Secondary trigeminal neuralgia: have you thought outside the box?

A case series.

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Abstrakt (GERMAN)

Trigeminusneuralgie (TN) ist eine den Patienten schwächende neurologische Erkrankung, die starke Gesichtsschmerzen verursacht. Eine primäre TN (PTN) kann idiopathisch sein oder resultiert aus einem anormalen Gefäßkontakt mit der Wurzel des Trigeminusnervs. Sekundäre Trigeminusneuralgie (STN) wird durch andere Erkrankungen wie Demyelinisierung und andere pathologische Zustände verursacht, welche den Nerv komprimieren können, wie Tumore oder Schädelbasisläsionen. Allgemeinzahnärzte (GDP = General Dental Practitioners) sollten mit den Anzeichen und Symptomen einer TN vertraut sein und diese in ihren Differenzialdiagnosen bei der Untersuchung von Zahn- bzw. Gesichtsschmerzen miteinbeziehen. Dieser Beitrag stellt fünf Fälle einer sekundären TN mit Gesichtsschmerzen vor. Einige wurden anfänglich als Zahnschmerzen und/oder Kiefergelenkdysfunktion-Syndrom (TMJDS) falsch diagnostiziert.
Die meisten Patienten mit einer TN stellen sich zunächst dem Allgemeinmediziner vor. Ärzte und Zahnärzte müssen eine TN als mögliche Diagnose in Betracht ziehen, wenn sich die klassischen Symptome zeigen. Eine TN kann das erste Anzeichen einer schwächenden oder ernsthaften Krankheit sein, sodass eine frühzeitige Diagnose wichtig ist, nicht nur um den Schmerz zu kontrollieren, sondern auch um sekundäre Neuralgien auszuschließen. Die anfängliche Behandlung einer TN ist pharmakologisch, aber die Chirurgie spielt eine wichtige Rolle.

Abstract (ENGLISH)

Trigeminal neuralgia (TN) is a debilitating neurological condition causing severe facial pain. Primary TN (PTN) can be idiopathic, or results from aberrant vascular contact with the root of the trigeminal nerve. Secondary trigeminal neuralgia (STN) is caused by other conditions such as demyelination and other pathologies which compress the nerve, such as tumours, or skull base lesions. General Dental Practitioners (GDP) should be familiar with the presenting signs and symptoms of TN and consider it in their differential diagnoses when investigating dentofacial pain. This paper will show five cases of secondary TN presenting with facial pain. Some were initially misdiagnosed as dental pain and/or

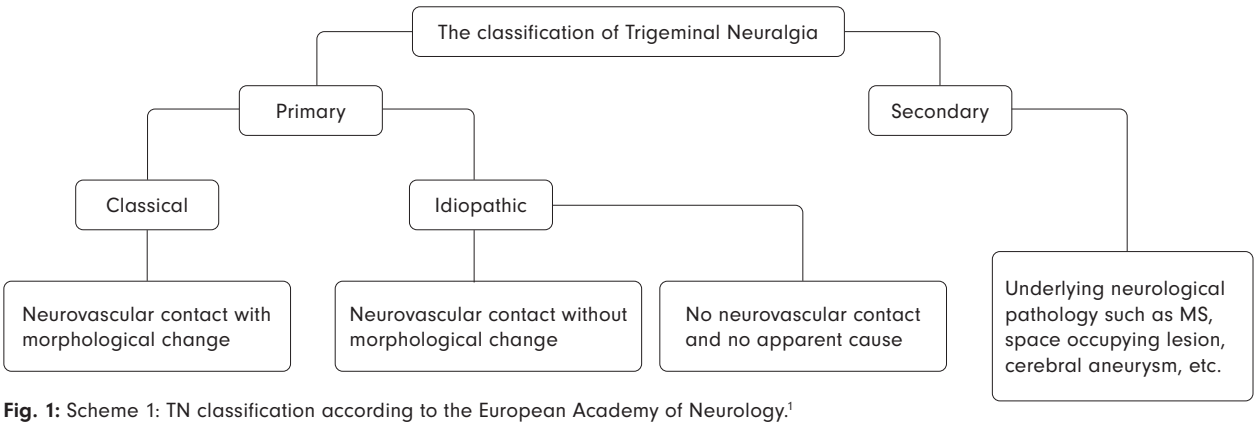


Fig. 1: Scheme 1: TN classification according to the European Academy of Neurology.[1]

