NECROTIZING SIALOMETAPLASIA

Definition

Necrotizing sialometaplasia was first described in 1973 by Abrams, Melrose and Howell and a further five cases were reported the following year by Dunlap and Barker. It is a rare, self limiting, variably ulcerated, benign, inflammatory process, predominantly affecting salivary tissue. The importance of the lesion is that it may be mistaken for a malignancy and lead to inappropriately radical surgery. A famous dignitary, President Clevelend of the United States of America, may have suffered from this disease. The entity is classified under “tumour-like” in the WHO Classification of tumours of the salivary glands.

Epidemiology

Necrotizing sailometaplasia is extremely rare: there are barely 200 cases reported in the world literature.

Mean age of occurrence in men is about 50 years and 36 years in women. The youngest reported case is 15 years. There appears to be an increased incidence in males. A preponderance for Caucasians reported by Lynch et al (1979) was thought to be spurious, but in Brannon’s series of 69 cases compared to 115 in the literature in 1991, there was a 5:1 preponderence of Caucasians over Afro-Carribeans.

The vast majority (80%) of cases affect the minor salivary glands of the palate, while other sites include retro-molar pad, gingiva, lip, tongue and cheek. The condition has also been reported in major salivary glands. A sub-acute variant has also been described.

Clinical Presentation

Clinically, patients present with a rapidly-growing swelling, which may (or may not) ulcerate, usually in the palate. Ulceration does not occur in the sub-acute variant which has been described. A purulent exudate may be an early feature at the site of the lesion. Pain may also be a feature at the onset and may be intense and referral of the pain to the ear, eye and pharynx are variable features which have been reported. However, development of the lesion may be painless and there are even reports of anaesthesia of the greater palatine nerve as the presenting feature. This is thought to be caused by involvement of the vasa nervorum in the vasculitic aetiological process. The lesions may

occur bilaterally and metachronously. When ulceration occurs, it usually remains superficial, but a single case of full-thickness necrosis of the palate has been reported. The lesion heals spontaneously over a period of two to twelve weeks. Drug therapy with intra-lesional steroids appears to offer no benefit on recovery time of the lesion or associated anaesthesia.

A sub-acute variant of the condition has been described in which the lesions are usually painful, ulceration is not present and histopathology demonstrates a sub-acute inflammatory infiltrate. However, these cases may simply represent one end of a spectrum of disease.

Differential diagnosis of an ulcer presenting with these features could include: direct traumatic ulceration, major aphthous ulceration, syphilis, tuberculosis, deep mycosis, agranulocytosis, neutropaenia and nicorandil-induced oral ulceration. The most important differential diagnosis, is malignancy, in particular squamous cell carcinoma, low-grade mucoepidermoid carcinoma and oncocytic malignancies.

Rarely, the condition has also been reported at extra- salivary sites, which include: the nose, nasopharynx, trachea, larynx and lung. At extra-salivary sites, the lesion may be described as adenometaplasia. A similar lesion occurs in the skin termed syringometaplasia, and similar histopathological appearances have been described in the breast following trauma.

Aetiopathogenesis:

Although the aetiopathogenesis of necrotizing sialometaplasia remains unknown there is general consensus that an ischaemic event in the salivary gland precedes the development of the lesion. In experimental models, ligation of the arterial supply to major salivary glands in rodents may result in a similar histopathological picture and similar lesions may also occur spontaneously in dogs and experimentally in rabbits and rats. The disease has been reported in patients with sickle cell disease, where infarction may be a feature in crisis, Buerger’s disease and Raynaud’s phenomenon, vasculopathies which both predispose to ischaemia. It has been suggested that necrotizing sailometaplasia of the palate may represent an ulcerative or necrotizing stage of leukokeratosis nicotina palate, although this now seems unlikely.

Other predisposing factors in which ischaemia may play a part include: smoking (and alcohol), vascular damage due to trauma, hot food, intubation, fellatio, bronchoscopy, local anaesthetic injection and recurrent vomiting. Addition of a vasoconstrictor to local

anaesthetic solutions, local radiotherapy, cocaine use, pressure from local space occupying lesions and surgery have also been implicated. The lesion may be more florid in pregnancy.

There may be an association with other tumours, specifically: Warthin's tumour, Abrisokov's tumour, carcinoma of the lip, rapidly growing mesenchymal malignancy and salivary gland tumours. There is also an association with preceding upper respiratory tract infection within the previous few weeks, particularly acute on chronic sinusitis and allergy. It is possible that the ischaemic event in these cases is due to immune complex disease, similar to the aetiology of erythema multiforme or benign trigeminal sensory neuropathy.

