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NECROTIZING SIALOMETAPLASIA: LITERATURE REVIEW AND CASE REPORTS

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The authors describe necrotizing sialometaplasia, a benign inflammatory lesion primarily involving the minor salivary glands of the hard palate. The lesion presents itself as a deep-seated palatal ulcer with clinical and histologic features mimicking those of a malignant neoplasm. The lesion is believed to be the result of vascular ischemia initiated by trauma. An incisional biopsy is required to confirm the diagnosis, and the lesion heals by secondary intention within four to 10 weeks.

Necrotizing sialometaplasia is a benign, self-limiting inflammatory condition manifesting itself mainly as an ulcerative lesion on the palate. Its significance lies in the fact that its clinical and histologic features mimic those of a malignant neoplasm, particularly mucoepidermoid carcinoma or squamous cell carcinoma. In 1973, Abrams and colleagues defined necrotizing sialometaplasia as a reactive necrotizing inflammatory process involving the minor salivary glands of the hard palate. Necrotizing sialometaplasia is most likely the same lesion that Saunders described in 1958 as an ulcerative form of nicotine stomatitis.

The histologic features described by Abrams and colleagues include coagulation necrosis of glandular acini, squamous metaplasia of salivary ductal epithelium, pseudoepitheliomatous hyperplasia of the overlying epithelium and mucous pooling with an associated granulomatous inflammatory response.

In the largest study to date, Brannon and colleagues analyzed the clinicopathologic findings of 69 cases and reviewed the literature on another 115 cases of necrotizing sialometaplasia. The mean age of these patients at diagnosis was 46 years; men outnumbered women by a ratio of nearly 2:1; and whites outnumbered African-Americans by a ratio of nearly 5:1. Seventy-seven percent of these cases involved a deep-seated ulcer on the palate; however, an antecedent swelling or mass was not uncommon.

Other involved sites have included the maxillary sinus, retromolar pad, mandibular lip, tongue, buccal mucosa, mucobuccal fold, tonsillar fossa, nasal cavity, incisive canal, trachea, and larynx. Bony involvement of the hard palate is infrequent, but it does not preclude the diagnosis of necrotizing sialometaplasia. Researchers have also reported involvement of major salivary glands after surgical intervention on the involved gland for unrelated problems. Lesions that are histologically analogous have also been reported in non-neoplastic breast parenchyma.

HISTOLOGIC FEATURES

Anneroth and Hansen clarified the histopathogenesis of necrotizing sialometaplasia by proposing five histologic stages: infarc-
Figure 1. Pathogenesis of necrotizing sialometaplasia is shown. Top left: Necrotic stage. Glandular tissue undergoes necrosis. Surviving glandular acini are evident and an occluded blood vessel is occasionally found. Top right: Sequestration stage. An extensive infarct results in sequestration of the necrotic tissue. Slight elevation of overlying epithelium may correspond to a prodromal symptom of swelling. Bottom left: Ulceration stage. The necrotic glandular tissue is expelled, resulting in an ulcer. Bottom right: Reparative stage. Repair begins with downward growth of the overlying epithelium and metaplasia of the ductal epithelium. (Figures adapted with permission of the publisher from Anneroth and Hansen. Copyright 1982 Munksgaard International Ltd.)
tion, sequestration, ulceration, reparative and healed. It is unusual to observe these well-demarcated stages in any given biopsy specimen. More commonly observed is a spectrum of histologic features that include ulceration, pseudoepitheliomatous hyperplasia, necrotic acini, ductal metaplasia and inflammatory changes. In addition, Brannon and co-workers' described histologic features that included coagulation necrosis of acini in early lesions and squamous metaplasia of ducts and reactive fibrosis in late lesions.

