Neuralgia-inducing cavitational osteonecrosis

A possible diagnosis for an orofacial pain complaint?

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CLINICAL PROBLEM

A 45-year-old woman visited her general dentist because of severe pain in the right mandibular posterior region. Her first molar contained a large mesial-occlusal-distal amalgam restoration, and the patient experienced symptoms consistent with irreversible pulpitis. In addition, radiographs showed changes associated with the mesial root. The second molar contained a conservative occlusal amalgam restoration, and the premolars contained no restorations. The clinician performed endodontic therapy in the patient's first molar; the pain remitted for a few weeks after treatment but then returned.

The dentist performed endodontic treatment again in the first molar, which resulted in no change in the patient's pain. He referred her to an endodontist, who also treated the tooth endodontically, then performed an apicoectomy and a retrograde sealing of the tooth. Again, the patient experienced short-term pain relief, but owing to pain recurrence, the patient's general dentist extracted the tooth.

The patient continued to experience pain, and her general dentist performed endodontic treatment in the second molar. However, the pain persisted. The dentist referred her again to the endodontist, who concluded that the second premolar was the source of the pain and performed endodontic therapy in that tooth. Subsequently, the patient's general dentist extracted the second premolar and second molar, but the pain continued. The patient later sought care from her general dentist for persistent severe pain in the edentulous right side of the posterior mandible.

Did this patient experience the phenomenon known as neuralgia-inducing cavitational osteonecrosis (NICO), or did her pain complaint represent another orofacial pain condition?

EXPLANATION

Review of NICO concepts. Ischemic osteonecrosis (literally "dead bone from poor blood flow") is a condition reported in the orthopedic literature as not being a true bone disease. Instead, researchers believe it is a result of systemic and local disorders or events that ultimately lead to ischemia and infarction of bone marrow, bone or both.[1,2] Proponents of NICO have extended similar concepts to the maxillofacial region with the claim that osteonecrosis can occur in the maxilla and mandible as a result of trauma and infection. For example, Bouquot and McMahon[3] reported that a patient with NICO might have experienced pulpal, periodontal or sinus infections; undergone tooth extractions, endodontic procedures or periodontal surgeries; experienced blows to the facial region; received vasoconstrictors during procedures involving administration of local anesthetics; or a combination of these.

In the 1840s, Bond[4] explored concepts related to maxillofacial osteonecrosis, which Noel[5] later termed "bone caries." Other practitioners have used terms such as "bone cavities" to describe conditions associated with bone destruction, but without inflammatory signs.[6-8] These bone cavities often were located in old extraction sites and were accompanied by neuralgialike pain.[6-8] Ratner and colleagues[9] expanded this concept by reporting that these lesions usually were not detectable radiographically and that the eti-

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ology was an infectious process. Bouquot and colleagues[10] introduced the term "NICO" to describe a low-grade osteomyelitis of the jaws, characterized by bone cavities and associated with orofacial neuralgia.

More recently, researchers have described NICO as a nonsuppurative osteomyelitis secondary to bone marrow ischemia and associated with hereditary coagulopathies, acquired coagulopathies or both.[3] Several authors[11-14] expanded this description to include autoimmune concepts on the basis of antibodies to peripheral nerve myelin, as well as on the presence of anticardiolipin antibodies, thrombophilia (that is, an increased tendency to form blood clots) and hypofibrinolysis (that is, a decreased ability to dissolve clots as they form).

Clinical and radiographic features of NICO. The prevalence of NICO is unknown; however, Ratner and colleagues[15] reported that 800 patients met their criteria across a nine-year period. Study results indicate a 3:1 female to male predominance among patients aged 35 through 60 years (80 percent of cases reported).[16,17] Bouquot and McMahon[3] reported that patients suspected of having NICO often have difficulty describing and localizing the pain, which may spread locally across time or refer to distant sites. This pain is purported to be due to intraosseous fluid dynamics and inflammatory mediators rather than to damaged nerves.[3] This condition usually is not visible on radiographs, although advocates report seeing a regional osteoporotic lesion or an ill-defined radiolucency on radiographs of old extraction sites.[18] Bouquot and McMahon[3] reported that approximately 60 percent of the lesions exhibit hot spots on bone scans as a result of increased uptake of a radioactive isotope (technetium 99m).

