Odontalgia Simulating Trigeminal Neuralgia: practical approach based on serial cases

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ABSTRACT
Introduction: The most frequent cause of orofacial pain is from dental origin, which can present either with nociceptive and/or neuropathic features, often confounding the health professional in the correct diagnosis, becoming a challenge even to the more experienced clinician. Objectives: To emphasize the importance of a specialist in Temporomandibular Joint Disorders and Orofacial Pain in the hospital facility, in order to perform differential diagnosis of dental pain in patients with clinical hypothesis of trigeminal neuralgia. Case Presentation: The authors propose a guide for the correct evaluation of dental pain based on a series of five cases illustrating how odontogenic pain can mimic a trigeminal neuralgia, often generating misdiagnosis and, several times, irreversible treatments. Conclusion: Multidisciplinary approach is mandatory in many patients with symptoms suggesting trigeminal neuralgia, minimizing the risks of misdiagnosis. Once the correct diagnosis is established, the treatment will focus on the resolution of its causes.

Keywords: Odontalgia; Facial pain; Referred pain; Trigeminal neuralgia

RESUMO
Introdução: A causa mais frequente de dor orofacial é de origem dentária que pode apresentar-se com características nociceptivas e/ou neuropáticas, confundindo muitas vezes o profissional de saúde no correto diagnóstico, tornando-se um desafio até mesmo para o clínico mais experiente. Objetivos: Enfatizar a importância da presença do specialista em Disfunção Temporomandibular e Dor Orofacial no corpo clínico hospitalar com o intuito de realizar o diagnóstico diferencial de odontalgias em pacientes com hipótese clínica de neuralgia trigeminal. Relato de caso: Baseado numa série de cinco casos é ilustrado como a dor odontogênica pode mimetizar uma neuralgia trigeminal, capaz de gerar um diagnóstico equivocado e, tantas vezes, um tratamento irreversível. Os autores estabeleceram um guia para uma correta avaliação diagnóstica das dores de origem dental. Conclusão: Uma equipe multidisciplinar é imprescindível na abordagem de pacientes com sintomas sugestivos de neuralgia trigeminal para minimizar os riscos de um diagnóstico errôneo. Uma vez estabelecido o correto diagnóstico, o tratamento se concentrará na resolução de suas causas.

Palavras-Chave: Odontalgia; Dor facial; Dor referida; Neuralgia trigeminal

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Received Feb 3, 2022
Corrected Mar 9, 2022
Accepted Mar 27, 2022
INTRODUCTION

Trigeminal neuralgia (TN) is the most frequent cause of facial neuralgia, with estimated prevalence of 4.3 cases per 100,000 people, affecting more women than men in a 3:1 ratio. TN rarely affects individuals under the age of 40 years, since 90% of symptomatic cases occur above this age, which incidence increases progressively after 60 years. The correct diagnosis may consist in a great challenge to the clinician, since several other orofacial painful conditions can simulate the diagnosis of TN, especially in patients with pain of dentoalveolar origin.

Trigeminal Neuralgia is described by the International Classification of Headache Disorders – 3rd Edition (ICHD-3) and the International Classification of Orofacial Pain, 2020 (ICOP) as a short-term, high-intensity, lancinating, electric shock-like, unilateral pain limited to the inervation regions of the fifth cranial nerve. It may be triggered by innocuous stimuli such as touch and/or most often arise spontaneously with sudden onset and abrupt ending. In some cases, the symptoms can remain for more than 2 minutes and/or present a persistent and continuous painful sensation. The paroxysmal event can occur several times a day, with a high potential for worsening in the frequency, duration and intensity of pain.

Orofacial tissues such as tooth elements, periodontal tissue, nasal mucosa, skin of the facial region, temporomandibular joint and adjacent muscles are largely innervated by the trigeminal nerve, which corresponds to the fifth cranial nerve. They can often be a source of orofacial pain (OFP) of peripheral origin, using the trigeminal sensory system to respond to nociceptive peripheral stimuli of these tissues. OFP conditions represent a large spectrum of painful disorders that can overlap each other, sometimes mimicking other disorders that converge to the same trigeminal pathways.

