CASE REPORT

Bilateral necrotising sialometaplasia

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SUMMARY

Necrotising sialometaplasia is a benign, necrotising, self-healing inflammatory condition categorised as idiopathic disease of salivary glands. This condition holds diagnostic importance because of its clinical and histopathological presentation, which is ambiguous, and can be misdiagnosed as carcinoma particularly squamous cell carcinoma or mucoepidermoid carcinoma. This report describes a case of bilateral necrotising sialometaplasia occurring in a 38-year-old male patient.

BACKGROUND

First reported by Abrams *et al*,² necrotising sialometaplasia (NS) is a benign, necrotising inflammatory disease which resembles malignancy clinically and histopathologically. According to Mesa *et al*¹ it represents <1% of all the biopsied oral lesions, an incidence of 0.03% based on findings in 10 000 oral biopsy specimens. Its resemblance to malignancy clinically and histopathologically warrants an unnecessary clinical approach which can be avoided with greater familiarity with the disease's clinical and pathological features.²

This rare disorder, classified under the group of tumour-like lesion by the WHO, predominantly affects men and could occur in any age group ranging from 17 to 80 years with a mean age of 50 years in men and 36 years in women.³ NS involves the minor salivary glands, most commonly of the hard palate. Vast majority of palatal lesions arise spontaneously whereas most extrapalatal lesions appear postoperatively or after trauma or radiation therapy. Up to 10% of cases have been reported in major salivary glands.⁴ The NS presents commonly as an ulcer on the palate. The location and clinical appearance may simulate malignancy. Palate involvement usually appears as a single, unilateral ulcer on the posterior hard palate or at the junction of the hard and soft palates. Lesions may be ulcerated crater like, with raised erythematous borders. Deep ulcers covered with necrotic slough are also a clinical presentation.⁵ Among the extrasalivary gland tissues, the lungs, breast and skin are involved and these lesions were designated as adenometaplasia. Skin involvement was termed as syringometaplasia or metaplasia of sweat ducts.⁶ Described here is a case report of NS in a 38-year-old man presenting as palatal ulcers.

CASE PRESENTATION

A male patient aged 38 years presented with the symptom of ulcers on both sides of the palate since 1 week. The history of present illness reported that it started as an asymptomatic swelling about

9–10 days back which turned into ulcers within 2 days. His medical and dental histories were non-contributory. No adverse habits were practised by the patient. On intraoral examination, there were two ulcerative lesions opposite to teeth #16 and #26 on either side of mid-palatine raphe (figure 1A). The ulcers were roughly oval in shape measuring about 11 mm in diameter with raised borders, covered with necrotic slough surrounded by a keratotic halo and non-tender on palpation (figure 1B, C). A working diagnosis of NS was considered.

INVESTIGATIONS

As the patient presented with ulcers clinically, infectious, immunological and metabolic diseases should be excluded. A complete haemogram was thus advised, the results of which would be suggestive of a definitive diagnosis. A complete haemogram was performed and all the values were within the normal range and venereal disease research laboratory (VDRL) test was non-reactive. These results exclude an infective, immunological and metabolic aetiology of the ulcers. An incisional biopsy was carried out on right side and sent for histopathological examination. On histopathological examination, stratified squamous parakeratinised epithelium exhibited pseudoeitheliomatous hyperplasia and connective tissue with duct-like structures and salivary gland acini was

Figure 1 Clinical intraoral examination revealed bilateral ulcerative lesions on the palate (A). Ulcers presented with raised borders and keratotic halo (B, C). Site of biopsy was from the left side palate (D). The lesion healed spontaneously and uneventfully (E, F).

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evident (figure 2A). Higher magnification shows squamous metaplasia of the duct lining cells (figure 2B). Epithelial islands in connective tissue exhibit no cytological atypia and the glandular acini have a benign morphology. Inflammatory cells were found in the intervening connective tissue stroma (figure 2C).

DIFFERENTIAL DIAGNOSIS

The clinical differential diagnosis of ulcer of traumatic, inflammatory, infectious processes and malignant neoplasms were considered. Clinical details such as the course (acute or chronic), symptoms (pain or no pain) and patient's background with eating disorders (EDs) and depression were documented. On the basis of clinical and haematological findings, a differential diagnosis of non-specific or malignant ulcer was considered.

TREATMENT

The lesion was self-healing and healed uneventfully (figure 1D, E).

OUTCOME AND FOLLOW-UP

The patient was called after 1 month and complete healing of the lesions had occurred (figure 1F). Based on clinical and histopathological features (figure 2), a final diagnosis of 'bilateral NS' was given.

