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Necrotizing sialometaplasia: a case report of a non-ulcerated histopathological presentation

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Abstract

A 27-year-old woman presented with the chief complaint of severe pain in the palate region, which had been present for two months. Upon examination, she was found to have a firm, non-ulcerated nodule measuring about 2.5cm at the palatal junction. Incisional biopsy was recommended because the clinical differential diagnosis was mucoepidermoid carcinoma or squamous cell carcinoma. Anatomopathological examination revealed squamous metaplasia of the salivary gland ducts with preservation of the lobular architecture. Immunohistochemistry showed metaplastic ducts with low reactivity for p53 and Ki67, as well as positivity for CK AE1/AE3, CK7, p63, S-100, and SMA. The final diagnosis was necrotizing sialometaplasia. No treatment is required for this disease. Thirty-nine days after biopsy, total remission was observed with no signs of relapse after two years.

Keywords: histopathology, immunohistochemistry, wound repair, surgical pathology

Introduction

First described by Abrams et al. [1] necrotizing sialometaplasia (NS) is characterized as a rare inflammatory condition [1-3]. Although its etiology is not yet fully defined, it is known to be related to traumatic factors that may cause vascular obstruction, with consequent infarction and ischemic necrosis of the salivary glands [4]. Possible causes of obstruction include intubation, local anesthesia, local radiotherapy, smoking, alcohol, as well as Raynaud and Buerger disease [5]. However, episodes of vomiting have been described as a cause as well [6].

The clinical features of NS consist of a nodule or crater-shaped ulcer surrounded by an erythematous halo; on rare occasions, there may be destruction of the underlying palatine bone [7]. Histologically, it may mimic malignant tumors such as squamous cell carcinoma [1,8,9] and mucoepidermoid carcinoma [10-12] as NS is composed of marked squamous metaplasia of the salivary ducts in addition to acinar necrosis [13,14]. According to Keogh et al. [5] after an initial biopsy for diagnosis, there is no recommended treatment for SN ulcers or nodules as the lesions will heal within the following weeks.

Herein, we report a non-ulcerated case of SN and describe the clinical, histological, and immunohistochemical features in an attempt to call attention to this unusual diagnosis.

Case Synopsis

A 27-year-old woman presented to the dental clinic complaining of severe pain of the palate, which had started two months prior. Upon physical intraoral examination, a firm, 2.5cm diameter, non-ulcerated nodule was found at the palatal junction (**Figure 1A)**. The patient reported no basic systemic diseases or