Among the disturbances that most affect the oral region, odontogenic pain of inflammatory and/or infectious nature can easily generate some of the manifested symptoms in other non-odontogenic diseases, such as TN. It is important to highlight that the tooth element is constituted by a mineralized organic tissue, where the root canal and the pulp cavity (containing the dental pulp) can be found. They exhibit a nervous and vascularized tissue. The tooth element is firmly inserted into the alveolar bone through periodontal ligaments corresponding to musculoskeletal structures. Pulpar dental pain emerges due to the release and activation of many pro-inflammatory endogenous chemical mediators, such as bradykinin, prostaglandins, substance P and interleukines. Beyond that, peripheral sensitization can occur due to exogenous substances from bacteria, increasing the intrapulpar pressure. These substances directly promote further vasodilation, increased vascular permeability, and other inflammatory reactions, causing pain. It is noteworthy to point out that pulpar and peri radicular pain can also occur after the application of mechanical, thermal, chemical and electric stimuli. Therefore, odontogenic pain can mimic both neuropathic and musculoskeletal pain characteristics.

This study aims to reinforce the importance of a dentist specialized in Temporomandibular Joint Disorders and Orofacial Pain (TMJD and OFP), both in the hospital as well as in the outpatient facility, adding a multidisciplinary assistance, in order to perform a differential odontogenic diagnosis in patients with initial diagnostic hypothesis of TN.

CASE PRESENTATION

Case 01
Caucasian male patient, 51 years old. Patient reported pain in the left V3 area started one year before consultation, severe with Visual Analog Scale (VAS 10/10), paroxystic, electric shock-like, often ultrashort (few seconds), rarely lasting up to 3 minutes. It occurred several times a day, with worsening when chewing or brushing his teeth with no increase with light touch or while speaking. As previous history, he reported a car crash few months before the initial pain, when was diagnosed a cominutive fracture of the face, although the patient did not correlate the pain in the face to the accident. After a neurological consultation, the patient had the hypothesis of idiopathic trigeminal neuralgia, and performed a magnetic resonance imaging (MRI) showing no abnormalities. The recommendation of carbamazepine 200 mg TID resulted in moderate improvement of symptoms with minor side effects. However, following a multidisciplinary evaluation, the patient was referred to a dentist specialized in TMJD and OFP for differential diagnosis of odontalgia. At odontological clinical exam, the patient related spontaneous pain, increased by cold liquids. The percussion test elicited major pain at the inferior molar tooth. A Cone Beam Computed Tomography
(CBCT) scan (Prexion Elite, Yoshida, Japan) of the lower dental arch was requested and depicted a transverse hypodense line crossing from vestibular to lingual, in the center of the crown of tooth 47 (Lower Right Second Permanent Molar), suggestive of fracture. In addition, a periodontal hypodensity suggestive of an inflammatory lesion was found (Figures 1 and 2). The scanning parameters were 90KVP, 5mA, a spatial resolution of 150 μm and a field of view of 50 x 50 mm.

After final diagnosis of longitudinal fracture involving the dental root and crown associated with irreversible acute pulpitis, patient was managed with extraction of tooth element 47 (Figure 3), resulting in complete relief of pain soon after the extraction.

