

# Trigeminal Trophic Syndrome: Report of 3 Cases Affecting the Scalp

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## Practice Points

- Trigeminal trophic syndrome (TTS) should be considered in the differential diagnosis for any ulceration found in the distribution of the trigeminal nerve.
- Trigeminal trophic syndrome is a possible organic cause of delusions of parasitosis when symptoms are restricted to the distribution of the trigeminal nerve.
- The most pressing issue regarding treatment of TTS is the prevention of continued self-mutilation.

*Trigeminal trophic syndrome (TTS) is a rare condition that results from a prior injury to the sensory distribution of the trigeminal nerve. Patients typically respond to the altered sensation with self-mutilation, most often of the nasal ala. We describe 3 patients with TTS who presented with self-induced ulcerations primarily involving the scalp. Two patients developed delusions of parasitosis (DOP) based on the resulting symptoms of TTS, which is a unique association. Trigeminal trophic syndrome may occur at extranasal sites and in any branch of the trigeminal nerve. The condition should be considered when ulcers are encountered in this nerve distribution. Symptoms such as formication may mimic DOP. Trigeminal trophic syndrome may be differentiated from DOP by the restriction of symptoms and ulcerations to the distribution of the trigeminal nerve.*

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The trigeminal nerve, also known as cranial nerve V, consists of 3 major branches: the ophthalmic (V<sub>1</sub>), maxillary (V<sub>2</sub>), and mandibular (V<sub>3</sub>) nerves. Trigeminal trophic syndrome (TTS) is a rare condition that results from self-induced ulcerations and follows damage to the sensory root of the V<sub>1</sub> or V<sub>2</sub> branches of the trigeminal nerve. The pathogenesis of TTS is not well understood and symptoms may develop weeks to years after initial injury to the trigeminal nerve. Insults that often result in TTS include cerebrovascular infarction, infection, neoplasm, or trauma; additionally, ablation of the trigeminal nerve for management of trigeminal neuralgia often leads to TTS. Patients with TTS frequently present with crescent-shaped ulcerations on the nasal ala.

The diagnosis and management of TTS often is challenging and therefore may require multiple approaches. A comprehensive history and physical examination are essential to early diagnosis, thereby allowing for exclusion of malignant, autoimmune, psychiatric, or infective etiologies that can mimic TTS. We describe 3 patients with TTS who presented with self-induced ulcerations primarily involving the scalp. It is notable that 2 of 3 patients appeared to develop delusions of parasitosis (DOP) based on the resulting symptoms of TTS, which is a unique association.

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## Case Reports

**Patient 1**—A 63-year-old woman with multiple chronic illnesses presented to our clinic for evaluation of a large ulcer on the right side of the forehead. Her symptoms began 6 years prior to presentation when she was diagnosed with herpes zoster affecting the right V<sub>1</sub> branch of the trigeminal nerve including the right eye. She subsequently experienced postherpetic neuralgia in the following months and developed a large wound on her forehead. The wound healed completely several months later but recurred later that year. Multiple physicians were consulted and the patient was treated with terbinafine, metronidazole cream, ketoconazole cream, acyclovir, risperidone, moxifloxacin, and pain medication for the neuralgia.

The patient presented to our clinic 1 year later with an eroded plaque on the right nasal ala and a smaller ulceration on the scalp. At that time she was being treated with metronidazole gel for application to the affected area. She noted symptoms of formication that she was convinced were caused by a parasite infestation; she presented a container filled with cutaneous fragments that she stated contained the parasites. A diagnosis of DOP was made. The patient subsequently was lost to follow-up, as she did not want to return after being diagnosed with a psychiatric disorder. She was evaluated by the infectious diseases department 1 year later. No sign of parasite infection was seen, and all antibiotics and antifungal medications were stopped. Evaluation of a stool sample and skin scrapings was unremarkable.

One year later, she presented to the ophthalmology department with decreased vision in the right eye. A skin graft of the right upper eyelid was recommended, and the eyelid was sewn shut in an effort to protect the globe from self-mutilation. She also was seen by a plastic surgeon and was treated with antibacterial dressings, metronidazole, and moxifloxacin after a positive culture for *Serratia*.

