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Necrotizing Sialometaplasia Report of Five Cases Including Uncommon Localizations

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Necrotizing sialometaplasia (NS) is a self-limited inflammatory disorder of the salivary glands predominantly occurring as a palatal lesion (1,2). Since its first description by Abrams *et al.* in 1973 (3), many cases have been reported (4-17). Although NS is a benign condition, its clinical and microscopical features can mimic malignancy and may lead to unnecessary surgical treatment (2,6,7,11,16). In this report five additional cases, including uncommon localizations, are reported and attention is drawn to the possible influence of previous surgical interventions in the histogenesis of NS.

Among files covering five years (1996-2000) from the archives of the Department of Pathology of Dokuz Eylül University School of Medicine, seven cases were found with the diagnosis of NS. A review of the slides revealed that five of them fulfilled the criteria for classification as NS. Serial sections from paraffin blocks and Verhoeff's stain to selected slides were performed. Clinical data was obtained from the hospital files or pathology request forms.

Case reports

Case 1: A 26-year-old male was admitted to another hospital with the complaint of a palatal mass. A biopsy was performed with a diagnosis of papilloma. Histology revealed inflamed salivary lobules and squamous metaplasia in some of the ducts and acini. Inflammation associated destruction of the lobules was noted. Surface ulceration and pseudoepitheliomatous hyperplasia of the overlying epithelium were also present. The histopathological diagnosis was that of NS.

Case 2: A 33-year-old female presented with a complaint of nasal obstruction. Physical examination revealed perforation of the nasal septum. The clinical diagnosis was granulomatous disease. A biopsy from the margin of the perforation showed ulceration covered with fibrino-purulent exudate, squamous metaplasia and pseudoepitheliomatous hyperplasia of the adjacent overlying epithelium and associated squamous metaplasia of the sero-mucous glands with preservation of lobular morphology (Figure 1). The histopathological diagnosis was that of NS.

Case 3: A 46-year-old male had been operated for pT4N2b squamous cell carcinoma of the floor of the mouth. A month later a full thickness biopsy from the lower lip was received without a clinical diagnosis. Histopathological examination revealed focal ulceration and associated inflammatory granulation tissue. Beneath the adjacent hyperplastic mucosal epithelium, there were foci of sialometaplasia with well preserved lobular morphology (Figure 2).

Case 4: A 42-year-old female had been operated on after a diagnosis of moderately well differentiated squamous cell carcinoma of the lower lip. The wedge resection material showed a positive margin for the tumor and the patient was operated on again. This second operation also included suprahyoid neck dissection. Histopathological examination revealed residual foci of tumor tissue. Sections representing one surgical margin of this re-operation specimen contained the focus of NS. This lesion involved a single salivary lobule and was adjacent to surgical suture material (Figures 3,4). Lymph nodes were free of tumor. The diagnosis was that of

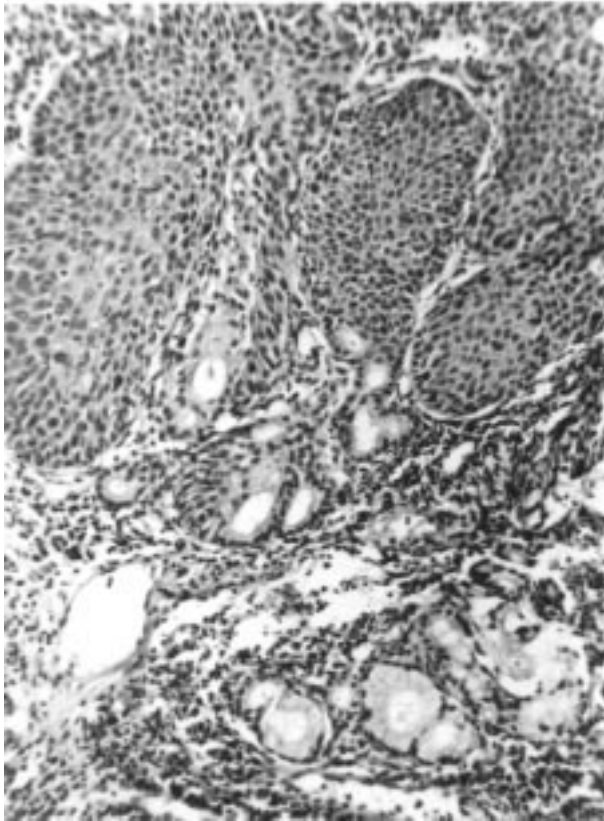


Figure 1. NS involving salivary lobules. Note some acini are still discernible among the foci of squamous metaplasia. H-E x 200.

