

## INVITED REVIEW

# Trigeminal neuropathy

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**Trigeminal neuropathies (TNs) are well recognized disorders characterized and manifesting as skin and mucosal numbness in the region innervated by the trigeminal nerve. Facial numbness indicates trigeminal sensory alteration affecting the trigeminal system. TNs always pose differential location difficulties as multiple diseases are capable of producing them: they can be the result of traumatism, tumors, or diseases of the connective tissue, infectious or demyelinating diseases, or may be of idiopathic origin. Their importance is explained by the fact that TN may represent the first manifestation of tumor disease, or of relapse in patients with prior neoplastic processes. As such, these manifestations are ominous, and patient life expectancy is often short. The clinical exploration reveals a loss of sensitivity in the cutaneous territory corresponding to the affected nerve, which can be partial (hypoesthesia) or complete (anesthesia). The sensory defect is occasionally associated with hyperesthesia (i.e., the patient suffers a decrease in sensory perception, but when sensation is perceived, it may cause considerable discomfort). Complementary studies are needed to establish the etiologic diagnosis, with laboratory tests to discard the possible causative diseases underlying the trigeminal neuropathy, and the opportune radiographic examinations in the form of plain X-rays or a routine cranial computed tomography scan.**

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## Introduction

Trigeminal neuropathies (TNs) are well recognized disorders characterized and manifesting as skin and mucosal numbness in the region innervated by the trigeminal nerve (Calverley and Mohnac, 1963).

Facial numbness indicates a trigeminal sensory alteration affecting one or more branches of the trigeminal nerve, Gasser's ganglion, the sensory roots or the sensory nucleus of the trigeminal nerve, the cortico-thalamic pathway, the thalamic nuclei, the thalamus-cortical pathway and the cerebral cortex (trigeminal system). TNs always pose differential location difficulties as multiple diseases are capable of producing them: they can be the result of traumatism, tumors, or diseases of the connective tissue, infectious or demyelinating diseases, or may be of idiopathic origin (Peñarrocha, 1997).

Though there are many potential causes for TN, the possibility of a neoplastic process must always be taken into consideration (Selby, 1975; Martí, 1986). This is particularly the case when numbness spreads gradually, even when trigeminal motor function and the corneal reflex are preserved – requiring the exclusion of a tumor of the skull base or located in the proximity of the trigeminal ganglion (Fisher, 1983).

The importance of TNs is explained by the fact that they may constitute the first manifestation of tumor disease, or of relapse in patients with prior neoplastic processes. As such, these manifestations are ominous, and patient life expectancy is often short (Laurencet *et al*, 2000).

## Clinical presentation and physical findings

The clinical exploration reveals a loss of sensitivity in the cutaneous territory corresponding to the affected nerve, which can be partial (hypoesthesia) or complete (anesthesia). The sensory defect is occasionally associated with hyperesthesia (i.e., the patient suffers a decrease in sensory perception, but when sensation is perceived, it may cause considerable discomfort) (Selby, 1975).

Robinson and Williams (1986) described a clinical documentation method to reflect inferior alveolar and lingual nerve paresthesia based on patient response to painful stimuli, in order to quantify the degree of involvement and plan management.

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The clinical exploration of these patients is very important to reject other associated injuries and other possible cranial nerve defects, particularly paralysis of the VI cranial nerve (abducens nerve), which limits abduction or separation of the eye ipsilateral toward the disabled side. Likewise, it is necessary to explore the VII and VIII cranial nerves. This type of defect is caused by tumors located in the region of the pontocerebellar angle (Alpers and Mangall, 1975; De Myer, 1976; Lazorthes, 1978; Aronson, 1980; Pelissou *et al*, 1988).

## Diagnostic testing

Complementary studies are needed to establish the etiologic diagnosis, with laboratory tests to discard the possible causative diseases underlying the trigeminal neuropathy (TN) (Table 1), and the opportune radiographic examinations in the form of plain X-rays or a routine cranial computed tomography (CT) scan – in order to discard alterations of the maxillary sinus, of Meckel's cavum, or of the pontocerebellar angle (Peñarrocha, 1997). Hutchins *et al* (1989) defend radiological evaluation in patients with TN, including CT and magnetic resonance imaging (MRI), to analyze the proximal region (brainstem, preganglionic region, Gasser's ganglion, and cavernous sinus) and distal zone (extracranial portion of three roots), and the trajectories of the V cranial nerve. The authors moreover stressed

the difficulty of identifying the location of the trigeminal injury based on the clinical manifestations.