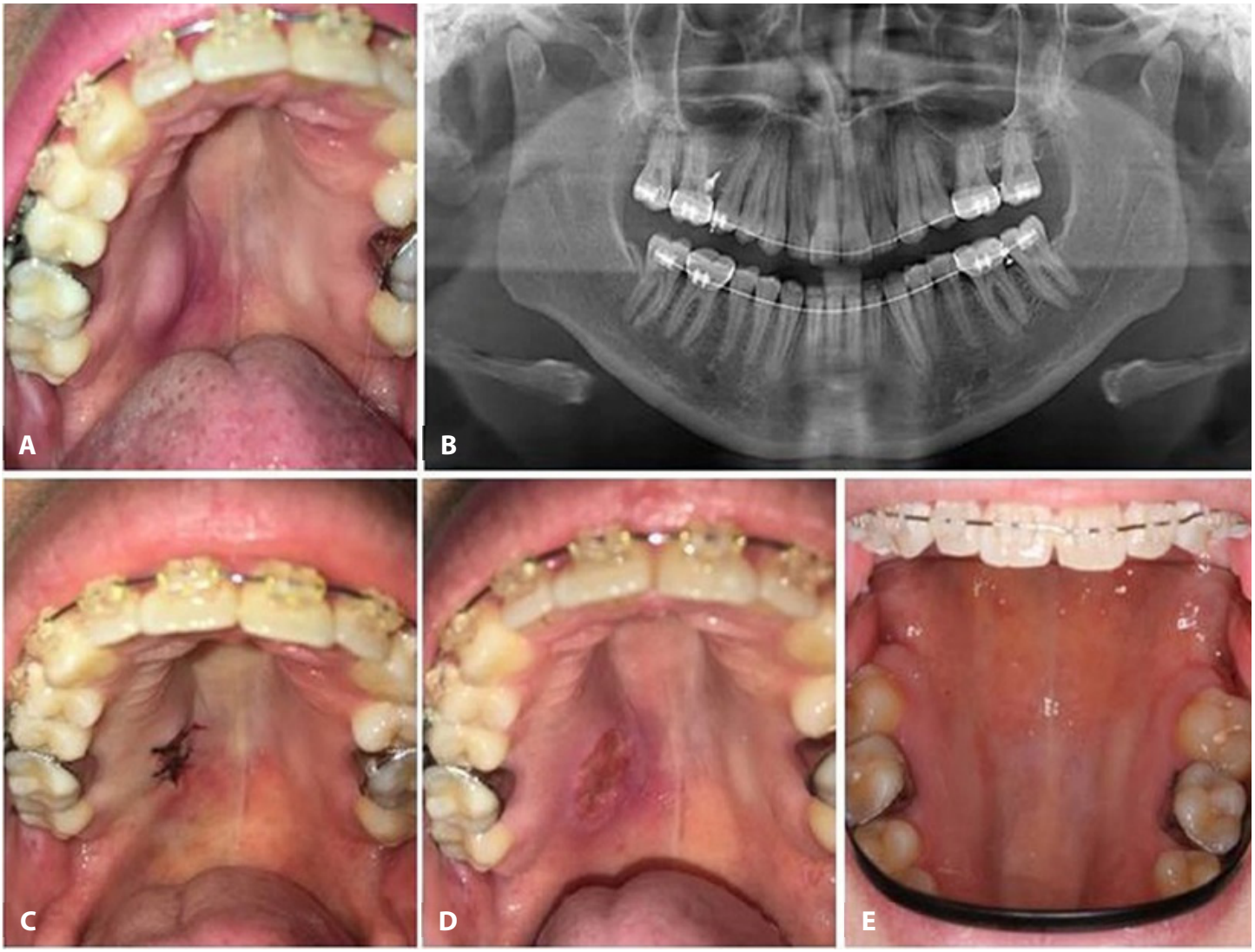

Figure 1. ***A)*** *Initial clinical picture of the palatal junction lesion.* ***B)*** *Initial panoramic radiograph image with no evidence of bone involvement.* ***C)*** *Immediately after the incisional biopsy* ***D)*** *Clinical aspect after one week of incisional biopsy.* ***E)*** *Note the oral mucosa without alterations after two years of follow-up.*

use of medication. In addition, there was no history of trauma to the region. She noticed the onset after being diagnosed with sinusitis, which was treated for 21 days with antibiotics and systemic corticosteroid. A complementary imaging exam, panoramic radiography, revealed no changes to the bone (**Figure 1B)**. The initial clinical differential diagnosis included mucoepidermoid carcinoma or squamous cell carcinoma. Therefore, an incisional biopsy was recommended (**Figure 1C**, **D)**. Anatomopathological examination showed a mucosal fragment lined with non-ulcerated, keratinized stratified epithelium and connective tissue showing preservation of the architecture. It showed squamous metaplasia of the salivary gland ducts, mucin leakage, and inflammatory infiltrate composed of lymphocytes, macrophages, and neutrophils, in addition to acinar necrosis. (**Figure 2A**, **B)**. Immunohistochemistry was performed (**Table 2**, **Figure 2C**-I). Based on these findings the final diagnosis was necrotizing sialometaplasia. Ten days after the biopsy procedure, a reduction in pain was reported and total remission occurred within 39 days. The patient is under routine observation and shows no signs of relapse after two years (**Figure 1E)**.

Case Discussion

We report a non-ulcerated form of NS involving the palatal junction of a 27-year-old woman. Its presence