The existence of neuralgia-inducing cavitational osteonecrosis as a distinct disease entity is controversial.

CLINICAL IMPLICATIONS

Proponents of NICO often begin treating patients by prescribing antibiotics that may diminish symptoms temporarily; however, the pain typically returns while the patient is receiving antibiotic treatment or after completion of treatment. Usually, a surgical approach involving bone decortication, curettage of the "diseased" bone marrow or both is recommended.[17] Pain relief may take several months to occur, if it occurs at all. The pain has a strong tendency to recur or to develop in additional sites, leading advocates of NICO to suggest repeated surgical procedures at the same site or at other involved areas. Bouquot and Christian[17] described a case report of a patient who underwent surgical curettage 32 times.

The existence of NICO as a distinct disease entity is controversial. No precise and widely accepted definition exists, and epidemiologic evidence of this condition is lacking.[19] Goldstein and Epstein[20] commented that the etiology and pathogenesis of NICO are based on anecdotal case reports (or case series), with analysis coming mainly from one laboratory without corroborative biochemical, histopathologic or neuropathologic findings. In addition, reproducible and diagnosable clinical features are lacking. Furthermore, it appears that the majority of published reports regarding NICO are based on descriptive series of observations that lack proper methodological approaches, control groups or statistical analysis.[21] Finally, the number of invasive surgical procedures performed in patients with NICO raises many questions about the validity of this diagnosis, as well as about the proposed treatment.

Experts in bone metabolism and pathology have postulated that bone cavitations represent normal anatomical marrow spaces (inappropriately diagnosed as disease by NICO proponents) that are found routinely on computed tomographic scans of adults, especially in surgical sites located in the posterior regions of the jaws.[22] These intrabony changes are part of a normal physiological process in which hematopoietic elements are replaced by fatty deposits in women at about 40 years of age as a result of menopause and osteoporosis. Also, mature bone contains so-called oil cysts, which are not true cysts but chemical products of normal adipose tissue representing part of the biochemical makeup of bone marrow.[22]

Therefore, the etiology, pathogenesis and treatment of NICO are speculative and not well defined, and the reported bone changes may represent variations of normal changes. As a result, one can argue that the symptoms of chronic pain attributed to NICO are better explained by established concepts of neuropathic pain; thus, they should be approached medically and not managed surgically.

CONCLUSION

Without a confirmed clinical diagnosis of localized bone pathosis, aggressive and invasive procedures are not warranted. Such interventions

may have no effect or may even worsen the pain by increasing sensitization of the central nervous system. In the case described above, the dentist must consider the probable diagnosis of neuropathic pain[23-25] and initiate the appropriate evidence-based management strategies for that type of pain.[26] Prudent clinicians will refer such patients to practitioners who have specific training and knowledge in the fields of oral medicine and orofacial pain so that the diagnosis can be confirmed. This will lead to appropriate therapy and avoidance of treatments that may be ineffective or that may aggravate chronic pain complaints. ■