## Trigeminal neuropathy variants

### Traumatic trigeminal neuropathy

While many alterations can give rise to TN, traumatism – accidental or of an iatrogenic nature – are the most frequent cause (Rushton *et al*, 1984), representing up to 40% of all cases (Peñarrocha *et al*, 1994). Most post-traumatic TNs manifest after oral surgery, particularly removal of impacted lower third molars (Sandstedt and Sørensen, 1995). The associated sensory defects are located mainly in the territory innervated by the inferior alveolar and lingual nerves (Blackburn, 1990).

The underlying cause is damage to the inferior alveolar nerve, attributable to the anatomical proximity between the third molar apexes and the canal housing the nerve (Sandstedt and Sørensen, 1995; Robinson, 1992). Likewise, due to the anatomical position of the lingual nerve in relation to the third molars, the former may be damaged during extraction procedures (Robinson, 1992; Walters, 1995; Brann *et al*, 1999). Schultze-Mosgau and Reich (1993) reported a 2.2% and 1.4% incidence of neuropathies involving the inferior alveolar nerve and lingual nerve, respectively, in a series of 1107 molar extractions. Fielding *et al* (1997), in a survey of 452 maxillofacial surgeons, found that 343 claimed to have patients with lingual sensory defects after the removal of impacted mandibular molars – such defects being permanent in 18.6% of cases. According to Kipp *et al* (1980), following the removal of 1377 mandibular molars, a total of 60 cases of dysesthesia or hypoesthesia were recorded – these problems being permanent in 13 cases. Surgery of this kind entails a risk, even when performed with maximum care, and patients should be informed of the fact.

The development of TN as a consequence of dental anesthesia is scarcely mentioned in the literature. Chang and Mulford (2000) published a case of iatrogenic TN secondary to the injection of local anesthetic. There also have been reports of iatrogenic TN following thermal lesions of Gasser's ganglion (Iñiguez *et al*, 1997). Regarding chin numbness after dental implant placement, cases have been documented in the literature as a consequence of direct inferior alveolar or mental nerve damage produced by the surgical drill or the implant itself (Bartling *et al*, 1999). One case has been described after dental anesthesia in the context of these procedures – without the implant directly affecting the nerve (Flanagan, 2002).

Older patients suffer significantly more pain, as reported by Sandstedt and Sørensen (1995) – this being similar to the situation found in postherpetic TN, where for unknown reasons the incidence increases with age, affecting 30–50% of all patients over 60 years of age (Chang and Mulford, 2000).

According to Karas *et al* (1990), TN is characterized by increased sensory alteration in women. In turn, Sandstedt and Sørensen (1995) found women to suffer more pain, and the latter moreover lasted longer than in

**Table 1** Etiology of trigeminal sensory neuropathy

Direct and indirect traumatism
Dental avulsion (lower third molars)
Inferior alveolar nerve block
Implantology
Endodontic treatment
Orthognathic surgery
Tumors
Malignant
Intracranial
Pontocerebellar angle
Gasser's ganglion
Trigeminal branches
Benign
Odontomas
Collagen diseases
Lupus erythematosus
Dermatomyositis
Progressive sclerosis
Sjögren's syndrome
Rheumatoid arthritis
Connective tissue diseases
Idiopathic trigeminal sensory neuropathy
Infections
Herpes zoster virus
Herpes simplex
Syphilis
Leprosy
Others
Multiple sclerosis
Vascular vertebrobasilar diseases
Sarcoidosis
Amyloidosis
Sickle-cell anemia
Chemical agents: endodontic treatments
Toxic agents: stilbamidine, trichloroethylene

males. Most of our patients were women, and no significant differences were observed on relating patient sex to the presence or characteristics of pain.