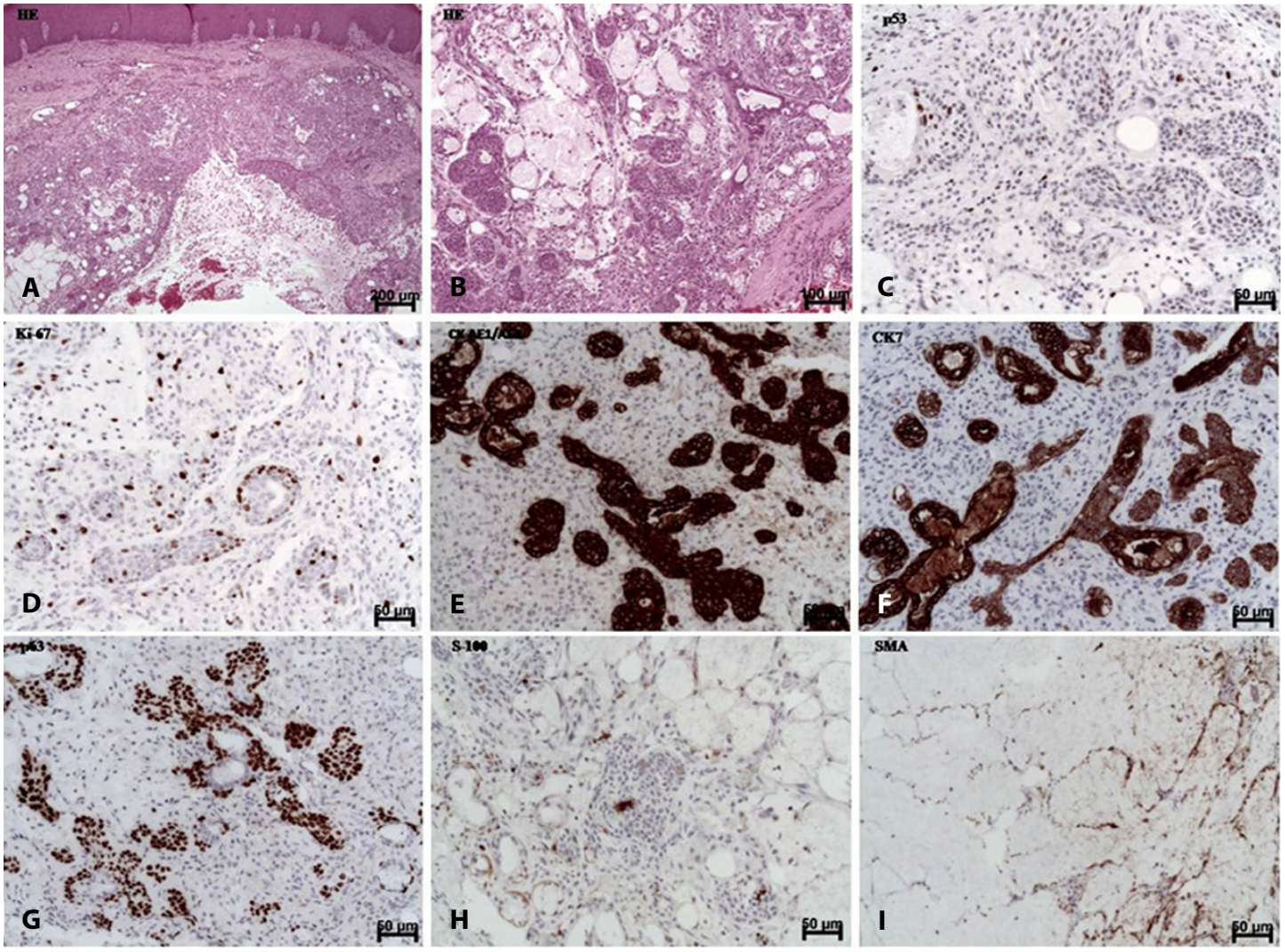

Figure 2. *Photomicrograph of histological sections on H&E and immunohistochemistry.* ***A)*** *Note absence ulceration and pseudoepitheliomatous hyperplasia and squamous ductal metaplasia and mucin extravasation, 10×.* ***B)*** *Detail of the anterior figure highlighting the acinar necrosis and ductal metaplasia, 20×.* ***C-I)*** *Immunohistochemistry for antibody p53, Ki-67, CK AE1/AE3, CK7, p63, S-100 and SMA, respectively, 40×.*

in this location is not a significant finding as NS has been described frequently in the palate [8], although other locations in the mouth have been described, including tongue, buccal mucosa, and retromolar area [5,15,16]. However, to the best our knowledge, there are only a few previous studies focusing on non-ulcerated lesions in the oral cavity [17-21].

Although NS can arise in any other mucosal area of the upper aero-digestive tract [1,8,10,22-25], the palate is most affected, about 70-80% [8,26-28]. On the other hand, it has been observed that NS at the palatal junction is rare and found only in 10% of cases [8]. This preference may possibly be explained by the higher supply of blood found in the palate [29,30]. Necrotizing sialometaplasia is a benign inflammatory condition that affects the salivary glands, especially the minor ones [1,8,27,31].

Clinically, there is not a specific clinical appearance specific to SN. Some authors claim that the lesions are characterized as deep ulcers, which can reach about 5cm in diameter, with well-defined edges and an erythematous halo [1]. However, the presence of necrosis is also a clinical feature commonly observed in SN cases [7]. Another clinical feature is the presence of asymptomatic or symptomatic ulcers with the appearance of an edematous well-defined unilateral or bilateral nodule, which may feel quite firm [5,27,32,33]. In the present case, the presence of a symptomatic, non-ulcerated nodule measuring

Table 1. *Reports of cases of non-ulcerated necrotizing sialometaplasia of the oral cavity published in the English language literature.*

Reference	Country	Age (years)	Gender	Location	Size (cm)	Duration	Treatment	Biopsy	Remission time
Alves et al 2011	Brazil	25	F	Hard palate	2.5	12 weeks	No	Incisional	30 days
Arpaci et al 2014	Turkey	58	M	Palate	3	3 months	NI	Incisional	NI
Indirani et al 2013-3*	India	38	M	Lip	2.5	1 month	NI	NI	NI
Madala et al 2014	India	28	F	Palatal junction	3	6 months	Excision	Excisional	NI
Shetty et al 2015	India	35	F	Hard palate	1	2 weeks	No	FNAC	4 weeks
Present case	Brazil	27	F	Palatal junction	2.5	2 months	NI	Incisional	39 days

Abbreviations: NI: not informed; F: female; M: male; FNAC: fine-needle aspiration cytology.
*articles with more than one case report.

