysms), and there is no gold standard or simple test for the TN diagnosis [8]. Follow-up has not been systematic, which is also a limitation.

Conclusion

We have shown that overdiagnosis of TN occurred in a significant proportion of patients referred for neurosurgical treatment. The main reason was overestimation of MRI findings – at the expense of careful history taking and clinical examination. Erroneous diagnosis is an important quality problem since patients may risk unnecessary and useless neurosurgery – in addition to delayed treatment of their underlying painful condition.

Implications

Before undergoing TN surgery all patients deserve a critical evaluation of the diagnosis – consisting of a thorough medical history, a physical examination and lastly a high quality MRI scanning.

Research funding: Author states no funding involved.

Author contribution: Not relevant.

Competing interests: Author states no conflict of interest.

Informed consent: This study is part of a quality study in patients referred for trigeminal neuralgia. Informed consent was obtained from the patient referred in the case history.

Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by Oslo University Hospital's data protection officer (Letter of Approval 17/20654).

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