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Case Reviews in Pain

Toothache or Trigeminal Neuralgia: Treatment Dilemmas

Christopher J. Spencer, John K. Neubert, Henry Gremillion, Joanna M. Zakrzewska, and Richard Ohrbach

Case Review

A 61-year-old woman presented to her general dentist with a complaint of pain associated with the maxillary left first premolar. The patient described a sharp, lancinating pain that was triggered by stimulation of the tooth in question. She also reported 2 specific episodes in which she experienced severe, shooting electrical shock-like pain followed by a hot sensation in the same area. One of these episodes was triggered by a cool breeze on her face and the other occurred while washing her face. Examination and radiographic assessment revealed a periapical osseous lesion resulting in a diagnosis of acute apical periodontitis. Nonsurgical endodontics was completed with no undue effects.

Approximately 2 months after the endodontic treatment, the patient began to have a recurrence of the paroxysmal sharp, shooting pain with a marked increase in the frequency of these episodes. The pain was triggered by light touch of the left cheek. Each episode lasted 1 to 2 seconds; however, she occasionally had 5 to 10 repetitive bursts. Clinical evaluation resulted in a diagnosis of trigeminal neuralgia of the left maxillary division. Initial treatment included 100 mg carbamazepine bid., which was gradually increased to a maximum dose of 600 mg bid. The patient derived modest benefit from the medication; unfortunately, cognitive changes necessitated a reduction in the dose. Gabapentin was introduced in a bedtime dosage regimen of 100 mg. This provided a marked reduction in pain for approximately 1 week. A gradual titration of gabapentin to 300 mg tid was efficacious for approximately 1 month. Neurosurgical consultation and MRI of the brain revealed no intracranial pathology and confirmed a diagnosis of trigeminal neuralgia. Surgical intervention is being considered.

Christopher J. Spencer, D.D.S.
Clinical Assistant Professor
University of Florida College of Dentistry
Parker E. Mahan Facial Pain Center
Gainesville, FL

Orofacial Pain: Unknown Etiology

Many acute, chronic, and recurrent painful maladies occur in the orofacial region. Lipton et al¹¹ reported that 22% of the U.S. population have orofacial pain on more than 1 occasion in a 6-month period. However, the etiology of pain for countless patients who have chronic orofacial pain disorders is unknown. In many instances, these patients may not recognize an injury or serendipitously report having a relatively minor dental procedure (eg, restoration or root canal) completed at the time of pain onset. Although pain involving the teeth and the periodontium is the most common presenting concern in dental practice, other nonodontogenic causes of orofacial pain must be considered in the differential diagnostic process.

Neuropathic orofacial pain, which is pain initiated or caused by a primary lesion or dysfunction in the nervous system, is relatively common. It is diagnosed in approximately 25% to 30% of patients presenting in a tertiary care University-based Facial Pain Center.¹⁹ Conditions representative of neuropathic orofacial pain are postherpetic neuralgia, trigeminal neuralgia, trauma-induced neuropathy, atypical odontalgia/nonodontogenic toothache, idiopathic oral burning, and Complex Regional Pain Syndrome (CRPS). In some instances, diagnosis can be difficult, as neuropathic orofacial pain is associated with significant interpatient variability regarding presentation and response to treatment. Additionally, neuropathic pain conditions are frequently associated with qualities that the patient is not familiar, thus making it difficult for the patient to communicate their pain experience. Typical descriptors used by patients include stabbing, burning, electric-like, and/or sharp, with numbness or tingling projected to a cutaneous area.^{15,16} However, aching pain does not preclude the possibility of a neuropathic basis for the patient's pain.