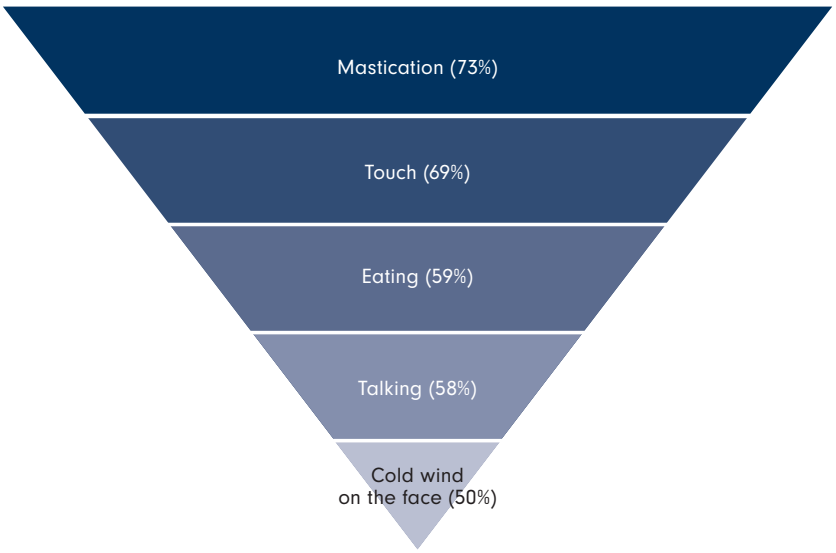


Fig. 3: The most common triggers reported in primary trigeminal neuralgia.[2]

temporomandibular joint dysfunction syndrome (TMJDS). Most patients with TN present initially to primary care practitioners. Doctors and GDPs must consider TN as a potential diagnosis, when the archetypal constellation of symptoms is present. TN can be the first presentation of a debilitating or sinister disease, so early diagnosis is important, not just to control the pain, but to exclude secondary neuralgias. The initial treatment of TN is pharmacological, but surgery has an important role.

Einleitung (GERMAN)

Die TN ist eine Gesichtsschmerzerkrankung, die durch krampfartige, schwere, elektrisch-schockartige Schmerzen als Reaktion auf harmlose sensorische Reize in den Ästen des N. trigeminus (CNV) gekennzeichnet ist, in der Regel immer einseitig. Die TN wird je nach Ursache als primär oder sekundär kategorisiert.[1]

Atypical presentations suggesting secondary TN or an alternative diagnosis
Age is under 50
Pain is constant
Pain wakes patient at night
>1 division of the trigeminal nerve is affected
Sensory disturbance or numbness is present along the distribution
Pain does not respond to conventional therapy
Presence of vasomotor phenomenon

Fig. 2: Atypical presentations suggesting secondary TN or an alternative diagnosis.[2]