The prognosis is dependent upon the severity of the lesion. Kipp *et al* (1980), after performing 1377 impacted lower third molar extractions, recorded sensory alterations in 60 cases – of which 64% resolved within 6 months. Some authors (Wofford and Miller, 1987) report that the incidence of spontaneous recovery 6 months after causal trauma is very small, and that if axon regeneration does not take place within 2 years, the regeneration potential is lost and the damage becomes permanent. According to Kipp *et al* (1980), less than 1% of all the patients who undergo lower third molar extraction suffer permanent dysesthesia and hypoesthesia. In these cases it is only possible to evaluate the potential for surgical nerve repair by means of microsurgery of the peripheral nerve (Gregg, 1990a,b).

Upton *et al* (1987) studied 52 cases with alterations of the inferior dental nerve secondary to sagittal osteotomy of the jaw and to extraction of lower third molars – no correlation being found between the terms used by the patients to describe the alterations and the predictions for regeneration. In addition, they did not observe any relationship between the topographic distribution of the sensory alteration and the predicted or actual residual deficit. The best possible treatment is prevention, while Chau *et al* (1989) described the different surgical skills required to minimize damage to the inferior dental nerve during sagittal osteotomy of the jaw.

With regard to possible treatments, Queral-Godoy *et al* (2006) reported in their study that 17 patients did not receive any treatment, while five received oral vitamin B complex once a day for a median of 7 days, and three underwent low-power laser sessions weekly, for 7–15 weeks. Robinson *et al* (2004) developed an algorithm to guide management decisions for such patients. In a small proportion of cases, damage to the inferior alveolar nerve is noted at the time of operation. As the neurovascular bundle is well supported within the mandibular canal, and even after sectioning the ends do not retract, primary repair of the nerve is not normally required. Medication or hemostatic agents such as Whitehead's varnish® (compound iodoform paint) or Surgicel® (oxidized regenerated cellulose; Ethicon Sarl, Neuchâtel, Switzerland) should also be avoided as they can cause chemical injury of the nerve (Loescher and Robinson, 1998).

Sandstedt and Sørensen (1995) studied 226 patients with trigeminal sensory alterations who applied for economic compensation from insurance companies. Of these cases, 79% were attributed to lower third molar extraction, and paresthesias were reported by 70% of the patients. Women and elderly individuals reported more discomfort after oral nerve damage. The pain involved may cause both functional and psychological problems for these patients (McGowan, 1995). Robert *et al* (2005) asked 535 Californian Oral and Maxillofacial Surgeons (OMFS), representing 86% of all OMFS, how many sensory injuries they had recorded during their professional career. Instances of injury to the

inferior alveolar nerve in a 12-month period were reported by 94.5% of the surgeons, while 53% reported instances of lingual nerve injury in a 12-month period. Cases of permanent injury of the inferior alveolar nerve were reported by 78% of OMFS; 46% reported permanent lingual nerve injury occurring during their professional lifetime. The overall estimated self-reported rate of injury was 4 per 1000 lower third molar extractions for the inferior alveolar nerve, and 1 per 1000 extractions for the lingual nerve for all cases (temporary and permanent). In most cases (80%) of inferior alveolar nerve injury the cause was known, but in a majority of cases of lingual nerve injury (57%) the etiology was not known. Self-reported rates of permanent injury were 1 per 2500 lower third molar extractions for the inferior alveolar nerve, and 1 per 10 000 lower third molar extractions for the lingual nerve. Injury rates were associated with treatment provider experience (i.e., extractions made per year), and years in practice.

#### Neoplastic trigeminal neuropathy

The importance of the diagnosis of neoplastic TN is that the disorder may manifest in the context of a systemic neoplastic process, and in some cases can precede the diagnosis of the malignancy (Martí, 1986; Halachmi *et al*, 2000). TN frequently reflects metastatic invasion or contiguity spread of the tumor lesion to the cranial nerves (Burt *et al*, 1992). TNs have been reported secondary to the following processes: tumors located in the region of the pontocerebellar angle (Matsuda *et al*, 2000), Gasser's ganglion, the trigeminal roots (Paquis *et al*, 1998), or nasopharynx and maxillary sinus (Dalmau and Grauss, 1986); and mandibular benign (Bodner *et al*, 1987) or malignant lesions (Heng and Heng, 1995; Halachmi *et al*, 2000; Reyes *et al*, 2003).