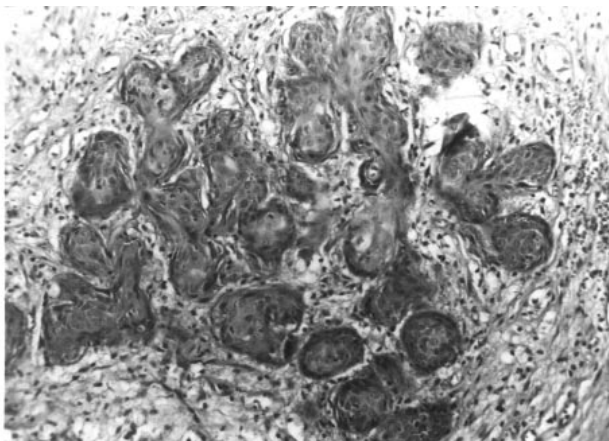


Figure 2. Squamous metaplasia involving a salivary lobule. Note the maintenance of the lobular morphology. H-E x 200.

residual moderately well differentiated squamous cell carcinoma with NS at the surgical margin.

Case 5: A 49-year-old woman presented with the complaint of sore throat, difficulty in swallowing and

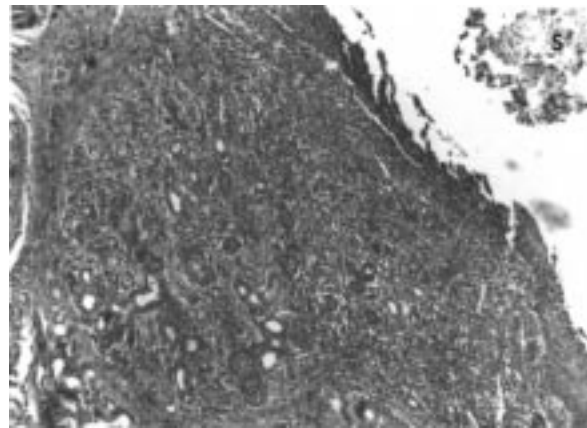


Figure 3. Focus of NS adjacent to surgical suture material (S). H-E x 100.

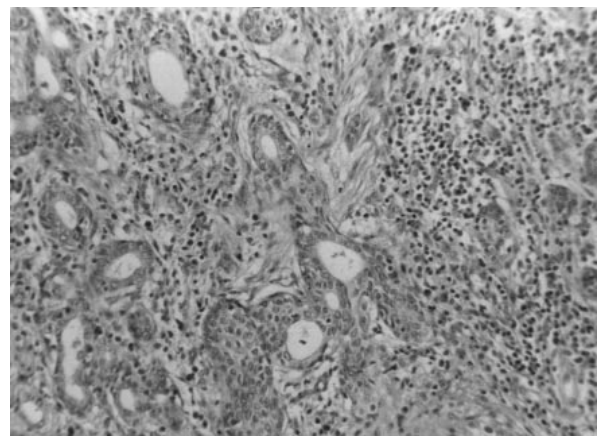


Figure 4. High power view of Figure 3. The squamous metaplasia involving ducts and acini associated with inflammatory cell infiltrate. H-E x 200.

dysphonia. Laryngoscopic examination revealed a lesion involving the left band ventricle and ventricle with extension to the anterior commissure. A punch biopsy was performed with the clinical diagnosis of carcinoma. The histology revealed mild dysplasia. In the repeat biopsy the diagnoses were NS and mild dysplasia (Figure 5). Then a third biopsy was performed and the clinical diagnosis of squamous cell carcinoma was confirmed. Total laryngectomy and a left radical neck dissection specimen showed a moderately well differentiated squamous cell carcinoma involving the left band ventricle and ventricle with transepiglottic invasion. The surgical margins of the specimen and cervical lymph nodes were free of tumor.

In 1973 Abrams *et al.* (3) reported a clinicopathological study of seven cases with a previously

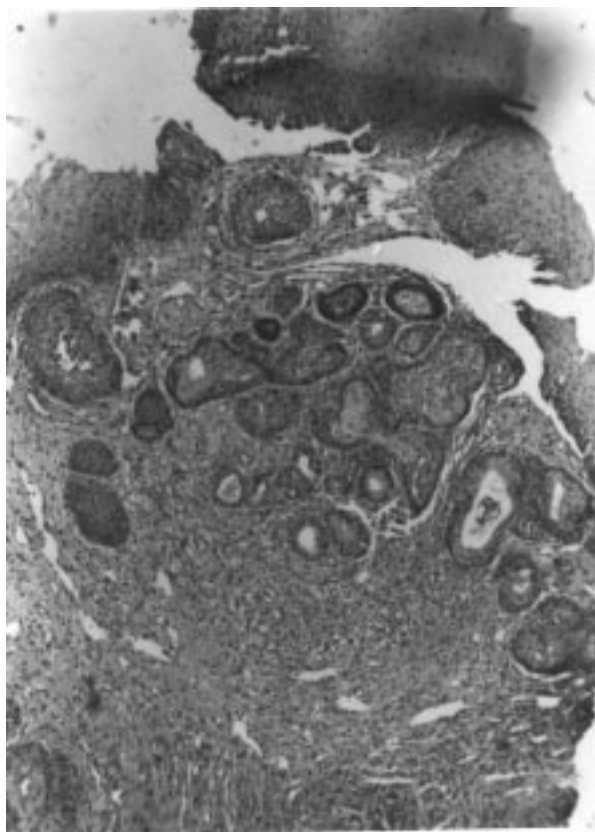


Figure 5. NS with lobular morphology beneath the laryngeal mucosal epithelium. H-E x 100.