### Case 02

Female patient, 51-years-old, Caucasian. She complained of a sudden pain in the right face in V2 and V3 areas starting approximately 20 days before his first consultation. Pain was excruciating, with electric shock-like pattern (VAS 10), seldom occurring at rest, but many times while eating, drinking or chewing either cold and/or hot foods. After a family physician evaluation (neurological consultation), the diagnosis was defined as TN. At that time, carbamazepine 400mg BID was prescribed associated with ketoprofen 150mg if needed. Six days later, the patient reported VAS 04, but stopped using carbamazepine due to adverse effects, and only continued with nonsteroidal anti-inflammatory drugs (NSAIDs) with the same previous partial improvement (VAS 04). The patient was instructed to search a service specialized in TMJD and OFP. A CBCT scan (Prexion Elite, Yoshida, Japan) was done, but depicted no major abnormality that could cause the pain. The scanning parameters were 90KVP, 5mA, spatial resolution of 150 μm and a field of view of 50 x 50 mm. During clinical consultation, the patient described spontaneous pain at the right region of the face, with tenderness after percussion of the first molars either superiorly as well as inferiorly. Both teeth responded to the cold (Endo Ice Spray -50°, Maquira, Maringá, Brazil), ceasing the pain soon after the removal of the stimulation. After heat stimulation, the lower right first permanent molar (46) had an intense painful response that lasted some minutes after the removal of the stimulus. At careful inspection, a fissure at the occlusal aspect was seen, suggesting a crack. Furthermore, a diagnostic anesthetic block has been done with lidocaine 2% at the inferior alveolar nerve, promoting a total pain relief. The patient was sent to endodontic treatment, where a crack on the occlusal surface was confirmed. At that time, the endodontic tissue showed major signs of inflammatory reaction (Figures 4 and 5). After the conclusion of the endodontic treatment, the patient was asymptomatic, and a prosthetic rehabilitation was done.

**Figure 1.** CBCT image on a coronal view of tooth 47 showing the dental fracture.

**Figure 2.** CBCT image on sagittal view of the tooth 47 showing longitudinal fracture (upper arrow) and apical hypodense region (lower arrow).

**Figure 3.** Post-surgery periapical x-ray of the tooth 47.
Final diagnosis was irreversible acute pulpitis (Figure 5), opting for endodontic treatment of tooth 46 (Figure 6), with total improvement of pain after three days.

**Case 03**

A 47-years-old Caucasian female patient. The patient reported pain in the left V3 area, mainly in mandibular region, with high intensity (VAS 10), started 21 days before her consultation. The most common pain triggers were chewing and cold liquid ingestion. It manifested as electric shock-like pain lasting few seconds up to 2 minutes many times a day in addition to a continuous burning pain. No relief factor was reported. She underwent a clinical consultation with a neurosurgeon that established the diagnosis of TN, with further prescription of carbamazepine 400mg TID plus phenytoin 100mg TID. The patient had moderate pain relief (VAS 03) despite major sedation. After brain MRI no neurovascular contact or other abnormalities were found. Nevertheless, neurosurgical procedure of trigeminal microdecompression was indicated, although she had been referred to dental evaluation. In intraoral dental examination, tooth 36 (lower left first permanent molar) had a brownish coloration, suggesting a possible endodontic disease. When pulp sensibility test was performed with coolant spray (Endo Ice spray -50°C Maquira, Maringá, Brazil) the pain was excruciating. Despite the patient reported a restorative treatment in this same tooth about 30 days before, a CBCT scan (Prexion Elite, Yoshida, Japan) of the left lower hemiarch was performed, which showed a large restorative material close to the pulp chamber of the tooth 36, beyond an increase in the apical periodontal space, highly suggestive of a pulp inflammatory process (Figure 7). The patient was oriented to cancel the surgical procedure due to the clinical finding of odontalgia. After endodontic treatment, the pain had a complete relief.