Two years later, the patient returned to our clinic for evaluation. The ulcer that previously was noted on the nasal ala had healed, but the scalp ulceration was considerably larger, extending from the right side of the upper eyelid to the parietal scalp (Figure 1). The ulcer was clean, well marginated, and triangular in shape without undermining and extended to the depth of the periosteum. A diagnosis of TTS was made. Treatment recommendations included neurosurgical consultation to determine if nerve ablation might alleviate the patient's symptoms. Amitriptyline was recommended to alleviate the psychological component that caused her skin picking. The patient did not return for follow-up and her ultimate disease course remains unknown.

**Patient 2**—A 69-year-old woman with a history of herpes zoster, postherpetic neuralgia, and human immunodeficiency virus presented with a large, non-healing, angulated, linear ulceration on the right side of the scalp (Figure 2). She admitted to picking and scratching the area. At presentation the differential diagnosis included factitious disorder, TTS, herpes zoster, squamous cell carcinoma, or erosive pustular dermatosis. A viral culture was obtained and a biopsy was performed to rule out cutaneous malignancy. Pending culture and biopsy results, daily application of antibiotic ointment and bandages was recommended, and the patient was asked to return for follow-up in 2 weeks. Viral cultures were negative



**Figure 1.** A sharply marginated ulcer extending down to the level of the periosteum, encompassing the distribution of the ophthalmic (V<sub>1</sub>) branch of the trigeminal nerve. Her eyelid was previously sewn shut in an effort to protect the globe from self-mutilation.



**Figure 2.** A large, nonhealing, linear ulcer along the distribution of the ophthalmic (V<sub>1</sub>) branch of the trigeminal nerve.



and the shave biopsy revealed epidermal hyperplasia with compact orthokeratosis, consistent with lichen simplex chronicus. The patient failed to return for her follow-up appointment but reported itching when contacting our clinic by telephone. Treatment with oral hydroxyzine (25 mg twice daily) was recommended until she could return for evaluation. The patient failed to keep her follow-up appointment and died several months later.

**Patient 3**—A 79-year-old woman with hypertension, hypothyroidism, and chronic kidney disease presented to our clinic for consultation. The patient had a 10-year history of trigeminal neuralgia that had resolved after a nonspecified brain surgery in 1997. She presented to her primary care physician 10 years later with blisters and pain over the temporoparietal area and left eye; a diagnosis of herpes zoster was made. She was referred to our clinic 6 months later for evaluation of tenderness on the left side of the scalp and ulceration over the auriculotemporal nerve distribution of the  $V_3$  branch of the trigeminal nerve (Figure 3A). Bacterial and multiple viral cultures were obtained and all were negative. After several months of symptoms, she began to question if she could have a parasite infestation. She brought with her several cutaneous fragments for inspection. Microscopic examination of the fragments revealed no parasites. A diagnosis of TTS was made and conservative therapy with hydrated petrolatum and mupirocin ointment 4 times daily was recommended. A trial of oral gabapentin 100 mg 3 times daily also was started. At 2-month follow-up, the ulcer and regional tenderness had resolved (Figure 3B), and the patient was no longer concerned about parasite infestation. She stopped taking the gabapentin after 3 months, but the ulcerations recurred 4 to 5 weeks later. The gabapentin was restarted and the lesions again healed. She remained clear with ongoing gabapentin therapy at 1-year follow-up. She reported no further concerns of parasitosis.

### Comment

Trigeminal trophic syndrome is a chronic condition that results from a prior injury to the sensory distribution of the trigeminal nerve. It typically manifests as a progressive ulceration of the nasal ala, scalp, forehead, eyelids, cheek, or upper lip.<sup>1,2</sup> The most common site of ulceration is the nasal ala. The tip of the nose usually is not affected because of its innervation by the anterior ethmoidal branch of the nasociliary nerve, an ophthalmic division of the trigeminal nerve.<sup>3,4</sup> Generally, the anterior ethmoidal branch is not affected in trigeminal nerve injury.