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1. Assouline-Dayan Y, Chang C, Greenspan A, Shoenfeld Y, Gershwin ME. Pathogenesis and natural history of osteonecrosis. Semin Arthritis Rheum 2002;32(2):94-124.
2. Lavernia CJ, Sierra RJ, Grieco FR. Osteonecrosis of the femoral head. J Am Acad Orthop Surg 1999;7(4):250-261.
3. Bouquot JE, McMahon RE. Neuropathic pain in maxillofacial osteonecrosis. J Oral Maxillofac Surg 2000;58(9):1003-1020.
4. Bond TE. A Practical Treatise on Dental Medicine. 2nd ed. Philadelphia: Lindsay and Blakiston; 1848:139-148.
5. Noel HR. A lecture on caries and necrosis of bone. Am J Dent Sci 1868;1(series 3):425, 482.
6. Barrett WC. Oral Pathology and Practice. Philadelphia: S.S. White Dental Mfg.; 1898.
7. Black GV. A Work on Special Dental Pathology. 2nd ed. Chicago: Medico-Dental Publishing; 1915:388-391.
8. Box RM. Post-extraction oral sepsis. Ontario Dent J Oct/Nov 1955:1-8.
9. Ratner EJ, Person P, Kleinman DJ, Shklar G, Socransky SS. Jawbone cavities and trigeminal and atypical facial neuralgias. Oral Surg Oral Med Oral Pathol 1979;48(1):3-20.
10. Bouquot JE, Roberts AM, Person P, Christian J. Neuralgia-inducing cavitational osteonecrosis (NICO): osteomyelitis in 224 jawbone samples from patients with facial neuralgia. Oral Surg Oral Med Oral Pathol 1992;73(3):307-319; discussion 319-320.
11. Glueck CJ, McMahon RE, Bouquot J, et al. Thrombophilia, hypofibrinolysis, and alveolar osteonecrosis of the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;81(5):557-566.
12. Gruppo R, Glueck CJ, McMahon RE, et al. The pathophysiology of alveolar osteonecrosis of the jaw: anticardiolipin antibodies, thrombophilia, and hypofibrinolysis. J Lab Clin Med 1996;127(5): 481-488.
13. McMahon R, Bouquot J, Mahan P, Saxen M. Elevated anti-myelin antibodies in patients with maxillofacial osteonecrosis (NICO) (abstract). J Oral Pathol Med 1998;27:345-346.
14. Glueck CJ, McMahon RE, Bouquot JE, Khan NA, Wang P. T-786C polymorphism of the endothelial nitric oxide synthase gene and neuralgia-inducing cavitational osteonecrosis of the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109(4):548-553.
15. Ratner EJ, Langer B, Evins ML. Alveolar cavitational osteopathosis: manifestations of an infectious process and its implication in the causation of chronic pain (published correction appears in J Periodontol 1987;58[2]:77). J Periodontol 1986;57(10):593-603.
16. Roberts AM, Person P. Etiology and treatment of idiopathic trigeminal and atypical facial neuralgias. Oral Surg Oral Med Oral Pathol 1979;48(4):298-308.
17. Bouquot JE, Christian J. Long-term effects of jawbone curettage on the pain of facial neuralgia. J Oral Maxillofac Surg 1995;53(4):387-397; discussion 97-99.
18. Bouquot JE, LaMarche MG. Ischemic osteonecrosis under fixed partial denture pontics: radiographic and microscopic features in 38 patients with chronic pain. J Prosthet Dent 1999;81(2):148-158.
19. Sciubba JJ. Neuralgia-inducing cavitational osteonecrosis: a status report. Oral Dis 2009;15(5):309-312.
20. Goldstein BH, Epstein JB. Unconventional dentistry, part IV: unconventional dental practices and products. J Can Dent Assoc 2000;66(10):564-568.
21. Zuniga JR. Challenging the neuralgia-inducing cavitational osteonecrosis concept. J Oral Maxillofac Surg 2000;58(9):1021-1028.
22. Marx RE, Stern D. Oral and Maxillofacial Pathology: A Rationale for Diagnosis and Treatment. Carol Stream, Ill.: Quintessence; 2003.
23. Horowitz SH. The diagnostic workup of patients with neuropathic pain. Med Clin North Am 2007;91(1):21-30.
24. Cruccu G, Sommer C, Anand P, et al. EFNS guidelines on neuropathic pain assessment: revised 2009. Eur J Neurol 2010;17(8): 1010-1018.
25. Greene CS, Murray GM. Atypical odontalgia: an oral neuropathic pain phenomenon. JADA. In press.
26. Dworkin RH, O'Connor AB, Backonja M, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. Pain 2007;132(3):237-251.