Secondary Trigeminal Neuralgia Due to Multiple Sclerosis in a Patient With Opioid Use Disorder Treated With Buprenorphine/Naloxone

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Trigeminal neuralgia (TN) is an exemplary condition of neuropathic facial pain.[1] Approximately 15% of cases of TN are secondary, with multiple sclerosis (MS) representing 2%–11% of all cases.[2] We present a case of a patient with secondary TN due to MS (TN-MS), who was minimally responsive to standard sodium channel antagonists. While responsive to opiates, the patient had a history of opioid use disorder (OUD).

Case Report

The patient was a 54-year-old woman diagnosed with MS at age 30 years. She presented to the emergency department with a 6-week history of progressively worsening left facial pain/V1 > V2 divisions. She first reported similar symptoms 5 years ago, describing the pain as severe, "electrical shock-like" lasting less than 1 minute/episode, recurring multiple times/day, with a Brief Pain Inventory-Facial[3] score of 140. The patient reported short-lived attenuation of pain with carbamazepine/gabapentin and, subsequently, a variety of anticonvulsants. Magnetic resonance imaging of the brain was remarkable for numerous (>20 lesions) T2/fluid-attenuated inversion recovery signal hyperintense lesions in the supratentorial and infratentorial regions of the brain (Figure 1). One of those lesions was located at the left dorsal mid pons at the expected location of the main sensory nucleus of the trigeminal nerve. Both blood alcohol and urine drug screens were unremarkable, except for opiates/oxycodone. We were asked to evaluate the patient because of "treatment resistance."

On psychiatric examination (Table 1),[4–13] the patient admitted to a history of stimulant, opioid, alcohol, and benzodiazepine use disorder throughout her 20s, although since MS diagnosis, she only met criteria for OUD. The patient was currently prescribed oxycodone/acetaminophen but greater than 100-mg morphine equivalent. Due to the latter and OUD, the patient was transitioned and titrated to buprenorphine/naloxone 8 mg/2 mg twice daily. After 1 week of treatment, the Patient Global Impression of Change (PGIC)[14] score was 3. At first-, second-, and third-month follow-up, her PGIC score was 2, and the blood alcohol and urine drug screens remained negative.

Discussion

Not atypical for MS-TN, our patient's pain involved areas innervated by V1.[6] Gently touching the face or even a slight breeze "triggered" paroxysms such that she was confined at times to wearing an eye patch over the affected eye. Similar to our patient, who was prescribed ocrelizumab, it has been reported that when demyelinating lesions develop in trigeminal sensory pathways, disease-modifying therapies have limited efficacy in TN-MS pain outcomes.[15] Furthermore, there is a dearth of evidence on prevalence of μ-opioid receptor agonists (MOR-As) in TN-MS. Nonetheless, a study reported that 100% and 16% of TN-MS patients were taking opiates with and without anticonvulsants, respectively.[16]

In other chronic, noncancer pain syndromes, rotation to buprenorphine has not been associated with changes to patients' pain control. In most studies, buprenorphine was associated with reduced pain severity, although the mechanism for this finding is unclear. It is possible, including in our patient, that reduced pain might be associated with buprenorphine's unique role in

Figure 1.

Magnetic Resonance Images Showing the Highlighted Node/Flare

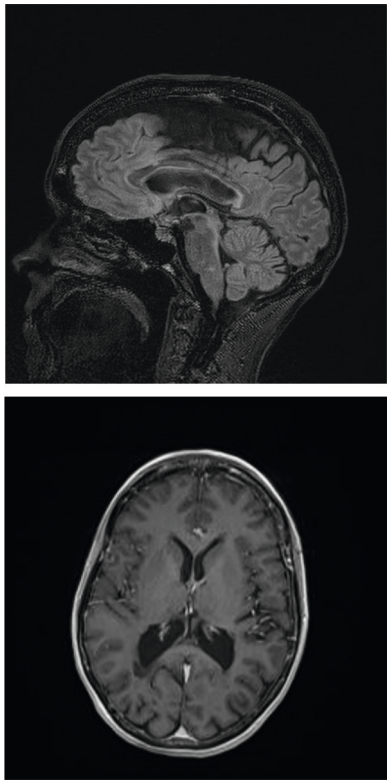

Table 1.