The final diagnosis of irreversible acute pulpitis was managed with endodontic treatment of tooth 36 (Figure 8), resulting in complete relief.
Case 04
Female patient, 34-years-old, Caucasian. She related painful hypersensitivity in the right face started 2 years before consultation with a dentist specialized in TMJD and OFP. At first, it had a low intensity (VAS 03), lasting up to 2 hours, with “pins-and-needles” pattern, occurring 3 to 4 times a week, relieved by NSAIDs. However, one year later, the pain worsened significantly (VAS 08) with allodynia and hyperalgesia in the right V2 and V3 regions. The pattern changed to electric shock-like pain, lasting few seconds (10s), in addition to a continuous burning pain. The patient reported no relief factors. The most common pain stimuli were chewing solid food and drinking cold liquid. After consulting a family physician (neurological consultation) she was diagnosed with TN. On MRI examination, the trigeminal nerve region had no neurovascular compression. The doctor prescribed carbamazepine 400mg BID with no significant improvement. On her own, she sought for a second opinion and for help in analgesic control, being evaluated by a dentist specialized in TMJD and OFP who evidenced pulp alteration in tooth element 46 (lower right first permanent molar). After thermal test with coolant spray Endo Ice spray -50° (Maquira, Maringá, Brazil), the patient had a severe painful sensation in the entire ipsilateral facial region, lasting for at least 5 minutes after the stimulation. The patient was oriented to stop the intake of carbamazepine and started ibuprofen 600mg TID plus codeine 30mg QID. A left mandible CBCT scan (Prexion Elite, Yoshida, Japan) was requested, which showed tooth element 46 with large restoration with restricted apical hypodensity compatible with inflammatory lesion (Figure 9). After final diagnosis of irreversible acute pulpitis, managed with endodontic treatment of tooth element 46 (Figure 10), the patient presented progressive resolution of pain until complete relief 4 days after treatment.

Case 05
Female patient, 31-years-old, Caucasian. According to the patient she was under treatment for TN on the right side (V3), diagnosed by a neurologist, using carbamazepine 400mg BID for almost 60 days, with partial relief (VAS 04).
She reported electric shock-like pain, lasting few seconds (10s) and rarely up to 2 minutes, and the pain is elicited by thermal stimuli. She went to a dentist specialized in TMJD and OFP in order to treat a limitation of oral opening, since the pain was assumed to be due to TN and was following treatment. As past history, the patient reported nocturnal bruxism. During extraoral inspection, it was observed pain in ipsilateral masseter and temporal muscles in addition to the presence of myofascial trigger points due to muscle contracture that reduced the amplitude of oral opening. On intraoral examination, partial coronary destruction of tooth element 15 (upper right second premolar) was observed, in addition to a significant carious tissue. When hyperalgesic test with coolant spray -50°C in this same tooth was performed, a lancinating pain was triggered, similar to the painful attacks of trigeminal neuralgia. CBCT scan (Prexion Elite, Yoshida, Japan) of the right maxilla was requested and showed an increase in the apical periodontal space in tooth element 15, suggestive of an inflammatory process in addition to sinusopathy in the ipsilateral maxillary sinus (Figure 11). In light of this finding, carbamazepine was requested to be discontinued. An endodontic treatment of the tooth 15 was performed with complete pain relief.

After final diagnosis, irreversible acute pulpitis, the option of management was endodontic treatment of tooth element 15 (Figure 12), resulting in complete pain relief.

**DISCUSSION**

The trigeminal nerve is a large cranial nerve, dividing into three major peripheral branches, namely: ophthalmic nerve (V1), maxillary nerve (V2) and mandibular nerve (V3). It is a mixed nerve, including both sensory and motor fibers. It receives sensory afference from the face and forehead to the mandible while the ramifications are widely distributed in the craniocephalic region, thus enabling the stimulation in a diversity of diseases that may affect these locations, and, often simulating pains from different causes, often promoting similar symptoms. The diagnosis of TN is based on a detailed anamnesis, with characteristic clinical signs and symptoms. Both ICHS-3 and ICOP describe specific criteria that guide clinical evaluation. Based on these criteria, classical trigeminal neuralgia (CTN) can be subdivided into purely paroxysmal TN or TN with persistent facial pain.

From the five cases here presented, four underwent MRI in order to detect the common neurovascular contact on the trigeminal root, as seen in most cases of TN. In all these cases, there was no imaging finding of such vascular compression. In a meta-analysis study using MRI with trigeminal ganglion and nerve analysis, 35.8% (OR = 16.6; 95% CI = 11.8–23.3; P < 0.0001) of asymptomatic control subjects (244 out of 681) presented neurovascular contact (otherwise called neurovascular conflict),
indicating that this method shows high sensitivity and low specificity\textsuperscript{15}. Thus, physicians should be aware of the occurrence of neurovascular contact alone as a diagnostic criterion\textsuperscript{15}.