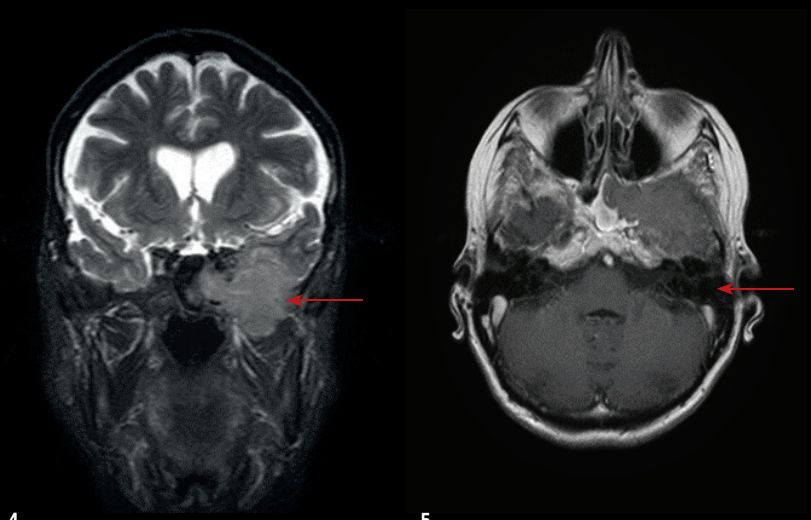
Selbst mit verfeinerten bildgebenden Verfahren ist es manchmal schwierig, eine eindeutige Ursache für die Neuralgie festzustellen; solche Fälle werden als idiopathische TN bezeichnet. Epidemiologische Studien berichten von einer jährlichen Zunahme der Inzidenz von 4,3 auf 27 neuer TN-Fälle pro 100.000 Einwohner, und sekundäre TN (STN) machte 14 bis 20 Prozent dieser Patienten in tertiären Versorgungsstudien aus. Das durchschnittliche Erkrankungsalter betrug 53 Jahre in PTN und 43 Jahre in STN.[2]

STN kann sekundär zu Grunderkrankungen wie Multipler Sklerose, Hirntumoren, Kompression des Nervs in der Schädelbasis im Bereich der Foramina, zum Beispiel bei Morbus Paget oder bei Neuropathie, auftreten.

Eine TN kann auch eigenständige Symptome verursachen, indem es den Sympathikus beeinflusst. Veränderungen des Gefäßtonus und der sekretorischen Funktionen können auftreten.[3] Im Bereich des Auges können Bindehautirritationen und Tränenfluss vorhanden sein, im Bereich des Oberkiefers können Gesichtsrötung, Schwellungen und erhöhtes Nasensekret auftreten, und übermäßiger Speichelfluss kann durch eine TN im Bereich des Unterkiefers entstehen. Die Angst vor den Schmerzen führt zur Vermeidung der Auslöser wie Rasur oder Zahnreinigung und Mundhygiene. Der Schmerz kann sich als Zahnschmerz tarnen und Patienten dadurch fruchtlose zahnärztliche Eingriffe hinter sich haben. Häufige Auslöser von TN sind unten dargestellt.

Eine hochauflösende Magnetresonanztomografie (MRT) des Gehirns und des Hirnstamms ist für alle TN-Patienten obligatorisch, um mögliche intrakranielle Ursachen einer TN wie MS, Tumore, Schlaganfälle und eine Kompression an der Schädelbasis auszuschließen. Oft sind Scans mit Kontrast erforderlich, um mikrovaskuläre Probleme darzustellen.[4] Der neurovaskuläre Kontakt ist häufig auf eine abnorme Schleife der Arteria cerebelli superior zurückzuführen, die die Trigeminusnervenwurzel berührt, wenn sie nach der Synapsierung am Ganglion Gasseri in der Meckel-Höhle (Cavum trigeminale) in den Pons eintritt.