DISCUSSION

NS is a benign, self-limiting disease of salivary glands, more commonly minor salivary glands often mistaken for a malignant neoplasm, such as mucoepidermoid carcinoma, as well as invasive squamous cell carcinoma. It is a disease of unknown pathogenesis; however, ischaemia is regarded as a major cause.⁷ Aetiological factors for ischaemia can be direct trauma, administration of local anaesthetics, ill-fitting dentures, alcohol,

smoking and cocaine use, radiation, intubation and surgical procedures, and upper respiratory infections. Bulimia has also been recognised as an aetiology of NS. In the literature review, most cases of NS associated with bulimia were white women and presented with ulcers of hard palate.⁵ Iatrogenic NS, which accounts for most of the major salivary glands and extrapalatal minor salivary glands, appears to be primarily, if not exclusively a vascular-based lesion.³

Histologically, the course of the disease can be divided into five stages: infarction, sequestration, ulceration, repair and healing. The stages can overlap and are dependent on the extent and severity of damage.⁸ The key features for histopathological diagnosis include pseudoepitheliomatous hyperplasia, squamous metaplasia of ducts and acini, preservation of lobular architecture, lobular infarction with or without mucin spillage and inflammation secondary to extravasation of mucin.⁹ The necrotic lobules are composed of small acini-sized pools of mucin that are surrounded by thin, necrotic septa and are frequently ringed by neutrophils.¹⁰ Mucin pools may coalesce and extend into the adjacent tissue and may elicit an inflammatory reaction. Granulation tissue may be prominent at the necrotic areas and near the ulcers.³ It has been reported that histological features may have some relation to the age of the lesion. Coagulative necrosis is a more dominant feature in the early lesions, whereas fibrosis and squamous metaplasia are features of an older lesion.¹¹

Any non-healing palatal ulcer in an adolescent or young adult patient with clinical signs of bulimia has to have NS foremost in the list of differential diagnoses.¹²

NS resembles squamous cell carcinoma histologically as the overlying epithelium is markedly hyperplastic and gives the appearance of pseudoepitheliomatous hyperplasia. But the

Figure 2 The photomicrograph of H&E stained section showing epithelium with pseudoepitheliomatous hyperplasia (A). Benign, squamous metaplasia of ductal and acinar elements and preservation of lobular architecture was evident (B, C).

squamous nests in connective tissue have a smooth, non-infiltrative periphery and the metaplastic cells have minimum pleomorphism and hyperchromatism. These histopathological features enable differentiation between the two lesions.⁹ Some nests may contain residual mucous cells and may lead to erroneous appearance of mucoepidermoid carcinoma.²

In the present case, clinically, the lesions are bilateral symmetrical and are very unlikely to occur in malignant neoplasms. Some metaplastic nests are composed of basaloid cells with hyperchromatic nuclei. Active regeneration and metaplasia in areas of necrosis may be associated with nuclear enlargement, prominent nucleoli, frequent mitotic figures and necrosis of either individual cells or groups of cells may be seen. When small biopsy specimen that include only these areas are sent of histopathology, these features may present a diagnostic challenge.³ Thus, it is mandatory to include these malignancies in the differential diagnosis.

Among the differential diagnosis, as aforementioned, squamous cell carcinoma and mucoepidermoid carcinoma hold importance. Any suspected lesion should be submitted for histopathology to prevent any unnecessary surgical procedure. Proper habit history, dental and medical history from the patient is obligatory. Differentiating features histopathologically include maintenance of lobular architecture, lobular infarction and completely or partially necrotic salivary gland lobules intermixed with metaplastic lobules in NS. Furthermore, NS lacks cystic spaces lined by mucous cells that are usually seen in mucoepidermoid carcinoma.¹³

Other features such as generalised bland appearance of squamous cell, the presence of residual glandular lumina in metaplastic nests and extraglandular mucin pools are also distinguishing features. Nicotinic stomatitis, associated with cigar and pipe smoking, has a quite similar histological and clinical presentation. It tends to be multifocal and grossly more punctate, with multiple foci localised to the palate.⁵ These latter lesions are not considered preneoplastic and resolve on cessation of smoking.