The present case illustrates an interesting conundrum whereby the practicing clinician must decide whether

Address correspondence to Judith A Paice, PhD, RN, Editor, Case Reviews in Pain; Director, Cancer Pain Program, Northwestern University, Feinberg School of Medicine, Chicago, IL 60611-2927. E-mail: j-paice@northwestern.edu
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the 2 pain complaints (tooth vs neuropathic pain) are related or are merely coincidental. Such comorbid conditions may result in diagnostic confusion and a perpetuation of the patient's pain condition. Although the etiology and pathophysiology of odontogenic pain is well known (ie, bacteria-induced destruction of tooth structure and subsequent activation of tooth nociceptors), mechanisms underlying trigeminal neuralgia are less understood. It is possible that coexistent sources of pain in this patient are indeed playing an additive role in the overall pain complaint. As such, this provides an interesting scenario whereby a persistent peripheral noxious stimulus (ie, tooth pain) can sensitize trigeminal ganglion neurons in the brainstem (ie, central sensitization) that may in turn influence the trigeminal neuropathic pain. Central sensitization involves an activity-dependent increase in the excitability of neurons in the dorsal horn of the spinal cord,^{4,17,21,22} and its trigeminal homolog in the brainstem.^{3,13} Central sensitization is reflected in the reduced threshold of activation and increased responsiveness of central neurons associated with an increase in receptive field size of the neurons.²² The increased excitability of central neurons, which receive convergent input from other, usually nearby tissues, typically results in expanded areas of referred pain as well as sensitivity to previously non-noxious stimuli (ie, allodynia). Importantly, these symptoms can persist beyond the initial noxious stimulus,²¹ which, if maintained, can continue to drive central sensitization.⁸

This case also highlights that trigeminal neuropathic pain may exist in many forms and may easily be mistaken to represent an odontogenic source. The pitfall for the practicing dentist is to focus on the odontogenic pain component while the physician focuses on the trigeminal neuropathic pain component. Failure to identify the source of the patient's entire problem may lead to erroneous and ineffective treatment. Therefore, it is important to consider all sources of pain in trying to delineate the etiology and ultimately recommend treatment. Optimum management can only be achieved by determining an accurate and complete diagnosis and identifying all of the factors associated with the underlying pathology on a case-specific basis.

John K. Neubert, DDS, PhD

Assistant Professor

Departments of Orthodontics and Neuroscience

University of Florida

Gainesville, FL

Henry Gremillion, DDS, MAGD

Associate Professor

College of Dentistry

University of Florida

Parker E Mahan Facial Pain Center

Gainesville, FL

Surgical Strategies for Pain Relief

There continue to be a variety of surgical treatments for patients with trigeminal neuralgia in whom efficacy and tolerability of medications is reduced. Surgical treat-

ments are broadly divided into 2 groups. The first group, ablative or destructive techniques, damage the trigeminal nerve. The tissue disruption resulting from the intervention can be partial or complete and/or selective or indiscriminate. The second surgical treatment, termed microvascular decompression (MVD), is a nondestructive procedure that attempts to relieve pressure on the trigeminal nerve.

Of the ablative procedures, percutaneous radiofrequency thermocoagulation/rhizotomy (RFT) is one example. This procedure involves the insertion of a needle under radiographic control through the foramen ovale into the trigeminal cistern. Once the needle is accurately located and checked by the use of radiology, then a lesion can be made. An electrical stimulus is passed through the needle tip which generates a temperature between 60°C and 80°C. This is maintained for 60 to 300 seconds. The position of the needle and the area of the lesion can, to some extent, be predicted by waking the patient at the start of the procedure to test the area that has been affected. For the majority of patients, only an overnight hospital stay is required as the procedure does not require a full general anesthetic but very heavy sedation. A recent randomized, controlled trial showed that pulsed radiofrequency (at lower temperatures than described above) did not give pain relief of sufficient quality and the trial was stopped early.⁷

A review of all the literature of surgical management of trigeminal neuralgia²⁵ showed that there were no randomized, controlled trials of treatments using RFT. The studies that have been conducted include independent observers to evaluate the outcomes.¹ A systematic review of all ablative procedures¹² suggests that RFT provides the longest-term and most complete pain relief, which at 5 years is just over 50%. The majority of patients will report sensory numbness, which may be confined to only 1 branch of the trigeminal nerve but can extend to all 3 branches. The extent of sensory loss can vary from mild paresthesia to the rare (2%) but extremely debilitating anesthesia dolorosa. If the first trigeminal nerve division is involved, corneal anesthesia may occur in up to 10% of cases, and this must be identified before the patient leaves the hospital, so that protective eyewear can be issued. This numbness can lead to corneal damage and subsequent loss of sight in 1% of patients. There is a 12% risk of masticatory weakness, resulting in difficulties with eating, but these tend to resolve over time. The risk of these side effects can be reduced by using lower temperatures, but this results in a shorter pain relief period.