Case 2



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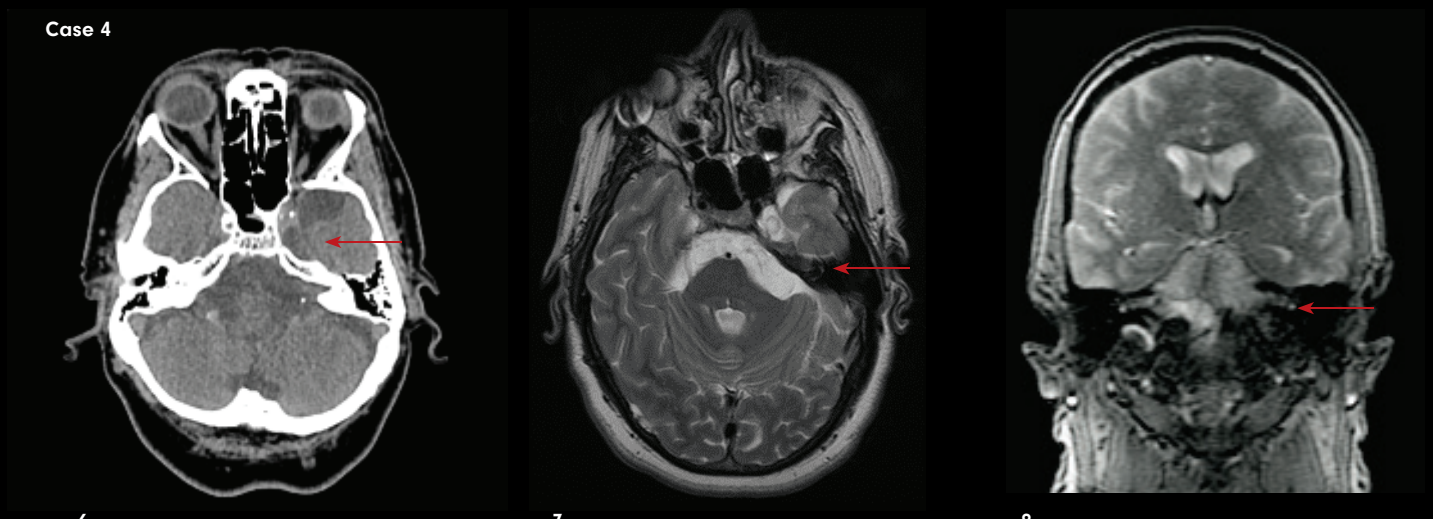
Case 4



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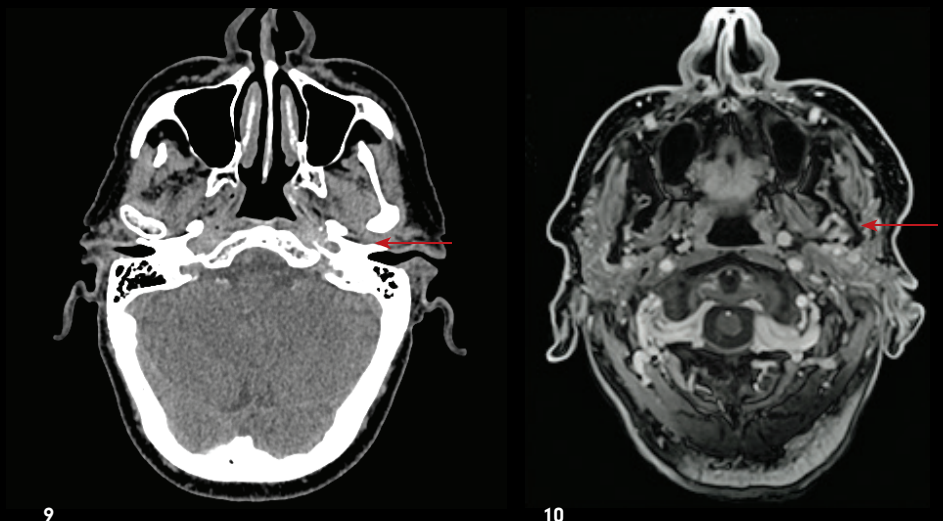
Case 5



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Figs. 4 & 5: T1 coronal and axial cuts of MRI of brain and skull base showing a large irregular skull base mass lesion (arrowhead) involving the pterygopalatine fossa and temporal lobe of the brain (as shown by arrow). – **Figs. 6–8:** Axial CT, MRI coronal T2 and MRI axial T2, respectively, of brain and skull base showing a large CSF isointense extra-axial mass (arrowheads) involving the Meckel's cave and temporal lobe on the left (as shown by arrow). – **Figs. 9 & 10:** Axial CT and MR slices showing thickened pterygoid muscles on the left (as shown by arrow).

