Trigeminal trophic syndrome of all three nerve branches: an underrecognized complication after brain surgery

Case report

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The authors report a case of trigeminal trophic syndrome (TTS) that occurred as a complication of a neurosurgical procedure. Three years after a second surgical treatment for a meningioma of the cerebellopontine angle, this 32-year-old woman developed TTS with progressive skin ulcers on the left ala nasi and the left side of the forehead and chin. Trigeminal trophic syndrome is an extremely rare cause of facial ulceration. It occurs as a consequence of trigeminal nerve damage or impaired central sensory connections. To the authors’ knowledge, this is the first report of lesions in the dermatomes of all three branches of the nerve after a neurosurgical procedure. Early recognition of this disorder is important, as treatment is difficult and often unsatisfactory. Many clinicians are not aware of this disease, thus, it may be more common than previously thought. The importance of recognizing and diagnosing TTS, as well as its treatment, are discussed. (DOI: 10.3171/JNS/2008/108/01/0170)

KEY WORDS • meningioma • neurotrophic ulceration • trigeminal nerve • trophic syndrome

TRIGEMINAL trophic syndrome was first described in German by Wallenberg in 1901 as an uncommon clinical entity in which cutaneous trophic ulceration develops within the trigeminal dermatomes. This syndrome was not described in English-language literature until 32 years later, when it was presented in 2 independent publications by Loveman and McKenzie. We report on a case of TTS that arose as a complication of the neurosurgical treatment of a meningioma. This case illustrates the difficulties faced in the diagnosis and management of TTS.

Case Report

History. Three years after a second operation for a meningioma of the left cerebellopontine angle (Fig. 1), this 32-year-old woman developed persistent, painless, deep ulcerations of the left ala nasi and left side of her forehead and chin. The first ala nasi lesion appeared in September 2002 and was followed 10 months later by a forehead lesion; the chin lesion appeared 15 months later. Once the ulcerations began to appear, over a 3-year period, she was examined by a general practitioner, a neurosurgeon, an otolaryngologist, a dermatologist, a plastic surgeon, and a maxillofacial surgeon, all of whom missed the diagnosis. She was finally seen in our department in October 2005. The patient recounted that a general practitioner had prescribed topical therapy (chloramphenicol ointment) and referred her to a dermatologist, who had treated her with antibiotics and a topical ointment. Another dermatologist had advised surgical treatment due to suspected basal cell carcinoma. Dermatitis artefacta was also suspected, and a psychiatric evaluation was recommended. The neurosurgeon who examined her did not recognize the lesion as a consequence of her previous neurosurgical treatment. A computed tomography scan of her brain obtained at that time was described as normal, with no signs of meningioma recurrence. The patient was hospitalized in the Department of Psychiatry for 3 weeks with a diagnosis of psychoorganic syndrome. She was treated with levomepromazine, flufenazin, biperiden, and tioridazin. Mild-to-moderate depression and anxiety, as well as obsessive–compulsive disorder were diagnosed.

Abbreviations used in this paper: TN = trigeminal nerve; TTS = trigeminal trophic syndrome.
The lesions were believed to be due to self-induced facial trauma, and postoperative trigeminal disorder was not considered. An otolaryngologist diagnosed basal cell carcinoma and suggested antibiotic therapy and surgery. A plastic surgeon suggested the same treatment. Finally, a maxillofacial surgeon at another hospital suggested reconstructive surgery despite the lack of a diagnosis. The patient visited our department for a second opinion about surgery (Fig. 2 left).

**Histological Examination.** Cytological and histopathological findings showed granulation tissue and inflammation with no evidence of a neoplastic, infectious, or autoimmune disease. A cultured swab specimen obtained from the ulcers was positive for the skin flora *Propionibacterium acnes* and *Staphylococcus epidermidis*. The diagnosis of chronic ulcerous inflammation was made on clinical grounds based on sensation loss and unilateral self-induced facial ulceration, particularly involving the ala nasi. The patient had complained of pronounced anesthesia and paresthesia, consisting of a crawling, numbness, itching, and tickling sensation over the left side of her face. She reported picking at and scratching the affected areas, particularly the ala nasi and nasolabial regions. On examination, which included tests of light-touch, pin-pick, and thermal perception, facial sensation in the distribution of the fifth cranial nerve and corneal reflex was absent. Facial motor function, including masseter function, was preserved.

**Treatment.** The patient was started on a course of carbamazepine because this drug is believed to affect both the paresthesia and the behavioral factors present in this syndrome. After 3 months of carbamazepine therapy (100-mg dose, twice daily) with the lesions covered with a sterile hydrocolloid dressing, the patient’s clinical symptoms had almost completely disappeared. The ala nasi defect required a reconstructive plastic surgical procedure, but this was postponed due to the patient’s pregnancy. Carbamazepine treatment was discontinued for the same reason. There was no recurrence 1 year after discontinuation of the carbamazepine (Fig. 2 right).

**Discussion**

Trigeminal trophic syndrome, also known as trigeminal neurotrophic ulceration, trigeminal neuropathy with nasal ulceration, trophic ulceration of the ala nasi, or ulceration en arc, is an unusual condition. It occurs when the fifth cranial nerve is injured at any point along its length—from its origin in the brain nuclei to its terminal branches. More than 100 cases were described in the literature between 1982 and 2007. The incidence of this syndrome will probably increase because TTS can occur after stroke as well as after nerve ablation for trigeminal neuralgia. To the best of our knowledge, only one previous case of postapoplectic lesions in the area of all three branches of the nerve has been described. The diagnosis of TTS is suggested in patients with facial ulcerations, especially of the ala nasi, that occur in a dermatome of a TN that has been rendered sensationless by a surgical procedure or other process affecting this nerve or its central sensory connections. It is unclear why only certain patients with facial anesthesia experience paresthesia, and why ulcers develop in only a few of these patients. In the opinion of Ferrara et al., the final diagnosis of TTS must be made based on a neurological examination because neurological impairment is the pathogenetic basis of the syndrome.

