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Trigeminal Trophic Syndrome Associated With the Use of Synthetic Marijuana

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Background: Trigeminal trophic syndrome (TTS) is an uncommon disorder of the trigeminal nerve tract and trigeminal brainstem nucleus. The syndrome is characterized by a triad of unilateral crescentic ulcers with anesthesia and paresthesias of the involved trigeminal dermatomes.

Case Report: A 24-year-old right-handed black female presented to our emergency department with a 4-week history of rapidly progressive painless desquamation/denudation of skin over her right face and scalp. Four weeks prior, she had been admitted to another institution for seizures and was diagnosed with seizures provoked by synthetic marijuana use. She was afebrile during her initial presentation at our institution. Dermatologic examination revealed denudation of the epidermis and partial dermis over the right frontal, parietal, and temporal scalp with associated alopecia.

Conclusion: To our knowledge, the association of disorders of the trigeminal nerve pathway, including TTS, with the use of synthetic marijuana has not been previously reported. The long-term neurologic effects of synthetic marijuana are difficult to predict, and the pathologic underpinnings of TTS are largely unknown. Further studies dedicated to exploring the underlying molecular and cellular mechanisms may translate into effective therapies and approaches to halt and reverse the process and prevent tissue destruction and cosmetic disfigurement.

Keywords: *Skin ulcer, street drugs, synthetic marijuana, trigeminal nerve diseases*

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INTRODUCTION

Trigeminal trophic syndrome (TTS) is an uncommon disorder of the trigeminal nerve tract and trigeminal brainstem nucleus. It is characterized by a triad of unilateral ulcers with anesthesia and paresthesias of the involved trigeminal dermatomes.[1,2] Patients with TTS typically have an intractable urge to excessively scratch the affected areas to overcome the unpleasant sensations, resulting in self-inflicted trauma in the form of multiple facial ulcers, often located at the nasal ala.[3,4] Additionally, the development of ulcers may be directly related to disrupted trigeminal innervation and, as such, be independent of trauma involving anesthetic regions.[2]

The etiologies of this condition are broad, with the most commonly reported etiology being ipsilateral peripheral or central trigeminal neural injuries, including postoperative complications involving the trigeminal nerve pathway.[2,5-7] Infections, stroke, and various brain lesions such as multiple sclerosis, intracranial tumors, and abscesses have been associated with TTS.[3,5,8] Although synthetic marijuana has been associated with multiple organ dysfunctions, to our knowledge, it has not been previously reported as an etiology for TTS.

CASE REPORT

A 24-year-old right-handed black female presented to our emergency department (ED) with a 4-week history of rapidly progressive painless desquamation/denudation of skin over her right face and scalp. Four weeks prior, she had been admitted to a regional hospital for witnessed seizures at home and was diagnosed with seizures provoked by synthetic marijuana use. The patient did not verify the duration or quantity of consumption. According to her family, her use was a recent phenomenon. During that hospitalization, she received intravenous lorazepam and was discharged on levetiracetam 500 mg twice daily. Soon after discharge from the hospital, she developed an irresistible itching on the right side of her face that led to uncontrollable rubbing. The patient reported regularly picking at and scratching the affected areas. The gradual peeling of the skin exposed large areas of pink denuded skin. She self-medicated with petroleum jelly and neosporin and reported modest relief of the itching with the application

of petroleum jelly. The patient also presented to her regional hospital ED where she was administered diphenhydramine, chlorpromazine, and 20-mg prednisone with little effect. The patient discontinued levetiracetam, as she presumed her condition to be a drug reaction. The symptoms progressed despite drug discontinuation.