There would be a great possibility of surgical intervention if any of these patients here studied had a neurovascular compression. Furthermore, the first line medications for TN, such as carbamazepine or oxcarbazepine may not improve the pain in many cases, since odontalgia usually is not relieved with anticonvulsants\textsuperscript{16,17}.

The main author previously published a report of a patient diagnosed with TN secondary to intracranial trigeminal schwannoma, with initial indication of neurosurgery for tumor resection. However, as the patient reported dental hyperalgesia while chewing, she was referred to a dentist specialized in TMJ and OFP. The pulp sensibility test was performed using thermal stimulation to cold, and one of the teeth responded positively, promoting excruciating pain for 3 minutes, resembling “trigeminal attacks”. On periapical radiological examination, a large restorative material was found in close contact with pulp tissue, which resulted in irreversible acute pulpitis. Endodontic treatment was indicated and completely ceased the symptomatology. The neurosurgical team, thereafter, decided to postpone any surgical intervention\textsuperscript{18}.

The medical team should be aware of the great responsibility of diagnosing TN, with the exclusion of causes of odontogenic pain that should always be evaluated (Table 1), as in cases when the dental pulp may present inflammatory reaction due to chemical, physical or even microbiological stimuli (pulpitis)\textsuperscript{20-22}.

### Table 1. Script model for anamnesis proposed for bedside patient (modified)\textsuperscript{18,19}

| 1) Ask about history of previous dental treatments and especially on recent restorations and/or trauma |
| 2) Ask the patient about fundamental questions: |
| a. Location of pain? Ask to point out with the finger where the pain is |
| b. Onset of pain? Spontaneous or evoked? (Irreversible pulpitis is spontaneous) |
| c. Intensity of pain? Mild, moderate or excruciating pain |
| d. Quality of pain? Examples: burning, electric shock, needling, pinprick, shooting, sharp or others. |
| e. Duration of the pain? Seconds, Minutes, hours or days |
| f. Frequency of pain? Daily, weekly or monthly |
| g. What improves pain? In cases of prolonged pulpitis, there is a typical relief with cold, although the pain becomes more localized |
| h. What makes the pain worse? Examples: cold, hot, chewing. |
| 3) Perform extraoral palpation in search of cervical lymphadenopathy |
| 4) Evaluation of the oral cavity in search of swollen gingival tissue, presence of dental darkening, structural abnormality in some tooth. |
| 5) Carry out the vertical percussion test to exclude acute periodontitis. |
| 6) Carry out the test of thermal hyperalgesia to the cold by spray vapocoolant. Remember to start the cold test on the contralateral side to the pain. |
| 7) Test thermal hyperalgesia at heat by heated rod, or even external heat source, in order to reproduce the pain. |
| 8) Request, as soon as possible, a panoramic, periapical or CBCT to identify clinically unexposed carious lesions, large restorations, endodontic and/or periodontal lesions. |
The dental pulp consists of loose connective tissue, which contains a vascular nervous bundle with important functions such as nourishing and giving sensory input to the tooth elements. After injury and/or aggression, it will trigger a neurogenic inflammatory response, leading to an overactivation of peripheral nociceptive nerve fibers and increased expression of intracellular algogenic substances such as substance P, CGRP, prostaglandin E2, prostaglandin F2a, interleukin 1, 6 and 8, TNF-α and MMP-9. This can easily mimic a trigeminal neuropathic pain. Moreover, it has been widely shown that sodium channels play a key role in regulating neuronal excitability. They are distributed throughout the primary afferent, and have their expression increased, both in the periphery (close to the site of nerve injury), as well as in central terminations of this fiber and in the dorsal root ganglion, producing an increase in neuronal excitability. At first, these changes were described primarily for Nav1.7 isoform, but more recently, changes have been described for Nav 1.8 and Nav1.9, leading to huge immune cellular response.