Classical and Secondary/Multiple Sclerosis–Induced Trigeminal Neuralgia (TN): Comparison With the Current Patient[4–13]

	Classical TN	MS-induced TN	Current patient
Prevalence[4–6]	0.16%–0.3%	2.4% (2%–5%); 20-fold increased risk without differences between relapsing-remitting, secondary, and primary progressive forms	NA
Gender[5,7]	More prevalent in women than in men (female:male ratio: 3:2)	Similar to classical TN: 1.6:1	Female
Age at MS diagnosis, mean, y[4]	NA	36	30
Age at TN onset, mean, y[4,5,8]	53–57	–45 to 46	49
Age at TN onset if after MS diagnosis, mean, y[4]	NA	48	49
Age at TN onset if before MS diagnosis, mean, y[4]	NA	39	NA
Diagnosis[6,9]	Pain restricted to the territory of 1 or more divisions of trigeminal nerve; paroxysms of pain that are sudden, intense, and very short (<1 seconds to 2 min, but usually a few seconds); described as a "shock" or an "electric sensation"; pain typically evoked by stimulating cutaneous or mucous trigeminal territories, ie, "trigger zones"; stimulus dependence is considered one of the most striking characteristics of TN/criterion of clinically established TN	Similar to classical although usually younger with onset ranging from 40 to 50 y; more likely to have sensory loss on a portion of the face; more likely to have bilateral pain; first branch alone may be involved, although the second or third branch are involved in approximately 90% of cases	Pain restricted to primarily left V1 region, less in left V2 region; aroxysmal, severe, short-lived (<1 min) "shock-like" pain complaints, occurring multiple times/day; pain triggered by wind, bright light to affected area; gently touching face, both V1 and V2 regions
Proposed pathophysiology[9]	Compression of sensory portion of trigeminal nerve: (1) close to its root entry zone in the pons, (2) adjacent small branch of the basilar artery, most often the superior cerebellar artery	Demyelinating plaque in fascicle of the trigeminal nerve as it courses through ventral pons	Demyelinating plaque located at left dorsal mid-pons at expected location of main sensory nucleus of trigeminal nerve
Physical psychiatric examination[6,10,11]	Paroxysmal attacks, lasting from fraction of a second to 2 min Distribution consistent with 1 or more divisions of fifth cranial nerve That is gentle touch of face, washing, shaving, talking, tooth brushing, chewing, swallowing Can be associated with tic douloureux	Similar to classical TN, but also more commonly: (1) bilateral involvement, (2) presence of trigeminal sensory deficits	Decreased gait speed, step length; bilateral internuclear ophthalmoplegia; intact bilateral V3, right V1 and V2; pain at trigger points in left V1 much greater than V2; lack of brisk facial muscle contractions Denied all primary psychopathology except for feeling "depressed" when experiencing TN symptoms; denied a history/current lethality; mental status examination was unremarkable, while the Mini-Mental State Examination score was 26
Evaluation[6,12]	MRI strongly recommended as a part of early workup; a combination of 3 high-resolution sequences: 3D T2-weighted, 3D TOF-MRA, and 3D T1-gadolinium—aids the detection of a possible NVC	Dedicated MRI is required to identify pontine demyelinating plaques.	MRI brain: greater than 20 lesions, numerous T2/FLAIR signal hyperintense lesions in supratentorial and infratentorial brain; 1 lesion located at left dorsal mid-pons at expected location of the main sensory nucleus of trigeminal nerve; no definite finding of an enlarged vessel contacting preganglionic left trigeminal nerve
Trigeminal reflex testing[6*]	Abnormal in 3% of patients	Abnormal in 89% of patients	Not available
Differential diagnosis[5]	Persistent idiopathic facial pain, primary stabbing headache	CNS (cerebellopontine angle tumor, arteriovenous malformation); dental causes; sinus causes (maxillary sinusitis); salivary gland causes; temporomandibular joint causes (temporomandibular disorders); neuropathic pain (posttraumatic trigeminal neuropathy, painful trigeminal neuropathies); trigeminal autonomic cephalalgias (SUNA, SUNCT)	Patient without other identifiable causes, as described in classical and MS-induced TN columns

(continued)

Table 1 (continued).

	Classical TN	MS-induced TN	Current patient
Treatment[10,12,13]	(1) Acute exacerbations of pain; in-hospital treatment may be necessary for titration of anti-epileptic drugs, rehydration, and IV infusion of fosphenytoin or lidocaine; (2) for long-term treatment, carbamazepine or oxcarbazepine is recommended as drug of first choice; (3) based on low to very low quality of evidence, lamotrigine, gabapentin, botulinum toxin type A, pregabalin, baclofen, and phenytoin may be used either as monotherapy or combined with carbamazepine or oxcarbazepine when first-line drugs fail due to either efficacy or tolerability	Dearth of well-controlled studies. First-line therapy: carbamazepine, oxcarbazepine; many patients never advance to the regimen required for pain relief because of intolerable adverse effects (carbamazepine: somnolence, dizziness, and postural imbalance; oxcarbazepine: less of above but greater risk of hyponatremia)	Past treatment includes gabapentin, oxcarbazepine, carbamazepine, lamotrigine, pregabalin, diazepam, amitriptyline, duloxetine, naproxen, meloxicam, cyclobenzaprine On admission: MS: dalfampridine, ocrelizumab 30 mg IV every 6 mo; TN: oxycodone-acetaminophen and tramadol In hospital: due to patient's history of opioid use disorder, both oxycodone-acetaminophen and tramadol were tapered and discontinued; began treatment with buprenorphine/naloxone, titrated to 8 mg/2 mg twice/d