Histopathology

The histopathological features and differential diagnosis of necrotizing sialometaplasia have been reviewed by many authors since the original description by Abrams Melrose and Howell in 1973.

The condition is characterized histopathologically by ischaemic lobular necrosis of sero-mucinous glands with maintenance of intact lobular architecture despite coagulative necrosis of the mucinous acini. Pale acinar outlines often persist, but the nuclei are hypochromatic or absent. Mucin extravasation into the adjacent tissues evokes an inflammatory reaction dominated by histiocytes and granulation tissue. Within the necrotic lobules the inflammatory component is often minimal, but is usually prominent in the surrounding tissues. Although squamous metaplasia of ducts and acini is a feature, (which complicates the diagnosis due to similarity to malignancy) the metaplastic cells have benign nuclear morphology, with minimal pleomorphism or hyperchromatism and few mitotic figures. Nests of squamous epithelium usually with a smooth periphery may be seen, which occasionally have an irregular outline. Pseudoepitheliomatous hyperplasia, where the overlying or adjacent epithelium is often markedly hyperplastic with thick elongated and complex rete processes, along with extensive ductal metaplasia may resemble epithelial malignancy and in the past, misdiagnosis may have let to inappropriate radical ablative surgery. It may be very difficult to distinguish necrotizing sialometaplasia from squamous cell carcinoma, low-grade mucoepidermoid carcinoma and oncocytic tumours.

Specific histopathological features may have some relation to the age of the lesion at biopsy. Coagulative necrosis is a more dominant feature in the early lesions, whereas

fibrosis and squamous metaplasia are features of an older lesion. Anneroth and Hansen suggested that the following five stages occur in most cases: infarction, sequestration, ulceration, repair and healing.

Management

The usual management of this condition is simple observation until the healing phase is complete. Necrotizing sialometaplasia may occur de novo, after trauma or a surgical procedure or in association with another lesions, either benign or malignant.
Because of the latter, whenever the diagnosis of necrotizing sialometaplasia is made, close follow up is indicated until healing is complete. Recognition of the histological picture and the varied clinical settings in which necrotizing sialometaplasia can be found is essential, to avoid histopathological misinterpretation and inappropriate treatment for this benign reactive condition. The prognosis is excellent, once the correct diagnosis is made. There are no known preventative strategies.

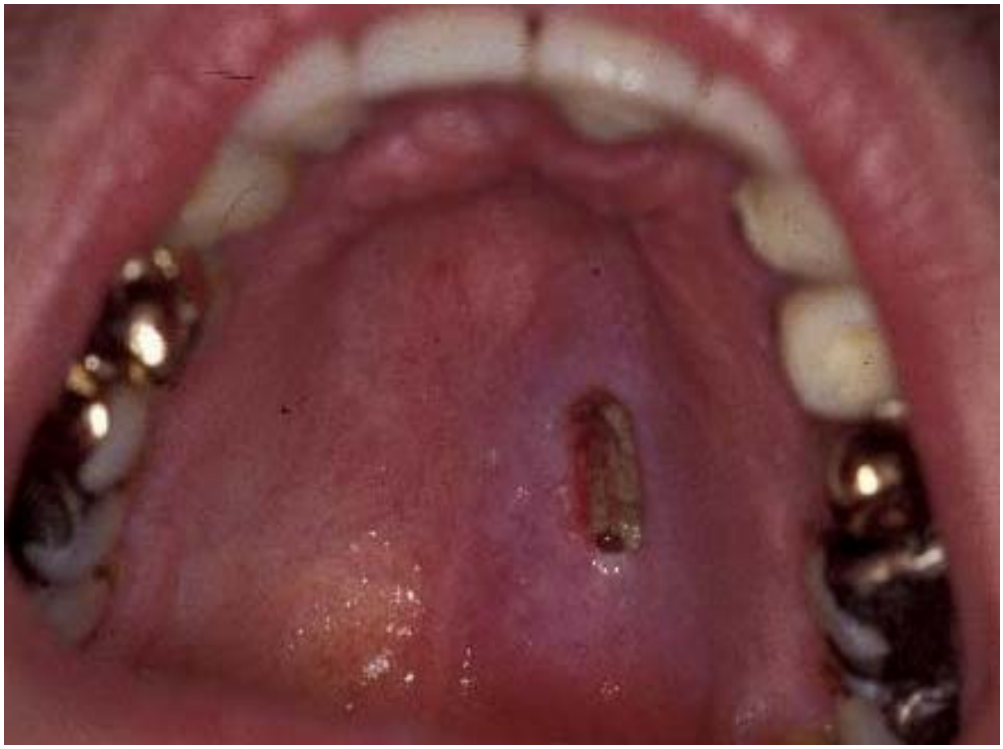

Figure 1. Necrotizing sialometaplasia at the typical site. The ulceration is full-thickness, deep and there has been involvement and exposure of the underlying bone.

