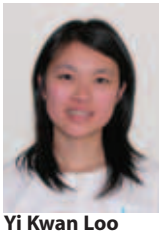

Yi Kwan Loo

Nicotine-Induced Osteonecrosis. A Case Report

Abstract: This paper describes a previously unpublished side-effect of nicotine replacement chewing gum and presents useful information about the effects of nicotine on the oral environment. It is important to consider this when diagnosing an area of ulceration.
Clinical Relevance: Patients who use nicotine chewing gum should be advised that prolonged contact with the alveolar mucosa should be avoided. They should be told that regular chewing helps dispersal of the nicotine.
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Nicotine has a known effect on gingival tissues. This case report describes a 64-year-old gentleman who developed osteonecrosis of the lower left lingual bone associated with lower left third molar (LL8) following placement of nicotine gum in the sulcus over a two week period. Cessation of the gum and careful monitoring led to healing of the lesion with loss of a sequestrum.

Smoking cessation interventions are a cost-effective way of reducing ill health and prolonging life.[1] Nicotine replacement therapy (NRT) is widely recommended to aid smoking cessation, having a success rate of 50–70%[2]. NRT is the pharmacological treatment of choice in the management of smoking cessation.[1] It aims to replace much of the nicotine from cigarettes temporarily, thus reducing the desire to smoke and decreasing withdrawal symptoms. There are many different formulations, such as chewing gum, transdermal patches, lozenges, nasal sprays, oral inhalers and sublingual patches.[1] This report demonstrates a case of osteonecrosis in the lower left lingual sulcus following use of nicotine chewing gum.

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Case report

A 64-year-old Caucasian male was referred by his general dental practitioner to a dental hospital emergency clinic for investigation and treatment of an ulcerated area. His medical history showed nothing abnormal. He drank 8 units of alcohol a week and took daily vitamin C, zinc, cod liver oil, garlic and multivitamin supplements. He had smoked 10–20 cigarettes a day for the last 45 years and wished to stop smoking.

Over the 2 weeks previous to noticing a problem, the gentleman had habitually placed 4 mg Nicorette® (McNeil Healthcare UK Limited) chewing gum in the lower left lingual sulcus. It was left here for 5–6 hour periods as he intermittently chewed the gum if he felt the urge to smoke. He had used the gum for 2 weeks and felt that it was helping him reduce his habit. In addition to the left lingual sulcus, the patient reported he had also stored the gum in his right lingual sulcus and upper labial sulcus. No areas of ulceration were noted here. He first noticed an anomaly in the lower left lingual sulcus whilst brushing his teeth. At this point there was no pain, although the patient had noticed a necrotic ulcerated area.

Despite cessation of the use of nicotine gum when the ulceration was noted, the area had not healed, and therefore the patient consulted his GDP. Photographs were taken at this appointment (Figure 1) and salt water and chlorhexidine mouthwash and Gengigel® gel (20 ml, Oraldent Ltd) were advised.

Figure 1. Clinical picture of the ulcerated area in the lower left lingual sulcus adjacent to the lower left third molar (LL8).

There was initial resolution over the first five days, however, the patient also experienced a constant pain which radiated to the whole left side of his face during this time. This continued for a week, following which healing appeared to slow.

The patient attended his GDP

Figure 2. Clinical picture of the lower left lingual sulcus after the patient stopped using nicotine gum.

Figure 3. Clinical picture of the occlusal view showing inflammation distal to lower left third molar (LL8).

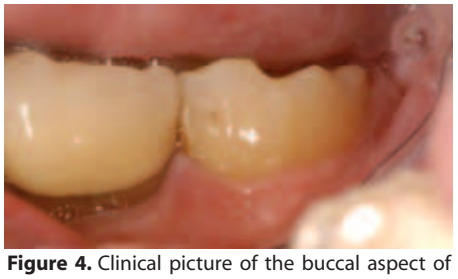

Figure 4. Clinical picture of the buccal aspect of the lower left second and third molar teeth (LL7 and LL8).

for review two weeks later. As healing of the ulceration had not occurred, he was referred to the dental hospital as a matter of urgency. The gentleman attended the emergency department the same day. At this point the ulcerated area was less painful, however, the patient and his wife, a theatre nurse, had concerns that the necrotic area may be a sign of osteomyelitis. Also, the tenderness was preventing him from eating on the left side.

Examination revealed palpable submandibular left lymphadenopathy and general tenderness at the left angle of the mandible. The patient reported that the area had previously been swollen. Intra-oral examination showed a painful necrotic area of maximum 2 cm diameter on the lingual aspect of the lower third molar (LL8) (Figure 2) and a pea-sized swelling distal to the tooth (Figure 3). This swelling was soft and tender. The patient reported that this swelling had previously been larger. The lower left second and third molar teeth (LL7 and LL8) had an undulating gingival margin and previous gingival recession was evident (Figure 4). The gingivae around the lower left second molar (LL7) was also tender. There appeared to be no discharge from the area. In general, the gentlemen had a restored dentition with a good level of oral hygiene.