*Series of reflex responses (R1 and R2 components of blink reflex after electrical stimulation of ophthalmic division, SP1 and SP2 components of masseter inhibitory reflex after electrical stimulation of maxillary or mandibular division).
Abbreviations: FLAIR = fluid-attenuated inversion recovery, MRI = magnetic resonance imaging, MS = multiple sclerosis, N/A = not applicable, NVC = neurovascular compression, SUNA = short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms, SUNCT = short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing, TOF MRA = time-of-flight magnetic resonance angiography.

opioid-induced hyperalgesia. Previous studies have reported antihyperalgesic outcomes of buprenorphine compared with other full MOR-As in animal models and humans. Participants were much more likely to complete study protocols, remain in treatment, avoid additional opioid use, and achieve analgesia if they continued to receive stable doses of buprenorphine after rotation rather than tapering off of buprenorphine. This outcome, including in our patient, was especially apparent in individuals with co-occurring OUD and chronic pain, which is consistent with the literature on OUD without chronic pain that found a greatly increased risk of return to illicit opioid use after buprenorphine taper.[17]

In conclusion, while uncommonly its first presentation, TN-MS is often a chronic/disabling symptom, similar to classical TN. For patients like ours with comorbid OUD and TN-MS, transition from a full MOR-A to/continuing buprenorphine can be a successful treatment strategy, although larger studies are needed to confirm this finding.

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References

1. Cruccu G, Finnerup NB, Jensen TS, et al. Trigeminal neuralgia: new classification and diagnostic grading for practice and research. *Neurology*. 2016;87(2):220–228.
2. Latorre G, González-García N, García-Ull J, et al. Diagnosis and treatment of trigeminal neuralgia: consensus statement from the Spanish society of neurology's headache study group. *Neurol Engl Ed*. 2023;38:S37–S52.
3. Lee JY, Chen HI, Urban C, et al. Development of and psychometric testing for the Brief Pain Inventory-Facial in patients with facial pain syndromes. *J Neurosurg*. 2010;113(3):516–523.
4. Laakso SM, Hekali O, Kurdo G., et al. Trigeminal neuralgia in multiple sclerosis: prevalence and association with demyelination. *Acta Neurol Scand*. 2020;142(2):139–144.
5. Lambru G, Zakrzewska J, Matharu M. Trigeminal neuralgia: a practical guide. *Pract Neurol*. 2021;21(5):392–402.
6. Di Stefano G, Maarbjerg S, Truini A. Trigeminal neuralgia secondary to multiple sclerosis: from the clinical picture to the treatment options. *J Headache Pain*. 2019;20(1):20.
7. Houshi S, Tavallaei MJ, Barzegar M, et al. Prevalence of trigeminal neuralgia in multiple sclerosis: a systematic review and meta-analysis. *Mult Scler Relat Disord*. 2022;57:103472.
8. Fallata A, Salter A, Tyry T, et al. Trigeminal neuralgia commonly precedes the diagnosis of multiple sclerosis. *Int J MS Care*. 2017;19(5):240–246.
9. Crucci G, Di Stefano G, Truini A. Trigeminal neuralgia. *N Engl J Med*. 2020;383:754–762.
10. Cruccu G, Gronseth G, Alksne J, et al. AAN-EFNS guidelines on trigeminal neuralgia management. *Eur J Neurol*. 2008;15(10):1013–1028.
11. Folstein MF, Folstein SE, McHugh PR. Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189–198.
12. Bendtsen L, Zakrzewska JM, Abbott J, et al. European Academy of Neurology guideline on trigeminal neuralgia. *Eur J Neurol*. 2019;26(6):831–849.
13. Rana MH, Khan AAG, Khalid I, et al. Therapeutic approach for trigeminal neuralgia: a systematic review. *Biomedicines*. 2023;11(10):2606.
14. Hurst H, Bolton J. Assessing the clinical significance of change scores recorded on subjective outcome measures. *J Manipulative Physiol Ther*. 2004;27(1):26–35.
15. Mousavi SH, Lindsey JW, Gupta RK, et al. Trigeminal neuralgia in multiple sclerosis: association with demyelination and progression. *Mult Scler Relat Disord*. 2023;74:104727.
16. Yang AI, McShane BJ, Hitti FL, et al. Patterns of opioid use in patients with trigeminal neuralgia undergoing neurosurgery. *J Neurosurg*. 2019;131(6):1805–1811.
17. Powell VD, Rosenberg JM, Yaganti A, et al. Evaluation of buprenorphine rotation in patients receiving long-term opioids for chronic pain: a systematic review. *JAMA Netw Open*. 2021;4(9):e2124152.