Necrosis of the glandular acini predominates in the infarct stage. An extensive infarct leads to sequestration of the necrotic acini, resulting in an ulceration (Figure 1, top left and right). The ulcer begins to heal via downward proliferation of the overlying epithelium, as evident microscopically by pseudoepitheliomatous hyperplasia (Figure 1, bottom left). However, if the infarct is limited in its extent, sequestration and ulceration do not occur. Healing is accomplished by phagocytic activity of histiocytes and polymorphonuclear neutrophils.

The repair of ductal epithelium and acini by squamous metaplasia with accompanying pseudoepitheliomatous hyperplasia can be confused microscopically with mucoepidermoid carcinoma or squamous cell carcinoma. The repaired lesion of necrotizing sialometaplasia results in a salivary gland with normal lobular architecture, but acini that have undergone metaplastic change and ducts that have been replaced by fibrous connective tissue with an accompanying chronic inflammatory infiltrate (Figure 1, bottom right). Histologically, the healed lesion may resemble chronic salivary lymphadenitis or degenerative age changes.¹⁹

**SYMPTOMS**

Initial symptoms vary and may include fever, chills, malaise or swelling.² Paresthesia or anesthesia of the involved area also has been reported.² More than half of the reported cases of necrotizing metaplasia are painful, although it is not uncommon for patients to have relatively large asymptomatic lesions.³ Palatal lesions can be quite large, averaging 1.8 centimeters in diameter.³ The length of time the lesion remains varies, generally ranging from four to 90 days. In one reported case, the lesion lasted 180 days.³ Necrotizing sialometaplasia heals by secondary intention over four to 10 weeks. The slow healing process is caused by the size of the lesion rather than the inherent nature of the condition. The dentist should closely follow up the patient until healing is complete.

The following case reports describe four patients who received diagnoses of necrotizing sialometaplasia.

**CASE ONE**

A 27-year-old woman fearing that she had a malignant lesion went to her dentist for evaluation of an ulcer on her right posterior palate. The ulcer measured 20 millimeters in length by 10 mm in diameter (Figure 2).
The lesion had been present for approximately three weeks and was asymptomatic; however, the patient described her maxillary molars as feeling “numb.”

The base of the ulcer was covered with necrotic debris and rested on palatal bone. The patient did not smoke; however, she did occasionally consume alcohol. She was unable to recall any prodromal symptoms, an antecedent swelling or trauma to the area. However, she volunteered the fact that she had performed several acts of fellatio.

The initial differential diagnosis included mucoepidermoid carcinoma, adenoid cystic carcinoma, squamous cell carcinoma, tuberculosis, tertiary syphilis and necrotizing sialometaplasia. Serologic test findings for syphilis and tuberculosis were negative.

An oral surgeon performed an incisional biopsy on the peripheral margin of the ulcer, without complications. Special staining for fungi, acid-fast bacilli and bacteria were negative. Microscopic examination of the tissue demonstrated a fibrinopurulent exudate and pseudoepitheliomatous hyperplasia at the surface of the ulcer. The base of the ulcer contained reactive fibrous tissue and pools of mucin. The key histologic feature present at the base of the ulcer was squamous metaplasia of the salivary ductal epithelium (Figure 3). There was no evidence of neoplastic changes.

The microscopic evidence supported a diagnosis of necrotizing sialometaplasia. The histologic features of pseudoepitheliomatous hyperplasia, reactive fibrosis and squamous metaplasia of salivary ductal epithelium indicated that the lesion was in the reparative stage, as proposed by Anneroth and Hansen. Similarly, these histologic features corresponded to a late-stage necrotizing sialometaplasia, as described by Brannon and co-workers. The patient was informed of the diagnosis, which alleviated her fear of cancer. The lesion healed within 10 weeks by secondary intention with no deformity or sequelae.

**CASE TWO**

A 55-year-old woman complained to her dentist of multiple asymptomatic ulcers on her soft palate beneath an “ill-fitting” maxillary complete denture (Figure 4). A biopsy specimen of the largest ulcer demonstrated acinar necrosis and squamous metaplasia of the salivary ductal epithelium (Figure 5). The histologic features were consistent with a diagnosis of necrotizing sialometaplasia. The ulcers healed within eight weeks without any deformity.