Treatment

At the initial consultation, advice regarding the likely aetiology was explained to the patient. The patient was warned that sequestra may form. Chlorhexidine gel (1%) was prescribed for topical placement at the affected area and review arranged. At the review appointment, healing had occurred. However, the prognosis of the lower left third molar may have been reduced as the patient reported loss of a sequestrum as shown in Figures 5 and 6. The sequestrum measured 10 mm by 4 mm.

Discussion

The case suggests that osteonecrosis can be induced by nicotine chewing gum. Nicotine medicated chewing gum such as *Nicorette® Gum, Nicorette® Plus Gum, Nicotinel®l Gum, Nicotinel®l Plus Gum, NiQuitin® CQ Gum, Boots Nicotine Gum* is available as 2 mg or 4 mg nicotine formulations. The chewing gum is sugar free, is available in fruit, liquorice and mint flavours and contains nicotine as polacrilin complex. Those who smoke 20 cigarettes or less are advised to chew one 20 mg piece slowly until the taste becomes strong. The gum should then be rested between the gum and cheek until the taste fades, upon which it may be chewed again. This can continue for approximately 30 minutes as and when an urge to smoke occurs. The 4 mg gum is aimed at people who smoke more that 20 cigarettes a day. After 3 months, the gum should be withdrawn gradually. Smoking cessation should be achieved within 9 months and 4 mg gum has been shown to have a significantly greater success than 2 mg gum.[2]

Known side-effects include dry mouth, mouth ulceration, increased salivation, hiccups, throat irritation, oesophagitis, peptic ulcers and gastro-intestinal disturbances. Lozenges have been associated with thirst, paraesthesia of the mouth and taste disturbances[1] and, more recently, hyperkeratosis of the lateral border of the tongue.[3,4] Osteonecrosis, however, has not been noted.

The release and thus absorption of nicotine from such gums is difficult to determine as it varies with chewing frequency, distance between the chewing surfaces, the angle at which it is chewed and the mouth temperature.[5] Indeed, subjects have been shown to alter their rate of chewing subconsciously in relation to the amount of nicotine absorbed.[6] Pharmacokinetic analyses demonstrate biphasic release and absorption followed by a slowing of

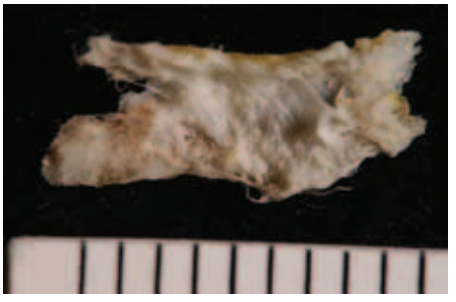

Figure 5. Buccal aspect of bone sequestrum.

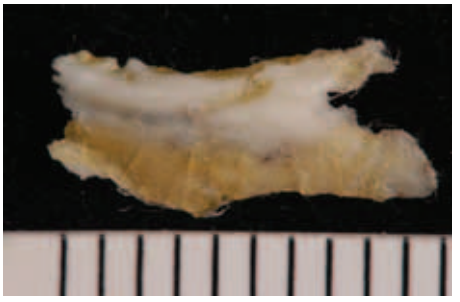

Figure 6. Lingual aspect of bone sequestrum.

release and absorption.[7]

Osteonecrosis is the process of bone death.[8] There are a number of known causes, such as radiotherapy, surgical and local trauma, apical or periodontal sepsis, Paget's disease, phosphorus exposure, haemoglobinopathies and lymphoproliferative disorders.[9] Bisphosphonates have also been recently implicated. Similar symptoms have been reported in cocaine traffickers as purity testing in the lingual sulcus causes decreased vascularity.

Nicotine has been shown to cause tissue destruction and impair bone healing.[10] It is vasoconstrictive and impairs angiogenesis,[11] thus impairing local blood flow vital to healing.[10,12,13] It also increases collagenase activity in gingival fibroblast cultures, reduces collagen production[14] and stimulates osteoclastic differentiation.[15] Nicotine has also been shown to bind to the root surfaces of smokers,[16] altering gingival[17] and periodontal ligament fibroblast attachment and proliferation *in vitro*.[18–21] It increases cytokine levels in response to lipopolysaccharide from *Aggregatibacter actinomycetemcomitans* and thus it may have a role in periodontal disease[22] owing to the inhibition of the expression of growth factors.[23]

Summary

Dentists are often presented with ulceration. This case report suggests that dentists should ask if patients use nicotine-containing gum if an ulcerated area is identified, as there may be periodontal consequences. Furthermore, patients using such gum should prevent the gum having prolonged contact with the oral mucosa by avoiding 'storage' of the gum in specific sites in the mouth.

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