She was afebrile during presentation at our institution. During neurologic examination, sensation of the trigeminal nerve dermatomes, V1-V3, was normal on the left side, but sensation was not assessed on the right side because of the bandages wrapped around her face. The rest of her cranial nerves were intact. Dermatologic examination revealed denudation of the epidermis and partial dermis over the right frontal, parietal, and temporal scalp with associated alopecia. In addition, denudation of the epidermis and partial dermis extending from the right glabellar region periorbitally (sparing the eyelid margins) and down the right lateral and medial cheek and nasal bridge including the right nasal ala and nares was noted (Figure 1). No vesicles or bullae were present. No lesions were observed in any other skin or mucosal areas, including the conjunctiva. The patient denied the presence of any oral or genital lesions associated with the facial lesions. Routine laboratory tests revealed no abnormalities with the exception of elevated serum erythrocyte sedimentation rate, 55 mm/h (normal 0-20 mm/h), and C-reactive protein, 92.1 mg/L (normal 0.0-8.2 mg/L). Serologic tests for human immunodeficiency virus antibodies were negative. Magnetic resonance imaging (MRI) of the brain was unremarkable. Biopsy revealed no evidence of infection, vasculitis, neoplasm, granulomas, or fungi. The patient exhibited no evidence of toxic epidermal necrolysis or Stevens-Johnson syndrome. She was treated with prophylactic cefazolin 1 g and petroleum-impregnated gauze. For seizure prophylaxis, she was started on 100-mg gabapentin 3 times daily and 50-mg lacosamide twice daily. She was discharged home 2 days later with home wound care services.

During her 3-month follow-up visit, the patient reported residual tingling and itching. At that time, she was self-medicating with fexofenadine, vitamin E capsule contents, and petroleum jelly. Dermatologic examination revealed hyperpigmented and hypopigmented patches, as well as 1-2 hypertrophic scar areas.

At the patient's 5-month follow-up visit, examination revealed alopecic hypopigmented plaques on the scalp, hypopigmented plaques on the face with areas of depigmentation, scar contractures, and 2 new discrete erosions with yellow discoloration that were secondary impetiginization (Figure 2). Culture of the erosions was positive for infection with methicillin-resistant *Staphylococcus aureus* that was treated with 100-mg doxycycline twice daily and intranasal mupirocin twice daily. She was evaluated by a plastic surgeon and received a 40-mg triamcinolone injection into the scar of the right medial cheek to soften the scar.

The patient continued to have breakthrough seizures. Her electroencephalograph was normal. Lacosamide was discontinued, gabapentin was continued, and zonisamide 300 mg once daily was initiated with effective seizure control. Repeat brain MRI with intravenous contrast and thin section imaging centered at the level of the trigeminal nerve origin from the brain stem was unremarkable.

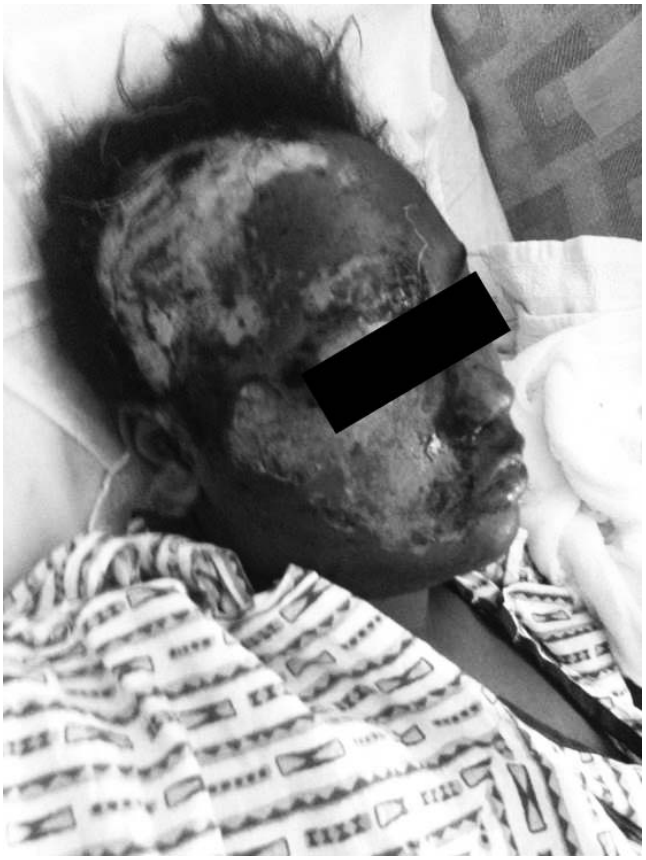

Figure 1. Lateral view of the patient's face during admission shows numerous contiguous ulcers in the right trigeminal nerve and V1-V3 dermatomal distributions. (To see this image in color, visit https://education.ochsner.org/publishing-services/toc/khan-17-0011-fig1.)

