Trigeminal Trophic Syndrome

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Definition

Trigeminal trophic syndrome (TTS) is an uncommon cause of facial ulceration resulting from damage to the trigeminal nerve system, leading to self-mutilating behaviour and ulceration of the skin in the distribution of cranial nerve V. Recently, an atypical form of TTS has been recognised.

Aetiology and Classification

Trigeminal Trophic Syndrome

TTS is described as the triad of anaesthesia, paraesthesia and secondary facial ulceration as a result of self-mutilation. The intractable anaesthesia and paraesthesia encountered by the patient leads to repeated manipulation of the area with resultant tissue damage. The condition occurs secondary to an insult of the trigeminal nerve, or its associated central structures. The nasal ala is the most common site of ulceration, felt to be related to its location at the junction of sensory innervation by the ophthalmic and maxillary branches of the nerve (McVeigh et al. 2018).

The majority of historical cases were reported to be iatrogenic, specifically resulting from ablative therapy for the treatment of trigeminal neuralgia; although this is now less common with modern ablation techniques (Kurien et al. 2011).

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Table 18.1 Causes of TTS

• Ablation of CN V or transection of the Gasserian ganglion
• Posterior circulation ischaemic stroke
• Post-craniofacial surgery
• Acoustic neuroma
• Post-encephalitis
• Syphilis
• Vertebral artery dissection
• Vertebrobasilar insufficiency
• Posterior fossa tumour (astrocytoma, meningioma, haemangioma)
• Syringobulbia
• Trauma
• Herpes zoster infection
• Amyloid deposition
• Leprosy
• Idiopathic

Ischemic damage of the posterior vascular territory, including posterior inferior cerebellar artery infarction and vertebral artery dissection, is another common precipitant of the condition (Sawada et al. 2014; Khan and Hachement 2019). In fact, TTS was first recognised by Adolf Wallenberg, most known for his clinical description of the lateral medullary syndrome, in 1901 (Wallenberg 1901). A number of other causes have been documented in the literature (see Table 18.1), and 5% of cases are described as being idiopathic (Slater 2006).

Atypical Trigeminal Trophic Syndrome

Recently, an atypical variant of TTS (ATTS) has been recognized. These patients present with severe, extensive facial ulceration that is responsive to treatment (Kentley et al. 2017; Gkini et al. 2019). Whilst no history of trigeminal nerve injury is identified, nerve dysfunction may be revealed following nerve conduction studies.

Clinical Presentation

Patients with TTS report distressing dysaesthesias, which may be described as burning, crawling, itching or tingling (Lane and Deliduka 2008). These altered sensations stimulate self-manipulation and due to impaired perception of pain and temperature in the area, repeated manipulation leads to trauma and ulceration (Sawada et al. 2014). An important consideration is that patients typically deny this self-mutilating behaviour, though it may be highlighted by those close to the patient

(Gkini et al. 2019). Patients may also report the sensation of a blocked nose due to impaired perception of nostril airflow (McVeigh et al. 2018).

Ulceration is most frequently seen unilaterally at the nasal ala, for reasons already discussed, and is more common on the right (Sawada et al. 2014). The characteristic evolution of the lesion is of a small crust that develops into a crescenteric or Y-shaped ulcer and may extend to involve the cheek and lip (Rashid and Khachemoune 2007). Ulcers may be single or multiple and are confined to one dermatome, usually the maxillary (V2), and particularly along the route of the infraorbital nerve (Garza 2008). The tip of the nose is spared, due to its innervation by a distal branch of the ophthalmic (V1) branch of the nerve (Curtis et al. 2012). Fibrosis of healing ulcers may cause facial distortion leading to ipsilateral ectropion or 'sneer-like facial expression' (Dicken 1997). Ulceration may also affect the forehead, eyelid, cornea or scalp. Whilst ulceration in the mandibular (V3) branch has been reported, this is uncommon (Sawada et al. 2014; Kavanagh et al. 1996).

In atypical trigeminal trophic ATTS, patients admit to manipulating their skin and describe a great sense of relief. They describe pain or abnormal sensation in the area which builds up until they pick at or manipulate the area which they describe as relieving the triggering pain or sensation. Lesions may be more widespread, affecting the face bilaterally or involving more than one dermatome (Kentley et al. 2017; Gkini et al. 2019) (Fig. 18.1).