In this context, in the review by Massey *et al* (1981), 47% of the patients reported dysesthesias prior to diagnosis of the cancer. This fact makes it necessary to explore the presence of a possible occult neoplasm in non-oncological patients diagnosed with mental nerve neuropathy – focusing attention on bronchopulmonary and breast malignancies and lymphoproliferative processes, which represent the most common underlying etiologies. Vadell *et al* (1989) presented five patients in the context of progressing neoplastic disease.

The degree of involvement and the location of the lesion are highly variable. Despite availability of the most recent early diagnostic techniques, it is difficult to differentiate 'benign' TN from 'malignant' tumor-associated presentations. Early clinical and radiological evaluation is of crucial importance (Kuntner *et al*, 1992). In the event of sensory defects in the territory of the trigeminal nerve, the presence of a primary tumor or of metastatic relapse of malignant disease at some point along the trigeminal trajectory must be discarded (Vadell *et al*, 1989).

Clinically, neoplastic TNs can manifest as numbness or numbness with pain, in an association of deficiency and irritative symptoms (Bullit *et al*, 1986; Schnetler and Hopper, 1989). Malignant mental neuropathy (MMN) is characterized by spontaneous, non-traumatic anesthesia

of the region innervated by the mental nerve. The sensory defect includes the skin and mucosa of the lower lip (Massey *et al*, 1981). Tumors affecting the trigeminal nerve may cause atypical neuralgia with sensory loss – the associated pain being intense, with progressive neurologic impairment (Peñarrocha *et al*, 1997). Calvin *et al* (1977) suggested that such pain may be caused by tumor compression of the sensory roots of the trigeminal nerve, resulting in areas of demyelization.

Different authors have stressed the importance of performing a complete radiological study of patients with TN, in order to discard the possible existence of a lesion in the brain, brainstem, preganglionic region, in Gasser's ganglion or in the cavernous sinus, or in the extracranial zone of the three trigeminal branches – with exploration of the entire trajectory of the fifth cranial nerve (Vadell *et al*, 1989; Manon-Espaillet *et al*, 1990; Peñarrocha *et al*, 1990; Cousin and Ilankovan, 1994; Reyes *et al*, 2003). In TN it is necessary in all cases to discard a possible tumor lesion – whether benign (Bodner *et al*, 1987; Heng and Heng, 1995) or malignant (Vadell *et al*, 1989) – at any point along the trajectory of the trigeminal nerve, and the lesion cannot be located based on the clinical signs and symptoms alone. Peñarrocha-Diago *et al* (2006) presented seven cases of TN secondary to tumors: in four cases there were antecedents of systemic neoplastic disease, while in the remaining three cases neuropathy was the first manifestation of the tumor. The lesion was located in the mandible in three cases (carcinomas), in the region of the skull base in one patient, and in the brainstem and brain in one case each. In one patient the lesion level could not be identified. The course was very poor in five cases. Recovery was only recorded in one patient in whom the symptoms were seen to disappear after acoustic nerve neurinoma resection.

From the prognostic point of view, the presence of MMN in patients with cancer often represents a very aggressive and even ominous sign, with rapid progression of the disease. MMN is of great importance as it may constitute the first sign of malignant disease, and in oncological patients it is predictive of short survival, due to the fact that in the majority of cases it reflects metastatic tumor spread (Peñarrocha *et al*, 1992b).

An infrequent cause of TN is neurinoma of the acoustic nerve. Such neurinomas are benign tumors that originate from the eighth cranial nerve within the internal auditory canal. They are the most frequent tumors of the pontocerebellar angle, representing 80–90% of all such lesions (Glasscock *et al*, 1987; Fetell and Stein, 1989), followed by meningioma. The differential diagnosis is based on the CT and MRI findings, and on the study of evoked auditory potentials. Other injuries of the angle must be discarded, such as neurinomas of the facial nerve and of the trigeminal nerve, the jugular glomus, cholesteatoma, and arachnoid cysts. The firm diagnosis is based on the histology of the lesion (Glasscock *et al*, 1987). The most common symptom is hearing loss; dysfunction of the cochlear nerve produces tinnitus. When these symptoms manifest jointly,