The patient's continued seizures despite several antiepileptic drugs with no clear provocative factors rendered her a clinical diagnosis of epilepsy.

One year after discharge, the patient underwent excision of a facial keloid with advancement flap and no recurrence. Two years after the onset of symptoms, she remains symptom-free with the exception of loss of sensation over the facial scars (Figure 3).

DISCUSSION

Synthetic marijuana, also known as spice, K2, herbal incense, mojo, or cloud 9, is not cannabis but rather a collection of laboratory chemicals that interact with the cannabinoid receptor in the brain to mimic the effects of marijuana and induce a marijuana-like high.[9,10] These chemicals are distributed as dried, shredded plant material to be smoked (herbal incense) or as liquids to be vaporized and inhaled in e-cigarettes and other devices (liquid incense).[11] The bioactive substances in synthetic marijuana can have particularly long half-lives, potentially leading to prolonged psychoactive effects and other neurologic complications.[9]

The pathophysiologic basis of TTS remains unclear because of unrevealing biopsies.[1] Furthermore, the exact etiopathogenesis is perplexing, as the time from trigeminal nerve pathway injury to development of TTS can range from

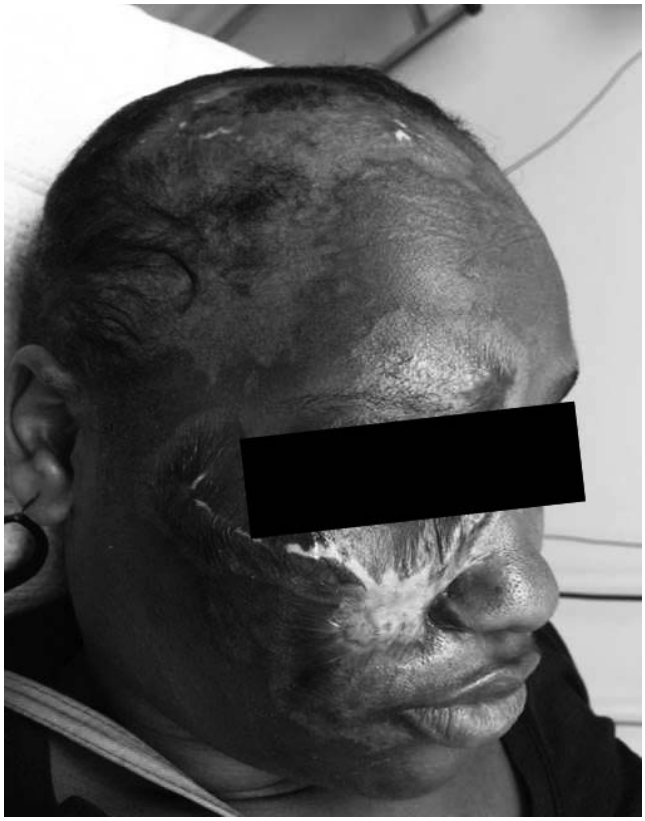

Figure 2. Lateral view of the patient's face shows healed lesions and alopecic hypopigmented plaques on the scalp and the face with areas of depigmentation and scar contractures 5 months after discharge. (To see this image in color, visit https://education.ochsner.org/publishing-services/toc/khan-17-0011-fig2.)