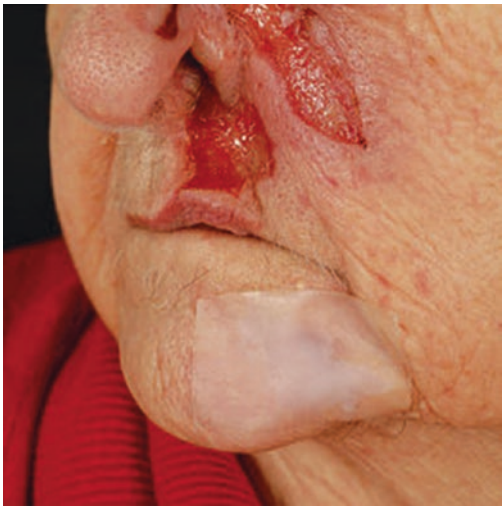

Fig. 18.1 A patient with Trigeminal Trophic syndrome

Why Is TTS so Debilitating?

The chronic and severe facial ulceration that accompanies TTS can be psychosocially devastating for patients and lead to secondary depressive symptoms, which should be managed by psychiatric assessment (Gkini et al. 2019). The dysaesthesia suffered by patients can be extremely distressing and must be addressed effectively. Secondary bacterial or viral infection is common, and in extreme cases, tissue loss may extend to the facial sinuses leaving the patient at risk of osteomyelitis and meningoencephalitis (Ziccardi et al. 1996).

Epidemiology

Prevalence

TTS is uncommon, with 107 published articles on the topic up to 2017 (Khan and Khachemoune 2019). The latency period between trigeminal nerve damage and development of TTS is reported to be between 2 weeks and 30 years (median 1 year) (Sawada et al. 2014; Sadeghi et al. 2004). Only a small proportion of those with trigeminal insult will, however, develop the condition and it is theorised that those that do are predisposed to skin picking (Kurien et al. 2011). Psychiatric conditions such as Alzheimer's disease may provoke TTS after a long latency period due to disinhibition of skin picking behaviour (Setyadi et al., 2007). According to historical data, 18% of patients that underwent trigeminal ablation developed TTS (Rashid and Khachemoune 2007).

Epidemiology

Patients of all ages are affected. There have been reports in patients between 14 months and 94 years developing TTS, with a mean of 57 years. A female preponderance of 2.2:1 has been documented (presumably due to increased incidence of trigeminal neuralgia in female patients) (Sawada et al. 2014; Slater 2006).

Course and Prognosis

The course of the condition is chronic and progressive; once ulceration appears it is persistent and follows the cycle of a non-healing wound driving further self-injury. Lesions may persist for many years and without the reversal of habitual mutilating behaviour, they are unlikely to spontaneously resolve. TTS is often highly refractory to treatment, though ATTS has been reported to display a favourable response to pregabalin (Gkini et al. 2019).

Diagnosis

General Considerations

TTS is a clinical diagnosis, however, it is essential to rule out other causes of facial ulceration. Inciting injury to the trigeminal nerve may be readily apparent from a careful history, or further extensive investigation may be required, including neuroimaging and neurophysiological studies. In the case of ATTS, it may be the case that no cause can be identified.

Differential Diagnoses

The differential causes of facial ulceration are extensive and should be carefully considered before making the diagnosis (Rashid and Khachemoune 2007).

Differential Diagnosis of TTS
• Bacterial infection: including mycobacterial (tuberculosis, leprosy), treponemal
• Viral infection: herpes simplex and zoster
• Parasitic infection: leishmaniasis
• Fungal infection
• Vasculitis
• Malignancy: squamous and basal cell carcinoma, lymphoma, sarcoma
• Granulomatous disease
• Pyoderma gangrenosum
• Psychodermatological disease: dermatitis artefacta, acne excoriée, delusional infestation

Diagnostic Process

History and Examination

A careful history should be taken from the patient to identify a possible precipitant of TTS. Careful attention should be paid to other neurological symptoms, including those of raised intracranial pressure and hearing loss that may indicate the presence of a tumour involving the trigeminal nerve or its ganglia. Enquiry regarding previous craniofacial surgery or facial rash should be made. The physician should ask about other psychological co-morbidities. Patients may benefit from psychiatric review to rule out conditions such as dermatitis artefacta and neurotic excoriation or obsessive-compulsive disorder. A full skin and neurological examination should be performed on all patients.