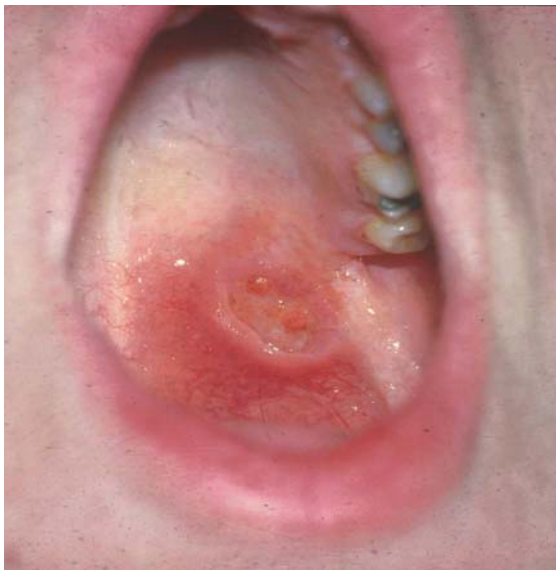

Figure 2. This lesion is more superficial. The clinical similarity to squamous cell carcinoma is obvious. Note, however, the surrounding inflammatory erythema.

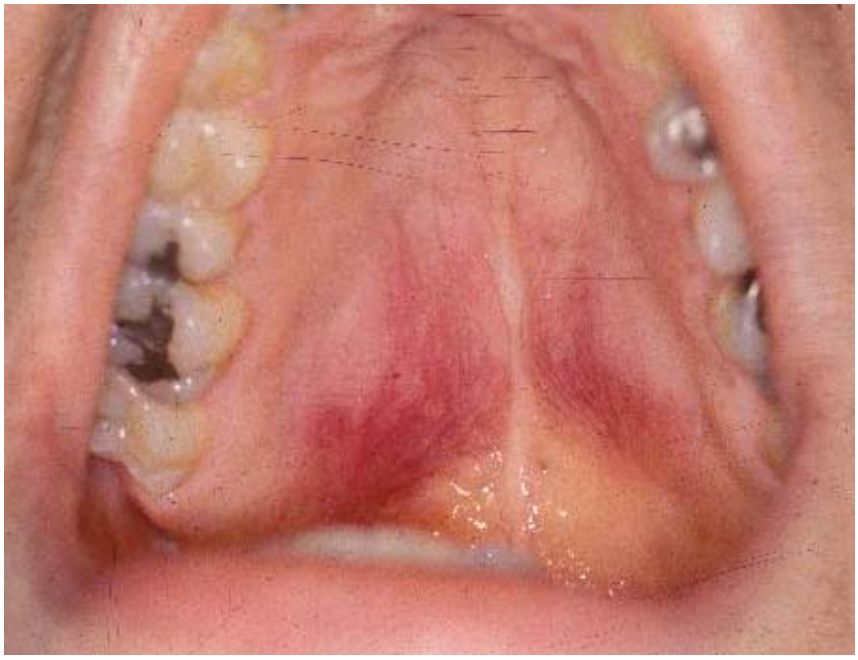

Figure 3. The sub-acute variant, unusually occurring bilaterally (note erythema also). Biopsy confirmed necrotizing sialometaplasia, but the lesions did not ulcerate.