The second treatment strategy, MVD, appears to offer the best long-term outcome, but not all patients can be offered this form of major surgery due to coagulopathies, infection, or general frailty. RFT, therefore, offers an alternative in patients who are not medically fit for surgery or who are fearful of a major operation and its risk of serious complications. Although mortality has been reported after RFT, this is very low in comparison to MVD. Patients must be aware that RFT may need to be repeated for them to remain free of pain. The major risk

is the sensory loss, which can affect the quality of life of more than 65% of patients.²⁴

In summary, the advantages of RFT include (1) safe in medically compromised patients, (2) highly specific for the targeted trigeminal nerve branch, (3) immediate pain relief, (4) low mortality rate, (5) relatively low recurrence rate, and (6) few complications outside the trigeminal nerve branch territory.²³ The disadvantages of RFT include (1) patients with coagulopathies are not suitable candidates, (2) a cooperative patient is necessary, (3) the equipment is expensive, (4) it is tedious to do because of the need to continuously request patient feedback, (5) sensory loss is inevitable, (6) risk of anesthesia dolorosa, (7) risk of corneal damage, (8) need to wear safety glasses, and (9) risk of masseteric dysfunction. Patients taking part in a hypothetical decision-making process on management of trigeminal neuralgia opted for surgery compared with continued medication, and MVD was only marginally more frequently chosen than other procedures.¹⁸

Prof Joanna M. Zakrzewska
Consultant Oral Medicine
Eastman Dental Hospital
UCLH Foundation NHS Trust
London, UK

Why Now? Biobehavioral Factors

This case illustrates the complex task of the clinician in determining which factors are important to consider at each stage of the progression of a pain disorder. The field of orofacial pain tends to be focused on the nociceptive and neuropathic aspects of the pain; this commentary addresses additional possibilities.

At the outset, the patient reported idiopathic onset (61-year-old individual with presumably no significant history of problems with the affected teeth or region) and clinical characteristics with overlapping diagnostic possibilities (sharp pain episodes triggered by tooth stimulation; sharp pain episodes triggered by stimulation to the face), coupled with a pathology (periapical tooth lesion, signifying pulpal death) from which nociception sufficient to explain the complaint could be reasonably inferred. Given these specific facts, focusing at that stage on only the somatic characteristics of the problem would be sensible. We learn that several months after somatic intervention for the obvious pathology, the pain episodes associated with the previously identified allodynia have recurred and escalated. A somatic diagnosis (trigeminal neuralgia) emerged, and medication appropriate to that diagnosis was implemented. It appears that the response to medication was variable over time, and an intervention was considered.

At the time of recurrence, the clinician's task became more difficult: A decision point emerged with respect to what additional evaluation and therapeutic possibilities should be considered. Although the first intervention (for the tooth pulp) indicated the clinician's reasonable belief that the allodynia suggestive of neuroplastic changes would resolve once the source of the nocicep-

tion was removed, the recurrence of the allodynia suggested that the initial presentation might not have been simply an acute disorder but rather possibly the acute presentation of a chronic process. The clear identification of additional somatic symptoms (eg, the neuropathic pain symptoms in this case) that point to a particular physiological process at the time of recurrence in any disorder can be seductive in that it overshadows consideration of possible chronicity as well as making the question of "Why now?" for the emergence of the initial complaint more salient. That is, the retrospective view at the time of recurrence opens the door to reconsidering what other factors might be contributing to the pain symptoms that may represent a chronic process.