progressively and with mild dizziness, due to vestibular central compensation of the alteration of the vestibular nerve, they are suggestive of a neurinoma of the acoustic nerve (Glasscock *et al*, 1987). Other manifestations, such as migraine, earache, double vision, nausea and vomiting (Fetell and Stein, 1989), dysgeusia (Schnarch and Markitzu, 1990), trigeminal neuralgia (Gelabert *et al*, 1989; Feinerman and Goldberg, 1994; Peñarrocha *et al*, 1997), unilateral burning mouth sensation (Ferguson and Burton, 1990), hemifacial spasm (Niski *et al*, 1987), facial paralysis (Ferguson and Burton, 1990), and orofacial numbness (Pérusse, 1994) are late presentations.

Computed tomography and MRI can detect very small neurinomas of the acoustic nerve. At present, MRI with gadolinium contrast injection is the best method for assessing the pontocerebellar angle and internal auditory canal (Pérusse, 1994).

When evaluating a patient with orofacial numbness, we must discard the possible presence of tumors along the entire trigeminal trajectory, with clinical and radiographic evaluation of the oral structures and paranasal sinus, as well as imaging studies (CT and/or MRI) of the base of the skull, the pontocerebellar angle, the trigeminal nuclei of the brainstem, the thalamic nuclei, and the brain cortex (Cohen *et al*, 1986; Schnetler and Hopper, 1989). While it is infrequent for typical TN to be the first manifestation of a neurinoma of the acoustic nerve, this possibility must be taken into account – particularly in the presence of hearing loss, tinnitus, and dizziness (Gelabert *et al*, 1989).

### Collagenosis

Among the manifestations of collagenosis, mention should be made of TN, which can present as hypoaesthesia or anesthesia, together with associated neuropathic pain (Varga *et al*, 1990). The neuropathy is purely sensory, without motor involvement (Farrell and Medsge, 1982; Ponce *et al*, 1988), with scant or no associated pain (Blau *et al*, 1969) of a unilateral (Vincent and van Houzen, 1980), bilateral (Searles *et al*, 1978), early (Roig *et al*, 1983; Varga *et al*, 1990) or late nature (Ponce *et al*, 1988), and with an intact corneal reflex (Farrell and Medsge, 1982). Its presence does not imply a poorer prognosis of the underlying systemic disease (Asworth and Tait, 1971; Farrell and Medsge, 1982).

In the presence of purely sensory TN, it is always necessary to consider the possibility of an underlying systemic disease, such as systemic lupus erythematosus (Font *et al*, 1990, 2003), Sjögren's syndrome (Kaltreider and Talal, 1969; Alexander *et al*, 1986; Graus and Dalmau, 1986; Flint and Scully, 1990; Font *et al*, 1990), progressive systemic sclerosis (Harris, 1967; Gumpel, 1970; Farrell and Medsge, 1982; Ponce *et al*, 1988), or mixed connective disease or overlapping syndrome (Hamza and Alarcon Segovia, 1976; Searles *et al*, 1978; Vincent and van Houzen, 1980; Farrell and Medsge, 1982; Hamza *et al*, 1983; Roig *et al*, 1983; Ponce *et al*, 1988; Varga *et al*, 1990; Peñarrocha *et al*, 1992b).

Sjögren's syndrome-associated neuropathy has been shown to manifest as a variety of forms of neuropathy, including sensory ataxic neuropathy (Kennett and Harding, 1986; Griffin *et al*, 1990; Kaplan *et al*, 1990; Sobue *et al*, 1993), TN (Kaltreider and Talal, 1969), multiple mononeuropathy (Peyronnard *et al*, 1982; Molina *et al*, 1985), radiculoneuropathy (Gross, 1987; Grant *et al*, 1997), painful sensory neuropathy without sensory ataxia (Denislic *et al*, 1995; Mori *et al*, 2001), autonomic neuropathy with anhidrosis (Kumazawa *et al*, 1993; Goto *et al*, 2000), and multiple cranial neuropathy (Touze *et al*, 1999; Chu *et al*, 2000; Urban *et al*, 2001).