2.5cm in diameter was observed, a similar size to those recorded in previous reports [17,19,34].

A search through the English literature of the last forty-six years demonstrated cases of non-ulcerated SN involving th e oral region (**Table 1**). The mean age of the patients was 35.2 years of age (range: 27-58 years of age). Women were slightly more affected (N= 4/66.6%) than men (N=2/33.4%). There was a predominance of cases affecting the palate (N=5/83.3%) and the mean size of the lesions was 2.41cm.

The pathogenesis of SN is not yet fully elucidated, but the primary cause is believed to be related to ischemia of salivary gland tissue [13,27,35,36]. This might result in the infarction of the salivary acini, and inflammation and metaplasia of the ducts [1,22,35,38]. In addition, in view of the histologic diversity found in NS, the expression of HIF1α, VEGF, and EGFR could represent all of the changes found in NS as ischemia, reperfusion, healing, or repair are all involved in the development [34].

Etiological factors related to development of NS are trauma, administration of local anesthetics, poorly adapted dentures, alcohol, smoking, cocaine, radiation, intubation, bulimia, surgical procedures, and upper respiratory tract infections [13,27,32,33,39,40]. However, the patient reported here took antibiotics and systemic corticosteroids to treat a sinonasal infection. It is important to state that such drugs are not likely to have caused ischemia of the salivary glands [41,42]. In addition, some systemic diseases also seem to be considered predisposing factors for NS, such as diabetes and HIV owing to immunosuppression, and sickle-cell anemia owing to an increase in blood viscosity, which favors tissue ischemia [43].

Histopath ologically, our patient's condition fulfilled the criteria for necrotizing sialometaplasia

Table 2. *Immunohistochemical panel of necrotizing sialometaplasia in our patient.*

Antibody	Result	Localization
P53	+	Metaplastic gland (Nuclear)
Ki67	5%	Metaplastic gland epithelium (Nuclear)
CK E1/AE3	++	Metaplastic gland ducts
CK7	++/++	Metaplastic gland ducts/viable mucous acini
P63	++/*	Metaplastic gland ducts (Nuclear)/ Myoepithelial cells
S-100	*	Metaplastic gland ducts
SMA	+/+	Myoepithelial cells of viable acini and non-metaplastic gland ducts

Weakly positive (+); intensely positive (++); focal areas (*); negative (-).

[1,3,5,7,33,35,43-46]. The nodule was composed of necrosis acinar, metaplastic glandular ducts and inflammation mixed amidst extravasated mucin. However, neither ulceration nor pseudoepitheliomatous hyperplasia were found in this case. These findings are in accordance with Alves et al. [17], Indirani et al. [19], and Shetty et al. [21]. The lack of these findings can be justified by the fact that the biopsy was performed in the early stages of the disease [17]. According to Anneroth and Hansen's hypothesis [47], the microscopic events of SN are divided into stages of infarction, sequestration, ulcer, repair, and resolution. The ulcer occurs in the third stage, whereas pseudoepitheliomatous hyperplasia occurs only in the final stage of healing. The typical clinical course was described by Rushinek et al. [48] who reported a nodule, that after one week without surgical intervention developed ulceration. Other cases of non-ulcerated NS have exhibited pseudoepitheliomatous hyperplasia [17,18,20].

The diagnosis of NS can be a serious challenge for pathologists, particularly when the biopsy is incisional, given the ability of NS to mimic malignant tumors such as mucoepidermoid carcinoma and squamous cell carcinoma [5,44], both clinically and histologically [45]. However, the absence of cystic spaces lined with mucosa cells, keratinization, and atypical mitosis help to distinguish between them. For this purpose, immunohistochemical markers, such as those used in the present study, may contribute to diagnosis. Our results showed low positivity for p53 and MIB1 (Ki-67) suggesting NS in the repair stage. In addition, CK 7, p63, and SMA showed epithelial and myoepithelial differentiation. According to Rizkalla and Toner [48], NS tends to heal spontaneously after three to 12 weeks. However, careful follow up is recommended.

Conclusion

Non-ulcerated SN is rare and it is important to recognize this condition and distinguish it from malignancies. Therefore, biopsy is necessary for accurate diagnosis.

Potential conflicts of interest

The authors declare no conflicts of interest.

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