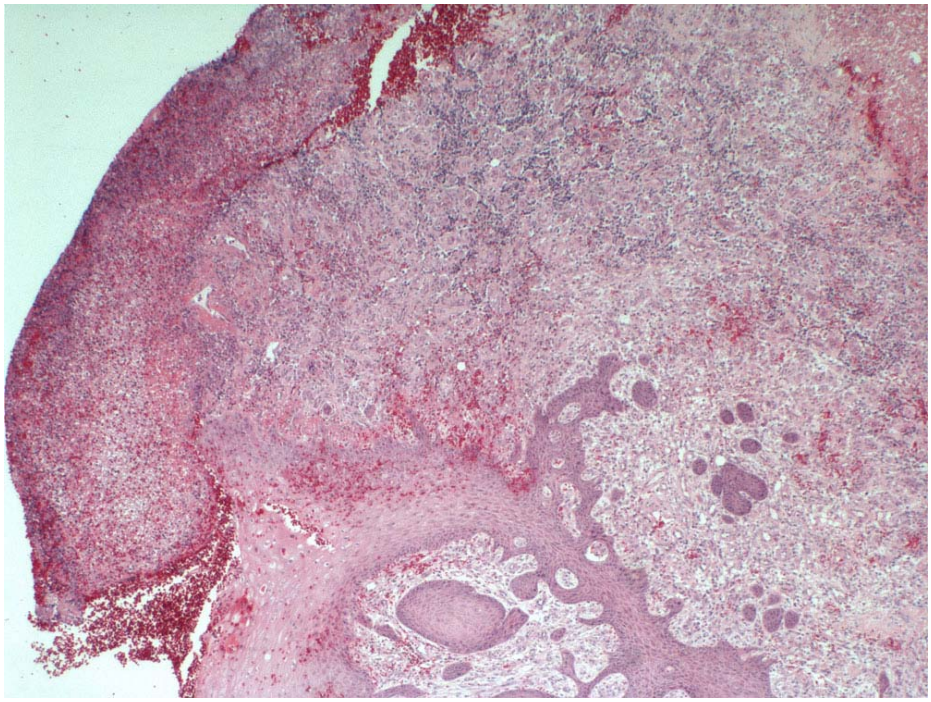

Figure 4. Ulcerated lesion with squamous proliferation at edge of ulcer.

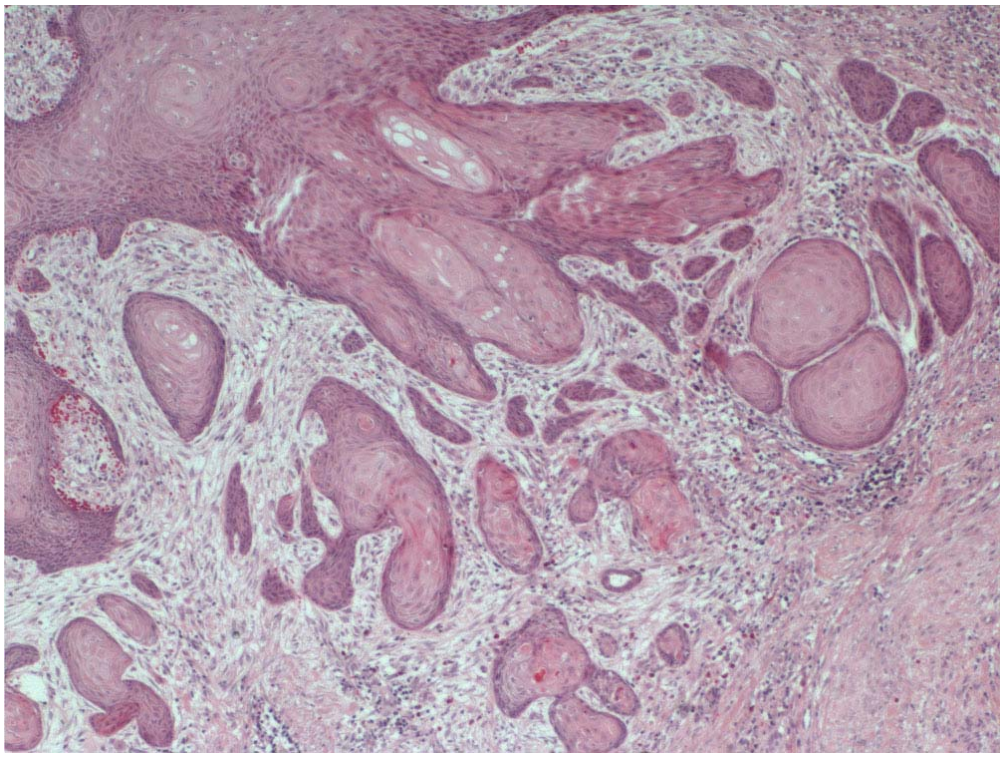

Figure 5. Note extent and worrying complex architecture of squamous proliferation.

Further reading

1. Abrams AM, Melrose RJ, Howell FV. Necrotizing sialometaplasia. A disease simulating malignancy. Cancer 1973; 32:130-5
2. Brannon RB, Fowler CB, Hartman KS. Necrotizing sialometaplasia. A clinicopathologic study of sixty-nine cases and review of the literature. Oral Surg Oral Med Oral Pathol 1991; 72:317-25
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4. Keogh PV, O'Regan E, Toner M, Flint S. Necrotizing sialometaplasia: an unusual bilateral presentation associated with antecedent anaesthesia and lack of response to intralesional steroids. Case report and review of the literature. Br Dent J 2004; 196:79-81
5. van der Waal JE, van der Waal I. Necrotizing sialometaplasia: report of 12 new cases. Br J Oral Maxillofac Surg 1990; 28:326-8