Facial involvement in mixed connective disease is relatively frequent, the condition being well documented in some cases of the recent literature (Hamza and Alarcon Segovia, 1976; Hagenah and Leonhardt, 1984; Alfaro *et al*, 1992). The patients have antibodies against nuclear antigens, targeted to nuclear ribonucleoprotein RNA (anti-RNPn) (Sharp *et al*, 1976). Normally, high titers of these antibodies are present during both the latent and active periods (Sharp *et al*, 1972). By definition, the presence of high anti-RNPn titers allows inclusion of the patient within the abovementioned disease condition. The time of appearance of such antibodies has not been well established. There are reports in the literature of patients presenting joint symptoms of more than one rheumatic disease, where the presence of anti-RNPn antibodies could only be demonstrated after an evolutive period of up to 2 years (Roig *et al*, 1983), and after treatment with aspirin and chlorophyll (Roig *et al*, 1983) or corticoids (Sharp, 1975; Alarcon Segovia, 1979). The appearance of anti-RNPn has been described 2 months after treatment with corticoids, tuberculostatic drugs, and carbamazepine, probably as a result of inherent progression of the disease, or through induction by some drug – possibly corticoids, as such a situation has been described before in the literature (Alfaro *et al*, 1992).

The reason underlying TN in connective diseases is not known. There are no postmortem studies of patients with collagenosis and trigeminal nerve dysfunction. Some descriptions of trigeminal sensory neuropathy in connective diseases (Lundberg and Werner, 1972) postulate that involvement would occur in the brainstem (at the bulboprotuberential level), caused by injury of the descending nucleus of the fifth cranial nerve, or of the thalamic tract in the presence of an onion-peel distribution of the facial sensory defect. Nevertheless, it is believed that the lesion would be located in the peripheral zone of the trigeminal nerve due to the frequent separation of the sensory alterations in the distribution of the different peripheral branches, and the lack of sensory dissociation or additional neurologic findings that imply normality of the brainstem (Farrell and Medsge, 1982). Thus, the majority of published cases correspond to trigeminal deficits of truncal topography, that prevail in the low branches, and that respect motor function (Roig *et al*, 1983) and tend to be bilateral.

Kaltreider and Talal (1969) described patients with Sjögren's syndrome and peripheral TN. The majority of these individuals had clinical and/or histological evidence of vasculitis in other locations (Weiss *et al*, 1978; Currie and Bradshaw, 1979). Vincent and van Houzen (1980) suggested that TN may be due to vascular alteration of Gasser's ganglion.

Possibly, in collagenosis the trigeminal nerve is more selectively vulnerable than other parts of the nervous system. The formation of immune complexes in the nerve or in the sensory root might induce isolated trigeminal sensory dysfunction. Alexander *et al* (1986) described 20 patients with primary Sjögren's syndrome and aseptic meningoencephalitis in whom the cerebrospinal fluid (CSF) showed high levels of IgG, oligoclonal bands in the gel electrophoresis study, and pleocytosis – all these findings being very similar to the situation observed in multiple sclerosis. Of these patients, nine had cranial neuropathies, one had trigeminal nerve involvement, and another presented facial nerve alterations.

Singsen *et al* (1977) presented a child with mixed disease of the connective tissue with an associated condition similar to 'aseptic meningitis'. It is interesting to indicate that four patients described by Bennett *et al* (1978) had membranous nephritis secondary to immune complex formation, and aseptic meningitis. Likewise, there is circumstantial evidence suggesting that the location of immune complexes in the CSF is related to the neurologic alterations of systemic lupus erythematosus (Keeffe *et al*, 1974). According to Asworth and Tait (1971), the lesion might be located in the nerve trunk due to the accumulation of immune complexes in the trigeminal nerve or root. Farrell and Medsge (1982) observed that when associated with progressive systemic sclerosis, TN is more frequent in patients with myositis, high anti-ribonucleoprotein antibody titers, leukopenia, hypothyroidism, Sjögren's syndrome and hypergammaglobulinemia. This suggests the participation of auto-immune processes in the pathogenesis of this sensory TN. Nevertheless, until further anatomical and direct immunoblastic information is obtained, the pathogenesis of these neuropathies in collagenosis remains speculative.

Treatment with corticoids improves the general clinical situation, the facial neuropathic pain (if present), and the biologic parameters, but the deficiency symptoms of TN remain unaltered (Bennett *et al*, 1978; Searles *et al*, 1978; Alfaro *et al*, 1992). Nevertheless, treatment must be specific of the underlying disease in each case.