The neurogenic inflammatory process after an acute pulpitis promotes both peripheral sensitization and central sensitization with the classic characteristics of allodynia, hyperalgesia and amplification of the receptive field of pain, changing typical symptoms and signs, due to the complexity of the pathophysiology that can easily mimic a trigeminal neuropathic pain. This can be easily seen in the reported cases.

Diagnostic criteria according to ICOP characterize the clinical condition of irreversible pulpitis defining the main characteristic as spontaneous and constant pain, outlasting the period of the stimulus (cold, hot or mechanical), delayed onset, throbbing, often difficult to be located by the patient. The masticatory function can promote pain intensification and, after performing the thermal or mechanical percussion test on the tooth element, there will be hyperalgesic response greater than 30 seconds. It is important to note that acute pulpitis in the initial stage usually irradiates to close structures while in the more advanced stage, when areas of necrosis appear. It becomes more localized and can be easily identified by the patient and confirmed by the thermal test of pulp sensibility with coolant spray -50°C which will trigger prompt hyperalgesic response of the affected tooth. However, some odontogenic conditions are considered to be of great diagnostic challenge, possibly mimicking TN symptoms, since the characteristic of pain is altered at this stage, becoming diffuse and referred in several regions of the craniocephalic trigeminal territory, such as teeth, face and head. The symptomatology is amplified by thermal stimuli to heat and chewing, but is relieved by cold.

CTCB scan can be an important diagnostic technique in many cases, sometimes identifying the source of irreversible pulpitis. When an inflammatory pulpar response occurs, this image modality can show a mild thickening in the periodontal ligament at the periapical region, as seen in cases 3, 4 and 5. This scan has shown superiority accuracy when compared to panoramic and periapical radiographs.

Dental sensitivity tests are used as supplementary resources in order to determine the real condition of the dental pulp in several circumstances to establish the differential diagnosis of odontalgia. Currently, several tests can be used. However, two of them are mostly used to perform pulp sensibility: a) the mechanical vertical percussion test and b) the cold test with coolant spray. Vertical percussion with solid instruments should be performed on a healthy adjacent tooth so that the patient has normal sensory perception followed by the test on the tooth with supposed alteration, as it will present hyperalgesia compared to the healthy tooth.

The cold test presents a greater predictor of the real pulp condition, since cold has a greater chance of changing the sensitivity in an inflamed pulp. The test should be performed by the surface of the tooth, always with the dry tooth, where a pellet of cotton frozen by the refrigerant spray -50°C will be applied with the aid of bipolar forceps until the patient feels the painful sensibility. Similarly to the previous one, the cold test should be performed on an adjacent tooth to compare the hypersensitivity that will pass seconds after the removal of cotton. Unlike the healthy tooth, in a pulpitis, a hyperalgesic response will occur for a prolonged time with a subjective report of pain by the patient.

Then, an adequate anamnèse should be taken and, mainly, attention should be paid to the smallest details that the patient has to inform about the characteristics of pain, as it may reveal some signs that this sensation is mimicking its main cause. Therefore, the evaluation of an interdisciplinary specialist in TMJD and OFP following the scheme of an adequate investigation prior to any neurosurgical procedure can avoid iatrogenic procedures and propose an appropriate treatment.
CONCLUSION

Pain resulting from pulp alterations is characterized as the most common etiological factor of orofacial pain. Thus, the correct diagnosis will lead to therapeutic success and avoid possible unnecessary interventional procedures.

Doctors should be aware that not all orofacial pains that present as electric shock-like and/or burning are pathognomonic of trigeminal neuralgia, since other etiological factors may be present with the same symptomatology through trigeminal sensory pathways. Therefore, the authors suggest that the medical evaluation of a patient with a diagnostic hypothesis of trigeminal neuralgia also include a detailed intraoral examination performed by a dentist specialized in Temporomandibular Joint Disorders and Orofacial Pain. In this way, the interdisciplinary team will be crucial for this group of patients.

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