Ulceration typically presents in areas that are supplied by specific terminal sensory branches of



**Figure 3.** A large temporoparietal ulcer along the course of the auriculotemporal branch of the mandibular ( $V_3$ ) branch of the trigeminal nerve (A). The ulcer healed within 2 months of conservative therapy with hydrated petrolatum and mupirocin ointment as well as oral gabapentin (B).

the 3 major trigeminal divisions. Major branches of the trigeminal nerve that provide sensory innervations to the scalp and face include the ophthalmic ( $V_1$ ), maxillary ( $V_2$ ), and mandibular ( $V_3$ ) nerves. One of the branches of the maxillary nerve includes

the infraorbital nerve, which has terminal cutaneous branches that innervate the nasal ala (external nasal branch), the upper lip (superior labial branch), and the medial cheek (superior alveolar branch).<sup>4,5</sup> Likewise, major branches of the ophthalmic nerve ( $V_1$ ) include the nasociliary and frontal nerves, which also have terminal sensory cutaneous branches (infratrochlear, supratrochlear, and supra-orbital) that innervate the scalp, eyebrow, and forehead. Ulceration is sometimes seen in these areas in patients with TTS. Our cases further illustrate that ulceration in TTS can develop in other areas and can affect all 3 branches of the trigeminal nerve, as reported elsewhere.<sup>5-7</sup>

Trigeminal trophic syndrome often occurs following trigeminal nerve injury due to ablation (eg, rhizotomy), infarction (eg, posterior inferior cerebellar artery occlusion, cortical or brainstem infarcts, vertebralbasilar insufficiency, syringobulbia, spinal cord degeneration), malignancy (eg, astrocytoma, acoustic neuroma, intracranial meningioma), infection (eg, herpes zoster, herpes simplex, *Mycobacterium leprae* neuritis, postencephalitic parkinsonism), trauma, or other idiopathic etiologies. The ulcers usually are painless, but painful ulcers are possible,<sup>5</sup> such as those in the 3 patients we described. Trigeminal trophic syndrome is more frequently seen in women and the elderly; the time between trigeminal injury and presentation of ulcers can range from a few weeks to 30 years.<sup>3,8</sup>

The differential diagnosis for patients presenting with ulcerations of the nasal ala, scalp, or other facial areas is broad and includes multiple disease categories (ie, neoplasms, infections, autoimmune disorders, psychiatric disorders).<sup>8</sup> At presentation, a malignant etiology should always be considered. The most common skin cancers that imitate TTS include basal cell carcinoma and squamous cell carcinoma. Other potential diagnoses should be ruled out in patients with a history of trigeminal nerve surgery, exposure to infectious agents, and history of foreign travel. Of note, TTS may be confused with psychiatric disorders including factitious disorder and DOP. It is important to rule out DOP, which was the suspected diagnosis in 2 of our patients. A misdiagnosis of TTS as DOP is possible due to patient reports of formication resulting from nerve damage. Patients may report the same concerns with both conditions, but DOP occurs without an organic cause; reports of infestation are not restricted to specific dermatomes. In both of our patients with suspected DOP, symptoms began prior to their concerns of parasitosis; they also had a documented history of herpetic injury to the nerve, which likely caused their symptoms. Restriction of lesions to a trigeminal

nerve distribution should exclude diagnoses other than TTS. It is interesting to note that 1 patient was taking risperidone without amelioration of her symptoms or belief about parasites.

It has not been explored if peripheral damage to the trigeminal nerve can result in changes to cerebral function that potentiates DOP. Some investigators have proposed that peripheral injury or irritation of the trigeminal nerve may result in changes in cerebral release of neuromediators, which may be responsible for some forms of migraine headaches.<sup>9,10</sup> It is possible that DOP might result from a similar mechanism or that it might simply be the result of formication.

Management of TTS is difficult and may require a multidisciplinary approach. To our knowledge, there are no randomized controlled studies. Currently, treatment involves dermatologic and neurologic evaluation, patient education about self-induction of ulcers, pain management for paresthesia, medical management, and surgical reconstruction of facial tissue loss. Treatment methods range from conservative to surgical (Table).

The most pressing issue is prevention of self-mutilation due to altered sensation in areas around the trigeminal nerve. Patient education about the cause of the symptoms is crucial.<sup>3,16</sup> The use of occlusive dressings and prosthetic devices (eg, face mask) to shield the ulcerated areas is important to prevent further injury. Patients should keep their nails short and wear cotton gloves at night to break the habit of picking the skin and to reduce trauma to the area.<sup>16</sup> Two reports demonstrated improvement in nasal ulceration with the use of a thermoplastic dressing.<sup>11,12</sup> Conservative management may be especially desirable in patients who are poor surgical candidates or patients with recurrent symptoms after surgical reconstruction of the mutilated area.<sup>11</sup>