#### *Idiopathic (primary) trigeminal neuropathy*

Idiopathic trigeminal sensory neuropathy (ITSN) is a benign disorder where the main clinical feature is facial numbness limited to the territory of one or more divisions of the trigeminal nerve, persisting from a few weeks to several years, and in which no underlying disease can be identified (Peñarrocha *et al*, 1992a; Domínguez *et al*, 1999; Dumas and Pérusse, 1999; Shotts *et al*, 1999). Trigeminal sensory neuropathy is

an uncommon but often significant orofacial symptom (Shotts *et al*, 1999). Facial numbness can only be accepted as a benign condition after excluding other possible causes and carrying out a careful follow-up of these patients over an extended period of time (Robinson *et al*, 2003), because there are multiple causes of facial numbness, and the possibility of neoplasm must always be kept in mind (Fisher, 1983). Three clinical subgroups of TSN have been recognized – an acute primary form (acute idiopathic TSN), a chronic form associated with connective tissue disease, and a chronic idiopathic form. The boundaries between these groups are not clearly defined (Flint and Scully, 1990). Much of the literature relating to ITSN is based on single cases reports and short clinical series (Robinson *et al*, 2003).

In a review of 61 cases of TN, Goldstein *et al* (1963) found no clear cause in seven patients. Blau *et al* (1969) and Horowitz (1974) described 10 and 7, patients respectively, diagnosed as benign trigeminal sensory neuropathy (BTSN), in whom no underlying disease was found. Peñarrocha *et al* (1992a) presented six patients with BTSN, and defined the criteria for the disease; they found no personal history of interest in relation to the neuropathy, and no neurologic alterations of other cranial nerves. Shotts *et al* (1999) described nine patients with TN, four were found to be secondary to distant malignancy, two associated with connective tissue disease, and in three there was no obvious cause for the neuropathy. Dumas and Pérusse (1999) in turn presented five cases of BTSN in a series of 35 patients with TN; in none of these were there other neurologic alterations, and the laboratory test and brain CT findings were normal.

The cause of this syndrome remains controversial. Blau *et al* (1969) postulated a virus as the cause of the syndrome. Mandal and Allbeson (1972) described a case of TN in the course of viral hepatitis. Peñarrocha *et al* (1993) described a recurrent form of TN, in which the numbness disappeared following treatment with acyclovir (Peñarrocha *et al*, 2001). Ecker and Smith (2002) suggested herpes virus reactivation in the etiopathogenesis of trigeminal neuralgia; there could be a similar mechanism in TN. These data further support the viral theory of spontaneous and transient trigeminal numbness, and raise the question as to whether patients with TSN should be treated with acyclovir.

Although the symptoms may last from a few days to several years, complete recovery is normal in half of all patients (Fisher, 1983; Peñarrocha *et al*, 1992a). According to Dumas and Pérusse (1999), the acute forms of BTSN are characterized by a rapid, painless onset with a good prognosis and full recovery, while the chronic forms are more insidious and can be associated with pain. According to Fisher (1983), pain was present during the initial stages in one of every three patients, and in cases of gradual evolution, severe chronic pain could appear. Peñarrocha *et al* (1992a) in turn described the presence of moderate, continuous pain in two out of six cases. Benefits from the use of tricyclic antidepressants have been described in cases with chronic pain (Bryson and Wilde, 1966), and in typical and atypical

trigeminal neuralgias (Zakrzewska, 1990). Robinson *et al* (2003) administered amitriptyline to patients with BTSN, but found no improvement.

### Infections

Reichart *et al* (1982), in 1982, studied in Thailand 750 leprosy patients and found trigeminal sensory alterations in 29 subjects – in 21 cases the second branch was affected, in 13 the first branch was involved, and in six cases the third branch was affected. The condition manifested in different combinations, and often proved bilateral. Classically (Harris, 1967), TNs have been described in syphilitic infections associated with chronic granulomas.