Although the evidence for the role of biobehavioral factors affecting musculoskeletal pain and chronic pain in general is very good,² there is very little known about how such factors might affect neuropathic pain. Yet, the available evidence does suggest that neuropathic pain is no different than other chronic pain conditions with respect to the potential importance of biobehavioral factors.¹⁰ Because of the evident pathology (periapical lesion) appropriate to the pain complaint at the time of initial presentation, it is understandable that the clinician focuses on further pathological contributions to the nociceptive pain (eg, trigeminal nerve impingement), and indeed the somatic contributions must be considered. However, because pain is clearly affected by multiple levels of processing in the brain,¹⁴ the suggestion of chronicity, coupled with uncertainty about how the symptom course will unfold in time after yet another somatic intervention, leads to the question of when should other possible contributions to pain experience and symptom expression be considered? So, we return to the question of "Why now?" Why, indeed, does pain expression suddenly unfold given the evidence of ongoing pathology heretofore not reaching into consciousness? Is it because of a change in the pathology (eg, pulpal status? degree of impingement upon the trigeminal nerve?) or perhaps because of a change in central processing independent of any ongoing nociceptive process?⁹

We have straightforward biobehavioral assessment methods for use in temporomandibular disorders that would appear to be as useful and relevant for other orofacial pain conditions.^{5,6} As is true for any pain condition, these methods assess the cognitive and behavioral processes associated with central changes that may be caused by persistent pain or that may affect the expression and course of pain. These assessment methods, however, are not used currently in any systematic way in most clinical settings; moreover, we as yet do not have the data demonstrating the clear relevance for their routine application for orofacial pain disorders as compared with use in temporomandibular disorders. The use of such methods will lead to that data, however, and certainly, for the given patient, to assess factors perhaps relevant to the question of "Why now?" might lead to insights leading to additional treatments (eg, cognitive behavioral therapy for catastrophizing, relaxation skills for stress-related anxiety responses) that might facilitate

better response to analgesics²⁰ and even perhaps to neuroleptic medications (though that is not yet been demonstrated), or perhaps augmenting the effects of interventional procedures, for example, and reduce risk of recurrence of the pain—which is known to occur in a substantial number of cases.

These are questions for which we do not as yet have answers. And yet, we do know enough about biobehavioral factors in general to at least move them around on our clinical decision board and utilize them, recognizing that we are still largely probing in the dark with respect to the best way to operationalize those processes. Better

to assess for the presence of cognitive and behavioral factors relevant to pain before significant intervention rather than after, as it allows such treatments to have at least a reasonable chance of success. Resorting to such treatments after failure of all somatic interventions puts too much of a burden on the treatment, the practitioner, and the patient.

Richard Ohrbach, DDS, PhD
Associate Professor
Department of Oral Diagnostic Sciences
University at Buffalo
Buffalo, NY