In cases of TTS, the most common causes of TN damage are trigeminal rhizotomy or alcohol or glycerol injections into the Gasserian ganglion. Other causes, such as infarctions of the brainstem, intracranial meningiomas, acoustic neuromas, astrocytomas, ophthalmic herpes zoster, syringobulbia, verteobasilar insufficiency, postencephalitic parkinsonism, and head trauma, are less common. Idiopathic TTS has also been described. Although psychiatric factors are important in factitious dermatitis, they are not considered important in TTS. The differential diagnosis of TTS from factitial skin disorders should be addressed. Patients with factitial skin syndromes differ from those with TTS in that such patients have normal skin sensitivity, must
undergo compulsive behavior modification, and have a bilateral and often symmetrical distribution of skin lesions.\textsuperscript{9,32} However, more information concerning the pathogenesis of neurotrophic ulcers is needed.

Trigeminal trophic syndrome is more common in women and the elderly; the average age of such patients is 57 years.\textsuperscript{14,30} Self-induced trauma (chronic manipulation of sensationless skin) is believed to produce the tissue destruction;\textsuperscript{7,28} therefore, the use of the term “trophic” is misleading. Patients often have paresthesias in the affected area, which prompt touching, rubbing, or picking to relieve the perceived irritation. In some cases, the anesthesia creates a sensation of nasal congestion and impaired airflow, which precipitates repetitive nasal manipulation.\textsuperscript{18,30} Once the ulcers appear, they are extremely persistent.\textsuperscript{9,23} Our patient had no pain, but in the context of deafferentation, pain would be somewhat unusual.

The mean period from the time of TN injury to the formation of the ulcer varies from several weeks or years to decades.\textsuperscript{2,7,25,28,33} Our patient developed relatively early manifestations of TTS, with skin changes in the areas of all three sensory branches of the TN. An understanding of the predisposing factors and clinical presentation of TTS is important for ensuring a timely diagnosis of this difficult-to-treat syndrome. Trigeminal trophic syndrome can be differentiated from malignant lesions (basal cell or squamous cell carcinoma and T-cell or natural killer–cell lymphomas), infectious diseases (herpes simplex or zoster viruses, syphilis, invasive fungi, or Mycobacterium tuberculosis), or autoimmune disorders (Wegener granulomatosis) on the basis of clinical history, tissue biopsy sampling, and serological evaluation.\textsuperscript{6} However, TTS may also manifest as an idiopathic lesion, most often as an ulcer of the ala nasi, which makes the diagnosis more difficult.

Trigeminal trophic syndrome is a rare condition and its management is often difficult. Patients are often unaware that they are hurting their own skin; thus, the mainstay of treatment involves instructing the patient not to manipulate the skin\textsuperscript{22} and to apply a sterile hydrocolloid and/or thermoplastic dressing to the lesion.\textsuperscript{21} Antibiotic therapy should only be used to treat secondary infections. Cotton gowns worn at night may also be useful. Because the pathophysiological basis of TTS is not fully understood, therapeutic options are limited, have not been rigorously tested, and are anecdotal at best.\textsuperscript{3} Pharmacological therapies may include pimozide,\textsuperscript{8,16} carbamazepine,\textsuperscript{26} chlorpromazine,\textsuperscript{14} amitriptyline, diazepam,\textsuperscript{10} vitamin B supplements and clonazepam,\textsuperscript{11} and selective serotonin reuptake inhibitors.\textsuperscript{25} Some authors have reported using transcutaneous electrical nerve stimulation,\textsuperscript{31} ionizing radiation,\textsuperscript{15} ipsilateral cervical sympathetic, and stellate ganglionectomy.\textsuperscript{17} Some patients require surgical reconstruction; surgical reconstruction with innervated skin flaps has been successfully performed.\textsuperscript{1,11,26} Tissue engineering with autologous cultivated epidermal cells has been used in the treatment of burns and chronic wounds; Schwertdner et al.\textsuperscript{24} was the first to report its use in the treatment of neurotrophic ulcerations. The residual ala nasi defect in our patient will require reconstructive plastic surgery; this had to be postponed, however, due to her pregnancy. The precise method of reconstruction has yet to be determined. Although there was no recurrence 1 year after discontinuation of the carbamazepine, the possibility of potential recurrence of the lesions remains.

Conclusions

Trigeminal trophic syndrome is an uncommon disorder that occurs after peripheral or central damage to the TN. It is characterized by a triad of unilateral crescentic ulceration with anesthesia and paresthesias of the trigeminal dermatomes. Self-induced facial ulceration remains difficult to diagnose and treat. Cytological and histopathological examination help to exclude other entities in the differential diagnosis. Treatment of TTS is aimed at suppressing paresthesia, preventing patient manipulation, and covering the defect with innervated skin flaps. It is important to differentiate TTS from autoimmune disorders, infectious diseases, factitial skin syndromes, and neoplastic processes that may mimic TTS. Many clinicians are not aware of this syndrome; however, once the diagnosis of TTS is made, they will probably never forget it.

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