Drug therapy of trigeminal neuralgia

An important characteristic of TN is that it does not respond well to conventional analgesics, even opioids. The mainstay of pharmacological treatment is membrane stabilising drugs such as carbamazepine, oxcarbazepine, gabapentin, pregabalin, and lamotrigine, sometimes augmented with baclofen. Intravenous infusions of the anticonvulsant fosphenytoin can be used to treat an acute TN episode.[5] Paroxysmal pain, the presence of trigger points, and symptoms responding to appropriate medication are good prognostic indicators. Patients with constant aching pain and presence of vasomotor phenomenon have less certain pain control following MVD.[3,4]

Surgical treatment

Surgical procedures have roles in managing intractable TN. Microvascular decompression (MVD) is the first-choice surgical intervention if microvascular contact has been demonstrated. It can be used for individuals for whom other less invasive methods such as radiosurgery and rhizotomy have been unsuccessful.[6] Craniotomy is performed to allow access to the posterior cranial fossa to identify and eliminate the microvascular conflict. The superior cerebellar artery is lifted from the nerve root and a Teflon™ pad is placed to separate the artery and nerve. This protects the nerve root form pulsation of the artery, which causes demyelination and hyperexcitability which is reversible when contact is eliminated. Pain relief is immediate postoperatively. MVD is the procedure with the longest lasting pain free status in patients, lasting up to five years for 50–73% of patients.[1,2] MVD carries a small risk of potentially serious complications.[2] Facial numbness and new or worsened CN dysfunction are the most frequent complications.[7]
Percutaneous rhizotomy, glycerol or alcohol injections and gamma knife surgery are other central options. Peripheral cryotherapy can be used as a rescue procedure when medication has not achieved sufficient control common in those with MS or atypical symptoms and neurosurgery is awaited. It is particularly appropriate in elderly or medically compromised individuals.[8]

Case series of secondary trigeminal neuralgia

Case 1
A 36-year-old female patient presented with severe facial pain initially thought to be right sided temporomandibular joint pain. This was exacerbated by cold, constant, and progressed to waking her up at night. Associated symptoms included otalgia, tinnitus and eventually hearing loss in the right ear. Dental causes of pain were excluded. An MRI scan revealed demyelinating plaques in the brain in keeping with a diagnosis of MS. She was treated with gabapentin and referred to neurology. She died of progressive MS after twelve years.

Case 2
A 68-year-old woman presented with predominantly typical features of TN affecting the left maxillary division. One atypical feature was that the pain woke her from sleep. Gabapentin was prescribed in view of an intolerance to carbamazepine. Subsequent MRI (Figs. 4 & 5) revealed an extensive middle cranial fossa tumour with a dumbbell appearance, partially intracranial and also extending into the pterygopalatine fossa through the foramen rotundum. Radiological findings were compatible with lymphoma or a metastatic deposit. CT of the neck, thorax, and abdomen showed extensive liver and bone metastases, with a small lesion in the lower lobe of the left lung which was thought to be the primary neoplasm.

Case 3
A 41-year-old male patient presented with intractable TN of the right maxillary and mandibular divisions of the trigeminal nerve. MRI showed an extensive arteriovenous malformation intracranially which was inoperable. The pain was refractory to initial medical management, and he underwent cryotherapy of the right inferior dental nerve under general anaesthetic as a holding procedure until gamma knife surgery could be arranged. At one-year follow-up he was pain free.

Case 4
A 60-year-old male long-distance lorry driver presented with left sided facial pain which started from within his mandible and cheek and did not resolve following extraction of multiple mobile teeth by his dentist. CT and MRI imaging with contrast showed an isointense CSF asymmetry of Meckel's cave consistent with a skull base epidermoid cyst (Figs. 6–8). It was not possible to control the pain with medication without affecting his ability to drive, and he experienced a spasm of pain whilst driving, he was forced to retire and was offered neurosurgical removal of the cyst. He was contemplating this significant surgical treatment whilst peripheral nerve cryotherapy remained an option.