References

1. Attal N, Cruccu G, Haanpaa M, Hansson P, Jensen TS, Nurmikko T, Sampaio C, Sindrup S, Wiffen P: EFNS guidelines on pharmacological treatment of neuropathic pain. *Eur J Neurol* 13:1153-1169, 2006
2. Blyth FM, MacFarlane GJ, Nicholas MK: The contribution of psychosocial factors to the development of chronic pain: The key to better outcomes for patients? *Pain* 129:8-11, 2007
3. Chiang CY, Park SJ, Kwan CL, Hu JW, Sessle BJ: NMDA receptor mechanisms contribute to neuroplasticity induced in caudalis nociceptive neurons by tooth pulp stimulation. *J Neurophysiol* 80:2621-2631, 1998
4. Cook AJ, Woolf CJ, Wall PD, McMahon SB: Dynamic receptive field plasticity in rat spinal cord dorsal horn following C-primary afferent input. *Nature* 325:151-153, 1987
5. Dworkin SF, Ohrbach R: Assessment of Orofacial Pain: Handbook of Pain Assessment. New York, NY, The Guilford Press, 2001, pp 475-498
6. Dworkin SF, Ohrbach R: Biobehavioral assessment and treatment of temporomandibular disorders, in Bays RA, Quinn PD (eds): *Temporomandibular Disorders*. Vol 4. Philadelphia, PA, WB Saunders Company, 2000, pp 389-409
7. Erdine S, Ozyalcin NS, Cimen A, Celik M, Talu GK, Disci R: Comparison of pulsed radiofrequency with conventional radiofrequency in the treatment of idiopathic trigeminal neuralgia. *Eur J Pain* 11:309-313, 2007
8. Gracely RH, Lynch SA, Bennett GJ: Painful neuropathy: Altered central processing maintained dynamically by peripheral input. *Pain* 51:175-194, 1992
9. Hasenbring MI, Plaas H, Fischbein B, Willburger R: The relationship between activity and pain in patients 6 months after lumbar disc surgery: Do pain-related coping modes act as moderator variables? *Eur J Pain* 10:701-709, 2006
10. Haythornthwaite JA, Benrud-Larson LM: Psychological assessment and treatment of patients with neuropathic pain. *Curr Pain Headache Rep* 5:124-129, 2001
11. Lipton JA, Ship JA, Larach-Robinson D: Estimated prevalence and distribution of reported orofacial pain in the United States. *J Am Dent Assoc* 124:115-121, 1993
12. Lopez BC, Hamlyn PJ, Zakrzewska JM: Systematic review of ablative neurosurgical techniques for the treatment of trigeminal neuralgia. *Neurosurgery* 54:973-982; 2004
13. Park SJ, Chiang CY, Hu JW, Sessle BJ: Neuroplasticity induced by tooth pulp stimulation in trigeminal subnucleus oralis involves NMDA receptor mechanisms. *J Neurophysiol* 85:1836-1846, 2001
14. Rainville P, Carrier B, Hofbauer RK, Bushnell MC, Duncan GH: Dissociation of sensory and affective dimensions of pain using hypnotic modulation. *Pain* 82:159-171, 1999
15. Rice AS, Maton S, Postherpetc Neuralgia Study Group: Gabapentin in postherpetc neuralgia: A randomised, double blind, placebo controlled study. *Pain* 94:215-224, 2001
16. Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L: Gabapentin for the treatment of postherpetc neuralgia: A randomized controlled trial. *JAMA* 280:1837-1842, 1998
17. Simone DA, Sorokin LS, Oh U, Chung JM, Owens C, LaMotte RH, Willis WD: Neurogenic hyperalgesia: Central neural correlates in responses of spinothalamic tract neurons. *J Neurophysiol* 66:228-246, 1991
18. Spatz AL, Zakrzewska JM, Kay EJ: Decision analysis of medical and surgical treatments for trigeminal neuralgia: How patient evaluations of benefits and risks affect the utility of treatment decisions. *Pain* 131:302-310, 2007
19. Gremillion HA: Neuropathic orofacial pain: proposed mechanisms, diagnosis, and treatment considerations. *Dent Clin North Am* 51:209-224, 2007
20. Wasan AD, Davar G, Jamison R: The association between negative affect and opioid analgesia in patients with discogenic low back pain. *Pain* 117:450-461, 2005
21. Woolf CJ, Wall PD: Relative effectiveness of C primary afferent fibers of different origins in evoking a prolonged facilitation of the flexor reflex in the rat. *J Neurosci* 6:1433-1442, 1986
22. Woolf CJ: Long term alterations in the excitability of the flexion reflex produced by peripheral tissue injury in the chronic decerebrate rat. *Pain* 18:325-343, 1984
23. Zakrzewska JM, Trigeminal neuralgia, in Zakrzewska JM, Harrison SD (eds): *Assessment and Management of Orofacial Pain*. Vol 14. Amsterdam, The Netherlands, Elsevier Sciences, 2002, pp 267-370
24. Zakrzewska JM, Jassim S, Bulman JS: A prospective, longitudinal study on patients with trigeminal neuralgia who underwent radiofrequency thermocoagulation of the Gasserian ganglion. *Pain* 79:51-58, 1999
25. Zakrzewska JM, Lopez BC: Trigeminal neuralgia. *Clin Evid Concise* 429-430, 2007; full details available at www.clinicalevidence.bmj.com