Investigation

- Skin swabs for microbiology (including mycobacterial and fungal) and viral PCR.
- Blood tests.

  - Full blood count, renal function, liver function, bone profile, inflammatory markers, haematinics, thyroid function, HIV, treponemal serology, autoimmune screen including anti-nuclear and anti-neutrophil cytoplasmic antibodies.
- Skin biopsy to rule out neoplastic and vasculitic conditions
  - Typical histological findings in TTS are of ulceration with adjacent lichenification and scarring with a mixed inflammatory infiltrate (Khan and Khachemoune 2019).
- Consider MRI and electrophysiological studies when the history reveals no cause, to confirm damage to the trigeminal nerve.

Treatment

Patients should be managed in a multidisciplinary setting with dermatologists, psychiatrists, psychologics, neurologists and, where necessary, plastic, maxillofacial and ophthalmic surgeons. Pain services may also need to be involved in case management.

Psychological Interventions

Patients with insight into their condition have been reported to have better outcomes (Brewer et al. 2016). Explaining the self-induced nature of the condition and instituting behavioural modifications such as habit reversal therefore play a key role in the management of the condition (McVeigh et al. 2018; Setyadi et al. 2007). Simple interventions such as trimming the fingernails and wearing scratch mittens may be beneficial (Sawada et al. 2014).

Wound Management

Simple hydrocolloid dressings play a role in wound management and also create an occlusive barrier from self-manipulation. However, the wound may reoccur once dressings are removed. Several studies have reported successful wound heading with thermoplastic dressings, which also play a role in addressing the patient's somatosensory symptoms (Brewer et al. 2016; Preston et al. 2006; Swan et al. 2009) Negative pressure therapy has also been reported as beneficial (Fredeking and Silverman 2008). Once wounds are healed, it is essential to address the underlying dysaesthesia to prevent recurrence.

Pharmacological Management

There are no randomised-controlled trials in the treatment of TTS, nor published guidelines. Gabapentin has the greatest body of evidence in the treatment of TTS; tiagabine and oxcarbazepine are reported as therapeutic options when the use of gabapentin is limited by side effects (Sadeghi et al. 2004). Carbamazepine and the use of SSRIs have been shown to be of benefit (Sawada et al. 2014; Gkini et al. 2019; Pedicelli et al. 2009; Fruhauf et al. 2008). The addition of topical tacrolimus ointment may use as an adjunctive therapy alongside gabapentin (Nakamizo et al. 2010). ATTS is described as being responsive to treatment with pregabalin (Gkini et al. 2019).

First-line therapeutic options for TTS	
Medication	Dose
Gabapentin[a]	Initially 300 mg 1–3 times daily Increased in steps of 300 mg every 2–3 days in 3 divided doses to maximum 3.6 g per day
Carbamazepine[b]	Initially 100 mg daily Increased slowly to 600–800 mg daily in 2 divided doses
Citalopram	20–40 mg daily

[a]Prolonged—release formulations of carbamazepine such as Tegretol® and Carbagen® SR are preferred

[b]Gabapentin and carbamazepine dose should be titrated to clinical response

Surgical Management

Plastic surgery has been considered a last resort and the recurrence of ulceration is common post-procedure (Tollefson et al. 2004). Rotational skin flaps from areas outside the affected dermatome, however, may be considered in refractory cases (McVeigh et al. 2018).

Transcutaneous electrical stimulation, autologous epidermal cell transplant and radiotherapy have all been trialled in refractory cases with varying degrees of success (Khan and Khachemoune 2019; Schwerdtner et al. 2005; Westerhof and Bos 1983).

Prognosis

TTS is a chronic condition that may be highly refractory to treatment. Where some studies have reported complete healing, follow-up times have been short, and patients frequently relapse (Sawada et al. 2014). As trigeminal nerve damage will

inevitably persist, patients must be followed up. Pharmacological treatment must be continued long-term alongside behavioural modifications and wound management to allow sustained healing of ulceration.

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