Opportunistic infections are common in patients with poorly controlled diabetes and may mimic NS. Clinically, deep ulcer of NS can be confused with granulomatous inflammatory diseases such as syphilitic ulcer and deep mycosis, which may show a sharp demarcation. With regard to syphilis, serological testing will rule it out and tuberculous ulcer is painful which is associated with characteristic general symptoms of diseases such as fatigue, slight fever and cough.¹⁴ However, the ulcer of syphilis is usually seen in the tertiary stage of syphilis that may present as a clean surfaced ulcer with perforation of the palate, a feature untypical of NS.¹⁵

Invasive fungal infections such as aspergillosis of the oral cavity are a rare form and typically present as a necrotic ulcer in immunocompromised patients, such as chemotherapy-induced granulocytopenia or AIDS.¹⁶

Another lesion which should be histopathologically differentiated from NS is subacute necrotising sialadenitis (SANS). SANS clinically presents as a non-ulcerated nodular lesion on the palate usually associated with abrupt onset of pain. Histologically it is characterised by focal acinar cell necrosis secondary to the inflammatory process and slight atrophy of ductal cells; neither ductal squamous metaplasia nor pseudoepitheliomatous hyperplasia is observed in SANS.⁷

Wegener granulomatosis is an autoimmune disease characterised by systemic vasculitis of small arteries and veins seen in the head and neck area as rhinitis and sinusitis, accompanied by

cough and haemoptysis. This lesion occurs on oral mucosa as a granular erythematous gingiva and exceptionally as a palatal ulcer.¹⁷

In addition to above oral lesions, NS is considered as a rare but increasingly associated with complication of EDs which has been reported in recent times.^{7 18 19} The complications of EDs include dental erosion, caries, decreased salivary flow, periodontal diseases, atrophic mucosa and sialosis.¹⁹

The present case had reported with bilateral palatal ulcers with raised margins and covered with necrotic slough. Granulomatous ulcer and malignant ulcers were considered among the differential diagnosis. The haemogram was within normal limits and VDRL was negative for syphilis. Histopathologically, the features were benign and were consistent with NS. No predisposing factors were associated with the present case. The lesion healed spontaneously and no recurrence followed.

Similar to the case presentation aforementioned, other reports of NS bilaterally on the palate have been described in the literature. In a case report by Johann and colleagues in 2006, a similar case of bilateral palatal ulceration was described in which the patient smoked and consumed alcohol heavily. The authors suggested that these habits may induce arteriosclerosis of the small vessels leading to ischaemia and development of NS.²⁰ A case of bilateral palatal ulceration in a female patient with bulimia has been reported. Mechanical irritation inflicted by the fingers to induce vomiting in patients with bulimia and the chemical irritation due to gastro-oesophageal reflux was considered as the aetiology.⁴ Similarly, Janner and colleagues in 2014 reported such a bilaterally presenting case in woman with bulimia and smoking history. Similar explanation of mechanical irritation was given by the authors for pathogenesis.²¹ However, in the present case, no such aetiological factor has been described as the medical, dental history and habits were all non-contributory.

The diagnosis can be further supplemented via immunohistochemistry demonstrating focal to absent immunoreactivity for p53, low immunoreactivity for MIB-1 and the presence of 4A4/p63 and calponin-positive myoepithelial cells.²² Squamous cell carcinoma is generally negative for CK-7, whereas, benign and reactive salivary gland epithelium is CK-7 positive. While NS is immunoreactive for MIB-1 and p53, the degree and intensity is far greater in squamous cell carcinoma. Similar to the pattern of immunoreactivity with MIB-1, the p53 shows far greater positivity in squamous cell carcinoma, whereas in NS it is faint and scant. Thus, both MIB-1 and p53 can stain positively in either benign or reactive squamous epithelium; labelling is generally more intense and is increased in malignancy, but alone, neither is diagnostic.⁷ Nonetheless, to date, H&E staining remains the gold standard.

CONCLUSION

NS, though rare, is an important disease for the general practitioners and oral pathologists to comprehend, as the disease closely resembles epithelial and salivary gland malignancies clinically and histopathologically. The clinical presentation obligates a biopsy, which when assessed microscopically differentiates this disease (benign, inflammatory, self-healing) from malignancy. Thus, the oral pathologists hold a key position in differentiating this tumour-like lesion from cancer and hence avoid any unnecessary surgical procedure.

Learning points

- ▶ Necrotising sialometaplasia is a benign, self-healing inflammatory disorder categorised as tumour-like lesion by the WHO.
- ▶ Grouped under idiopathic diseases of salivary gland, but a number of predisposing factors have been suggested by various authors over the years.
- ▶ Differential diagnosis of the lesion is important, and is mandatory to carry out a biopsy to rule out malignancies.
- ▶ The diagnosis can be supplemented by immunohistochemistry, but histopathology remains the gold standard.

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