Case 5
A 79-year-old male patient presented with severe pain on the left side of his face for the preceding three months. He had type 2 diabetes. The pain was localised around his TMJ and of sudden onset and triggered by eating, shaving and while going out in the cold weather. A diagnosis of TN was made on clinical grounds, and he was started on an increasing dose of carbamazepine. Subsequent MRI showed thickening and enhancement of the dural membrane and external auditory canal, with erosion of the condylar head and swelling of the masseter and pterygoid muscles, consistent with malignant otitis externa, resulting in skull base osteomyelitis (Figs. 9 & 10).

"[...] the management of TN ought to be multidisciplinary, but often patients are managed by various single specialties, such as OMFS, ENT, neurology, and neurosurgery. Excellent communications between specialties are important. [...]"

Discussion

The distinction between primary and secondary TN cannot be made on clinical grounds and detailed imaging is needed. Secondary neuralgias often have atypical features such as more constant pain, poor response to medication, and waking the patient from sleep. An underlying condition such as MS or a malignancy may already be confirmed, or the secondary neuralgia may be the first presentation of the underlying condition. The routine referral pathway may prove unsuitable for these patients especially if they are having frequent attacks of pain. In such cases primary care practitioners should phone the local maxillofacial department and seek assistance from the on-call staff. Most of the cases detailed above share important clues in the history and are in keeping with atypical symptoms.

In case 1, the pain was constant and woke the patient at night. Nocturnal waking and sensory loss were features of case 2. In case 3, the pain affected more than one division of the trigeminal nerve and in case 4 the pain did not subside following dental extractions. case 5 had an associated underlying malignancy.

Examples of space occupying lesion include benign and malignant lesions such as tumours of various origins, arachnoid or epidermoid cysts, cerebral aneurysms at the petrous portion of the internal carotid artery, or an extensive AV malformation. Neoplasms can be primary or secondary and include lymphomas, acoustic neuromas and metastatic deposits. 15% of TN patients have intracranial pathology compressing the trigeminal nerve and sometimes surrounding nerves and vessels. This makes a detailed neurological examination and cranial nerve examination at first presentation vital.[9]

Ideally, the management of TN ought to be multidisciplinary, but often patients are managed by various single specialties, such as OMFS, ENT, neurology, and neurosurgery. Excellent communications between specialties are important. Cryotherapy of the affected nerve may also be attempted with the aim to provide symptom control.

Multiple Sclerosis is a chronic inflammatory neurological disease in which demyelinating plaques are formed in the central nervous system. When these form at the root of the trigeminal nerve STN can result. TN occurs in roughly 2–5% of patients with MS and is sometimes bilateral. Conversely MS is detected in only 2–4% of cases of TN. Some patients with MS are found to have neurovascular compression of the trigeminal root. It is thought that MS increases the susceptibility of the nerve root to the effect of compression and leads more readily to painful paroxysms. These patients benefit less from pharmacological and surgical interventions than those with PTN.[10]

TN is frequently both misdiagnosed and underdiagnosed as classical symptoms may overlap with other various conditions. Common differential diagnoses include neurological, dentofacial and inflammatory conditions.[11] Misdiagnosis may lead to overtreatment as these patients present at secondary care having had extensive dental treatment before which included root canal therapy, extraction of multiple teeth or a diagnosis of TMJDS. Education of dentists of TN and its features can accelerate diagnosis. Sometimes pain thought to be associated with TMJDS or TN can in fact be related to an entirely separate condition which may need urgent management as shown by the last case. Fear of triggering the pain can mean patients speak without moving their mouths, omit oral hygiene, shaving, driving, or taking part in social activities. TN can lead to anxiety and depressive states and psychological specialist support following diagnosis is important. Regular follow up to review medication doses, effects, and side effects is needed.

Conclusion

TN is a life-changing condition. Dentists must be aware of its presentation, initial investigations needed and management as well as consider this diagnosis when assessing dentofacial pain such as in cases of presumed TMJDS. Clinical and radiographic examination, excluding dental pathology, is essential. Management of secondary TN according to the underlying pathology may need a multidisciplinary approach.

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