There have been reports of anesthesia of the peripheral branches of the trigeminal nerve secondary to odontogenic infections, from the maxillary secondary branch to pericoronaritis of the top of the third molar (Barrett and Buckley, 1986), and to maxillary sinusitis (Spillane and Wells, 1959). Regarding the mandibular branch, periapical alterations of the lower molars and premolars have been implicated (Barrett and Buckley, 1986). TN of herpetic origin in localized herpes zoster infection has also been documented (Peñarrocha *et al*, 1993).

### Other causes

There have been reports of paresthesia of the mental nerve secondary to sickle-cell anemia crises (Kirson and Tomaro, 1979; Friedlander *et al*, 1980), benign lymphogranulomatosis (sarcoidosis) (Cohen and Reinhardt, 1982), amyloidosis (Spillane and Wells, 1959; Gastaut and Michel, 1984), diabetic polyradiculoneuropathy (Casamassimo and Toker, 1988), and multiple sclerosis – such paresthesias being the first symptom or manifestation of the disease in 2–3% of patients (Roistacher, 1973; Durward *et al*, 1990). Likewise, alterations of the mental nerve have been described in located forms of Castelman's disease (Gabrielli *et al*, 1991), poisoning by trichloroethylene or stilbamidine (Goldstein *et al*, 1963), and cerebrovascular diseases such as spontaneous bleeding of the protuberance (Berlit, 1989) or ischemic vertebrobasilar damage (Nelson *et al*, 1986).

Paresthesia of the inferior alveolar nerve can be caused by periapical pathology or endodontic treatment (Lambrinidis and Molyvdas, 1987), or may be a consequence of extruded endodontic filler material. In such cases surgical removal is advised (LaBanc and Epker, 1984). Jerjes *et al* (2005) reported the case of a male who presented with gradual onset paresthesia in the distribution of the mental nerve. Radiographic investigation revealed a lesion associated with the apexes of the lower right premolar teeth. The patient subsequently underwent endodontic treatment of the lower right first and second premolar teeth. The control 6 months later showed almost complete bony regeneration of the area, with complete resolution of both lesions. The patient also showed complete recovery of sensation in the distribution of the right mental nerve. Mental nerve alterations have also been associated with the presence of a radicular fragment of a molar in

contact with the upper wall of the nerve canal, and with injuries close to the lower premolars (Marco *et al*, 1990).

Hypertrophy of the masseter muscles not secondary to parafunctional habits (chewing gum, bruxism) comprises an asymptomatic form, and only occasionally does an increase in volume to the level of the angle of the jaw require differentiation between this condition and pathology of the parotid gland. Facial hypoesthesia has been described in the lower half of the face in masseter hypertrophy. This sensory deficit can progress to complete anesthesia during mastication. Muscular hypertrophy can compress sensory divisions of the third branch of the trigeminal nerve, and possibly the buccal nerve, at the point where it crosses the external pterygoid muscle (Garcia-Albea *et al*, 1990). Compression has also been postulated as a cause of numbness and pain in the distribution territory of the inferior alveolar nerve, because of entrapment of the nerve in the lateral pterygoid muscle (Loughner *et al*, 1990).

The treatment of TN should be symptomatic in the case of pain associated with numbness, and should be of an etiologic nature if the underlying cause has been identified – in accordance with the different diseases that originate the neuropathy.

## Conclusions

Trigeminal nerve sensory defects are known as neuropathy trigeminal. Such injury of the trigeminal nerve manifests as numbness.

Traumatic TNs deserve special interest due to the frequency with which the trigeminal branches are affected in oral surgical interventions. Tumor origins are of great relevance, as mental or infraorbital neuropathies are possible manifestations of neoplastic disease.

Trigeminal neuropathy secondary to collagen diseases, of unknown etiopathogenesis, in many cases lead us to establish the diagnosis of the systemic background disease. Idiopathic benign trigeminal sensory neuropathies are related to infectious neuropathy secondary to herpes simplex viral infections. Finally, other diverse reasons for these alterations have also been discussed.

Patients describe facial numbness in the sympathetic trigeminal territory as a sensation similar to locoregional oral anesthesia. Sometimes they report dysesthesia or paresthesia, expressed as burning, itching, and even pain, in rare instances. Aside from the intrinsic and specific symptoms of each causal process of the neurologic disorder, a sensory deficit is established in the territory of the sympathetic branches, resulting in partial or total loss of sensitivity.

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