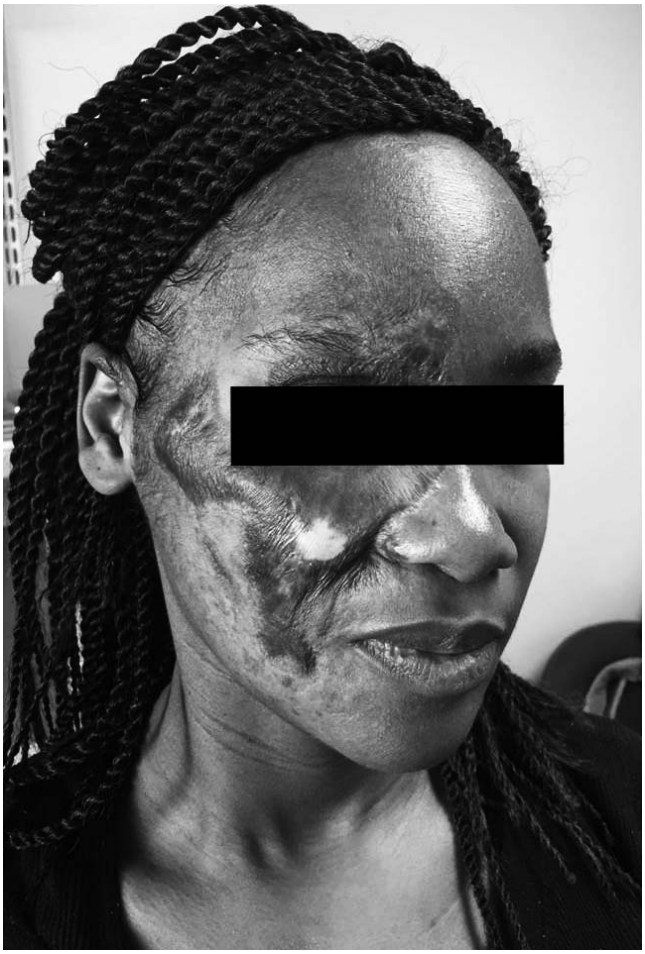

Figure 3. Lateral view of the patient's face shows healed scars 2 years after discharge. (To see this image in color, visit https://education.ochsner.org/publishing-services/toc/khan-17-0011-fig3.)

days to years.[2] While the paresthesias and anesthesia are attributed to dysfunction of the trigeminal nerve complex, the exact mechanism of skin ulceration and progressive tissue destruction is unclear. Repeated trauma because of underlying analgesia is common and can lead to eventual tissue loss.[12,13] Other unknown mechanisms may predispose patients to the development of ulcerations characterized by poor healing. Autonomic vasomotor dysfunction has been hypothesized to play a role in the development of TTS.[14] The authors of one case report suggest that self-manipulation did not appear to be a requisite for ulcer development in their patient.[2] Enhanced blood flow from transcutaneous electrical stimulation led to improved wound healing of chronic facial ulcers in their patient with trigeminal nerve transection. They hypothesized that when the gasserian ganglion is destroyed, sympathetic fibers from the internal carotid artery are somehow disrupted, resulting in a persistent low sympathetic tone that leads to constant cooling of the skin secondary to vasodilatation and a slower venous return that results in an unfavorable environment for wound healing.[14,15]

Synthetic marijuana use can have serious neurologic consequences. Our patient developed new-onset seizures after the use of synthetic marijuana that were refractory to 2 antiepileptic medications. She currently remains seizure-free after introduction of zonisamide. The prognosis of epilepsy after use of synthetic marijuana remains unknown, suggesting the need for long-term follow-up studies on this population.

To our knowledge, the association of disorders of the trigeminal nerve pathway, including TTS, with use of synthetic marijuana has not been previously reported. We propose that our patient's use of synthetic marijuana was directly responsible for the new-onset seizures and TTS as supported by the evidence of temporal association. The exact mechanism of injury to the trigeminal nucleus and/or nerve is unknown. No abnormalities were noted on head imaging in our patient. It is also unclear whether the TTS was an acute consequence of synthetic marijuana use or a result of chronic use with an accumulation of neurotoxicity. Typically, the ulcers in TTS present in the area of sensory overlap between the first and second divisions of the nerve (V1 ophthalmic and V2 maxillary). Cases of TTS involving all 3 branches of the trigeminal nerve have been reported in patients several months after a cerebellar stroke and surgical resection for ipsilateral cerebellopontine angle meningioma.[16,17] Our patient similarly developed extensive lesions involving all 3 sensory division dermatomes, predominantly in the first and second divisions. We speculate that the neurotoxins caused profound damage

to the trigeminal nerve complex. In the 1-year follow-up period, no recurrence of symptoms was noted after the patient stopped using synthetic marijuana. The long-term neurologic effects of synthetic marijuana are difficult to predict, and the pathologic underpinnings of TTS are largely unknown.[18,19]

CONCLUSION

We describe what we believe to be the first reported case of TTS associated with the use of synthetic marijuana. Further studies dedicated to exploring the underlying molecular and cellular mechanisms may translate into effective therapies and approaches to halt and reverse the process and prevent tissue destruction and cosmetic disfigurement.

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