Variable responses also have been reported with pharmacologic approaches to treatment. The use of carbamazepine<sup>13,17,18</sup> has shown mixed results.<sup>17,19</sup> Gabapentin was effective in one of our patients and in some other cases in the literature.<sup>5</sup> In our case, resolution of the patient's ulcer and regional tenderness was achieved with oral gabapentin 100 mg 3 times daily for 2 months. The scalp and facial lesions were still in remission at 2-month follow-up but recurred 4 weeks after stopping the medication. When gabapentin was restarted, resolution of the ulcer again was achieved and maintained with ongoing gabapentin therapy at follow-up 1 year later. In one report, treatment with gabapentin 2400 mg daily provided some relief in a patient with regional tenderness and formicationlike sensation in the left nasolabial fold, intranasal cavity, and periorbital region after failing

## Management of Trigeminal Trophic Syndrome

Treatment Method	Reported Outcome
<b>Conservative Management</b>	
Patient education	No cure reported but can prevent further damage to affected area and promote healing <sup>3</sup>
Prosthetic devices (eg, face mask)	Ulcer healed after 3 mo of consistent face mask use <sup>11</sup>
Occlusive dressing (eg, flexible mesh material)	Ulcers healed within 4 wk; clearance was maintained for up to 2–6 mo <sup>12</sup>
<b>Medical Management</b>	
Carbamazepine	Ulcer healed over 4 wk of treatment (100 mg twice daily) with no recurrence during 9 mo of continuous use <sup>13</sup> ; other studies have shown no success
Gabapentin	Decreased paresthesia following once-daily treatment (2400 mg) <sup>5</sup>
Amitriptyline	Healed ulcer and decreased paresthesia following once-nightly treatment (25 mg) <sup>14</sup>
Trolamine–sodium alginate emulsion	Ulcer healed following 6 mo of twice-daily application <sup>6</sup>
Transcutaneous electrical nerve stimulation	Ulcer healed after 6 wk of treatment applied to the affected area for 30 min 3 times daily; recurrence was noted <sup>15</sup>
<b>Surgical Management</b>	
Transplant of autologous cultured epidermal cells	Ulcer closed following 10 mo of treatment; healing was noted at 6-wk follow-up <sup>14</sup>
Reconstruction of affected area via skin flaps or grafts	Healing sustained for 2 y <sup>13</sup> ; some ulcers recur following surgery <sup>11</sup>

to respond to multiple medications.<sup>5</sup> A single report of twice-daily topical application of trolamine–sodium alginate emulsion over a 6-month period resulted in improved healing of the ulcer.<sup>6</sup>

Another unique way of treating TTS is the use of transcutaneous electrical nerve stimulation (TENS). Westerhof and Bos<sup>15</sup> showed improved wound healing and enhanced local blood supply to the ulcerated area with 30-minute treatments administered 3 times daily over 6 weeks. Ulcer healing was seen with continuous use of TENS.<sup>15</sup> Despite the promising results in this report, however, the use of TENS has been limited because of many patients' inability to tolerate the treatment.<sup>20</sup>

Surgical management of TTS includes the use of innervated skin flaps to correct the skin defect. Some good long-term results have been reported for

surgical reconstruction<sup>13,21</sup>; however, some patients continue to have recurrent symptoms despite surgical correction.<sup>11,22</sup> Reconstructed flaps can repair the skin defect but do not necessarily restore normal sensation to the area. Further investigation of novel treatment options for TTS is underway. Autologous cultured epidermal cells, mostly keratinocytes and fibroblasts, transplanted into the affected area have been shown to induce tissue regeneration after 10 months<sup>14</sup>; however, this method may have the same shortcomings as other surgical methods.

Another option for treatment of TTS is the use of flexible mesh dressings, which are noninvasive and easy to administer. Complete healing may occur in a matter of weeks.<sup>12</sup> Larger trials with long-term results are necessary to know if this approach has merit.

## Conclusion

This report of 3 patients with TTS supports the notion that injury along any of the 3 sensory branches of the trigeminal nerve can result in altered sensation, which can lead to self-mutilation. Because of this response, TTS often can be misdiagnosed as a psychiatric disorder and therefore should be distinguished from other disease processes that have similar presentations (eg, DOP). A history of trigeminal nerve injury and ulcerations confined to the trigeminal nerve distribution helps to distinguish TTS from other disorders. Overall management can be challenging. Nevertheless, treatment should aim at controlling compulsive picking of the skin and preventing further trauma by addressing paresthesia and numbness to achieve long-term healing.

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