**CASE THREE**

A 49-year-old man had a rapidly growing ulcerative mass on the right side of his hard palate. The lesion was asymptomatic and had been present for five to six days. There was no history of overt trauma, but the patient told the dentist that his teeth had been “cleaned and scraped” about one week earlier. A biopsy confirmed the diagnosis of necrotizing sialometaplasia, and the ulcer healed within eight weeks without sequelae.
CASE FOUR

A 36-year-old man had an asymptomatic ulcerating mass on the right side of his hard palate. Three days before the lesion developed, his maxillary right first molar had been extracted. The patient had received a greater palatine anesthetic block. Histologic features of the lesion were consistent with necrotizing sialometaplasia. Similar to the lesions in the other three cases, this lesion healed without complications within eight weeks.

DISCUSSION

The exact pathophysiology of necrotizing sialometaplasia is unknown, but ischemia of the vasculature supplying the salivary gland lobules is the most widely accepted theory. Etiologic factors resulting in ischemia have been reported, including direct trauma, administration of local anesthetic (because of vasoconstrictors and direct trauma from the needle), ill-fitting dentures, alcohol use, smoking, cocaine use, radiation, upper respiratory infection/allergy, intubation and surgical procedures for other associated lesions.

When necrotizing sialometaplasia is found with an associated lesion, the tumor or cyst itself may compromise the vascular supply, resulting in ischemia. Brannon and colleagues found partially occluded blood vessels within the immediate vicinity of the lesion. The occurrence of necrotizing sialometaplasia in patients with sickle cell anemia and Buerger’s disease, a form of arterial insufficiency, further supports the concept that ischemia is the main etiologic factor. Furthermore, two experimental studies were able to produce necrotizing sialometaplasia in submandibular and sublingual glands of rats by ligating the vasculature supplying these major salivary glands. Unfortunately, necrotizing sialometaplasia has been misdiagnosed as mucoepidermoid carcinoma or squamous cell carcinoma, with inappropriate treatment ranging from conservative excision to total maxillectomy. Recognition of necrotizing sialometaplasia, regardless of its clinical or microscopic presentation, is essential to avoid excessive treatment for this benign lesion.

On the other hand, some carcinomas can be mistaken for necrotizing sialometaplasia—as appears to be the case with President Grover Cleveland’s palatal ulcer. In July 1893, President Cleveland underwent a partial maxillectomy for what was described as an ulcer the size of a quarter. The surgical procedure was performed under secrecy on the yacht Oneida, while enroute from New York City to Buzzards Bay, Mass., where the president had a summer home.

The president’s absence of symptoms, lack of regional lymphadenopathy, clinical evidence of partial healing after conservative therapy and survival for 15 years without the benefit of radiotherapy or chemotherapy led many people to believe that the lesion may have been necrotizing sialometaplasia. However, this controversy may have been settled when Brooks and coworkers extensively examined the gross and microscopic specimens donated by the Mütter Museum of the College of Physicians of Philadelphia. Their final diagnosis was that the president had verrucous carcinoma of the hard palate and gingiva, not necrotizing sialometaplasia.

CONCLUSION

Necrotizing sialometaplasia is a benign self-limiting disorder of salivary glands. Unfortunately, it has been clinically and microscopically confused with a malignant neoplasm, resulting in inappropriate treatment. A simple incisional biopsy is required to confirm the histologic diagnosis and to rule out more serious disease processes. Usually, no treatment is required and the lesion heals by secondary intention within four to 10 weeks.

We have presented four cases of necrotizing sialometaplasia in which the patients’ initial complaint was a painless palatal ulcer. In two of the patients, an antecedent mass or swelling preceded the ulcer. The primary factors believed to have caused the ischemia were fellatio, an ill-fitting denture, scaling and root planing, and administration of a local anesthetic. All patients’ lesions healed within eight to 10 weeks without deformity.

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