unreported disorder of the minor salivary glands and introduced the term necrotizing sialometaplasia in order to describe this “new” disease. The main histopathological features of this entity defined by the same authors were as follows: 1. lobular infarction or necrosis; 2. simultaneous squamous metaplasia of ducts and acini; 3. bland appearing morphology of the metaplastic squamous cells; 4. prominent inflammatory component; 5. maintenance of the lobular morphology in spite of the inflammatory and metaplastic changes involving one or more lobule. Since this first report in 1973, the number of reported cases has gradually increased (4,6,7) and was reported to be over 180 in 1991 (9). Considering the additional reports in the English- language literature (11,12,13,15,16,17) the current number of reported cases may be estimated to be about 200.

Sites of involvement of NS in the head and neck include oral and non-oral sites. In a review of 184 cases (2,9) 77.2% of the cases occurred on the palate, while other oral tissues were involved in only 9.8% of the

cases. The involvement of the minor salivary glands of other head and neck sites was even less frequent. The least frequent sites of involvement of NS include the larynx and nasal cavity (11,15). Although NS is preponderantly a lesion of minor salivary glands, it may also be encountered in major salivary glands in a minority of cases (1). NS is solitary in the majority of the cases but metachronous lesions have also been reported (7).

The most widely accepted theory explaining the etiology of NS is ischemia (1,2,16). The factors believed to lead to ischemia were trauma; administration of local anesthetics; smoking, alcohol and cocaine use; infection; intubation; and surgical procedures for various lesions (1,6,16,18). Necrotizing sialometaplasia has also been reported in a patient with Buerger’s disease and Raynaud’s phenomenon (5) supporting the role of ischemia as an important etiological factor. In minor or major salivary gland tissues, the essential histopathological feature is the infarct of salivary gland lobules leading to the repair process involving squamous metaplasia (2). The proposed evolution of the lesions of NS include five stages: infarction, sequestration, ulceration, reparation and eventual healing (16). NS heals within four to 10 weeks usually without treatment (2,4,14,16). If it is biopsied during this period, it can be mistaken for squamous cell or mucoepidermoid carcinomas (14,16,18).

In reviewing our five cases, we noted that in none of the cases was the clinical diagnosis of NS considered. Among our cases, Case 1 was the classical presentation of NS. The lesion occurred in the palate without an antecedent history. In Case 2, it was not clear whether NS was the primary etiological factor leading to the perforation of the nasal septum or whether it represented a secondary reactive phenomenon. In Cases 3, 4 and 5 NS may be considered to be secondary to possible trauma during surgical interventions, for recent surgery in the area is also considered one of the possible precipitating events for NS (7). The importance of NS in Cases 3 and 4 (NS of the lip) lies in the fact that in these cases NS might be erroneously interpreted as residual or second primary tumors as these patients had previously been treated for squamous cell carcinomas of the floor of the mouth and the lip. Particularly in Case 4 misinterpretation of the NS, encountered at the surgical margin of the re-excision specimen, as a residual tumor might have resulted in unnecessary wide excision. Similar

cases have been reported occurring in the lip (8) and the trachea (12). In our case, NS was probably due to the traumatic effect of surgical suture material. Case 5 was also misleading. Three consecutive biopsies were required in order to reach the accurate diagnosis of a laryngeal tumor. NS in the second biopsy was probably due to the first biopsy procedure and this diagnosis was misleading for the surgeon as it obscured the underlying malignancy. We believe that the histological diagnosis of NS obtained subsequent to and from the site of a such previous "unsatisfactory" sampling should not be considered a definitive diagnosis, unless clinical features are unequivocally consistent with NS.

Although previously reported in the literature (1,2,5,11), in none of our cases were occluded vessels observed even with the aid of Verhoeff's stain.

The classical histopathological differential diagnosis of NS includes squamous cell and mucoepidermoid carcinomas. However, there are certain benign lesions requiring differentiation from NS (19,20). NS-like changes without a lobular configuration have been reported in herpetic tracheitis following intubation and have been called "necrotizing squamous metaplasia" (19). Another rare benign disease that has to be taken into account in the differential diagnosis of NS is a disorder termed "subacute necrotizing sialadenitis". This disease affects oral minor salivary glands and mostly occurs at the hard palate. It is characterized by loss of acinar

structures, acinar cell necrosis and atrophy of ductal cells. Twenty-two cases have been reported in the English-language literature (20). This lesion also is self-healing and resolves in 2 to 4 weeks (20,21).

In conclusion, we report here five cases of NS, including cases with uncommon localizations such as the nasal fossa and larynx. This disease may be confused with squamous cell and mucoepidermoid carcinomas, particularly in biopsies obtained subsequent to recent surgical interventions performed for those tumors. The histopathological features most helpful in the differential diagnosis of our cases were the bland appearing morphology of metaplastic squamous cells and preservation of lobular morphology. Awareness of the presence of such an entity is essential for avoidance of the misdiagnosis of malignancy.

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