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Necrotizing sialometaplasia: report of a self-limiting lesion with malignant appearance

CASE REPORT

Sialometaplasia necrotizante: reporte de una lesión autolimitante de apariencia maligna

Sialometaplasia necrotizante: relato de lesão autolimitante de aspecto maligno

Abstract

We report a case of a 45-year-old man with a palate ulcer for 10 days. The patient was an alcohol user and had a history of using cocaine for 17 years, discontinued for the last 7 years. An incisional biopsy was performed, and histological sections revealed an extensive ulcerated area covered by a fibrinopurulent membrane, with small nests of squamous cells in the connective tissue. These squamous cells exhibited eosinophilic cytoplasm, evident and sometimes multiple nucleoli, mild cellular atypia, and several mitotic figures. The clinical and histological characteristics indicated a Necrotizing Sialometaplasia diagnosis, and the patient underwent clinical follow-up. In the third week of follow-up, remission of the lesion became apparent. We emphasize the importance of histopathological and immunohistochemical examination in the correct diagnosis.

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Resumen

Presentamos el caso de un hombre de 45 años con úlcera en paladar de 10 días de evolución. El paciente era consumidor de alcohol y tenía antecedentes de consumo de cocaína desde hacía 17 años, discontinuada durante los últimos 7 años. Se realizó biopsia incisional y los cortes histológicos revelaron una extensa área ulcerada recubierta por una membrana fibrinopurulenta, con pequeños nidos de células escamosas en el tejido conectivo. Estas células presentaban citoplasma eosinófilo, nucleolos evidentes y en ocasiones múltiples, leve atipia celular y varias figuras mitóticas. Las características clínicas e histológicas indicaron el diagnostico de Sialometaplasia Necrotizante y el paciente fue sometido a seguimiento clínico. En la tercera semana de seguimiento se hizo evidente la remisión de la lesión. Destacamos la importancia del examen histopatológico e inmunohistoquímico en el correcto diagnóstico.

Palabras clave: Sialometaplasia necrotizante; Neoplasias de las glándulas salivales; Carcinoma de Células Escamosas de Cabeza y Cuello; Úlcera oral.

Resumo

Relatamos o caso de um homem de 45 anos com úlcera no palato há 10 dias. O paciente era usuário de álcool e tinha história de uso de cocaína há 17 anos, interrompida há 7 anos. Foi realizada biópsia incisional e os cortes histológicos revelaram extensa área ulcerada recoberta por membrana fibrinopurulenta, com pequenos ninhos de células escamosas que apresentavam citoplasma eosinofílico, nucléolos evidentes e por vezes múltiplos, atipias celulares discretas e diversas figuras mitóticas. As características clínicas e histológicas indicaram o diagnóstico de Sialometaplasia Necrotizante e o paciente foi submetido a acompanhamento clínico. Na terceira semana de acompanhamento, a remissão da lesão tornou-se evidente. Ressaltamos a importância do exame histopatológico e imunohistoquímico no correto diagnóstico.

Palavras-chave: Sialometaplasia necrosante; Neoplasias das glândulas salivares; Carcinoma Espinocelular de Cabeça e Pescoço; Úlcera oral.

Introduction

Necrotizing Sialometaplasia (NS), first described by Abrams et al. [1] in 1973, is a rare, benign, self-limiting, self-resolving lesion that primarily affects the minor salivary glands [1-3]. NS accounts for approximately 0.03% of oral biopsies [4]. While most lesions involve the mucous glands of the hard palate, cases have also been reported in major salivary glands, such as the submandibular gland [5].

Although the exact pathophysiology of NS remains unknown, it is thought to be associated with local ischemia triggered by factors such as dental injections, prosthetic use, alcohol, drugs, and smoking. Respiratory infections and bulimia have also been implicated as potential predisposing factors [6-9].

Clinically, NS usually presents as a circumscribed ulcer with raised borders and variable symptoms [6]. Its presentation can mimic various malignant entities with similar clinical features, including squamous cell carcinoma (SCC), mucoepidermoid carcinoma (MEC), and infectious diseases such as histoplasmosis, tuberculosis, paracoccidioidomycosis, and syphilis [8,10-12].

Biopsy and histopathological evaluation are essential for diagnosing this lesion [13]. The diagnosis can be challenging, depending on the size and orientation of the biopsy specimen. Alongside routine hematoxylin-eosin (HE) staining, immunohistochemistry can be employed to aid in diagnosis [12,14]. This is crucial to avoid diagnostic errors, as histopathologic differential diagnoses include SCC and MEC [12-14].

Once diagnosed, NS does not require specific treatment. However, symptomatic and conservative management is necessary, and lesions typically heal spontaneously within 2 weeks to 3 months [6,15].

This paper aims to report a case involving the challenging diagnosis of NS and to highlight the importance of histopathologic and immunohistochemical examination in achieving the correct diagnosis and proper patient management.

Case report

A 45-year-old man with a 10-day history of a palate ulcer was referred to the Oral Medicine Service of the São Sebastião Dental Specialties Center (São Paulo, Brazil). During anamnesis, he denied tobacco use but reported frequent alcohol consumption. He also disclosed a 17-year history of cocaine use, which had ceased 7 years before the onset of the ulcer.

Extraoral physical examination revealed no significant abnormalities. Intraorally, a painless ulcerated lesion (1.5 x 0.8 cm) with necrotic contents and slightly indurated borders was observed along the midline of the soft palate (Figure 1), raising initial concerns for syphilis and squamous cell carcinoma (SCC).

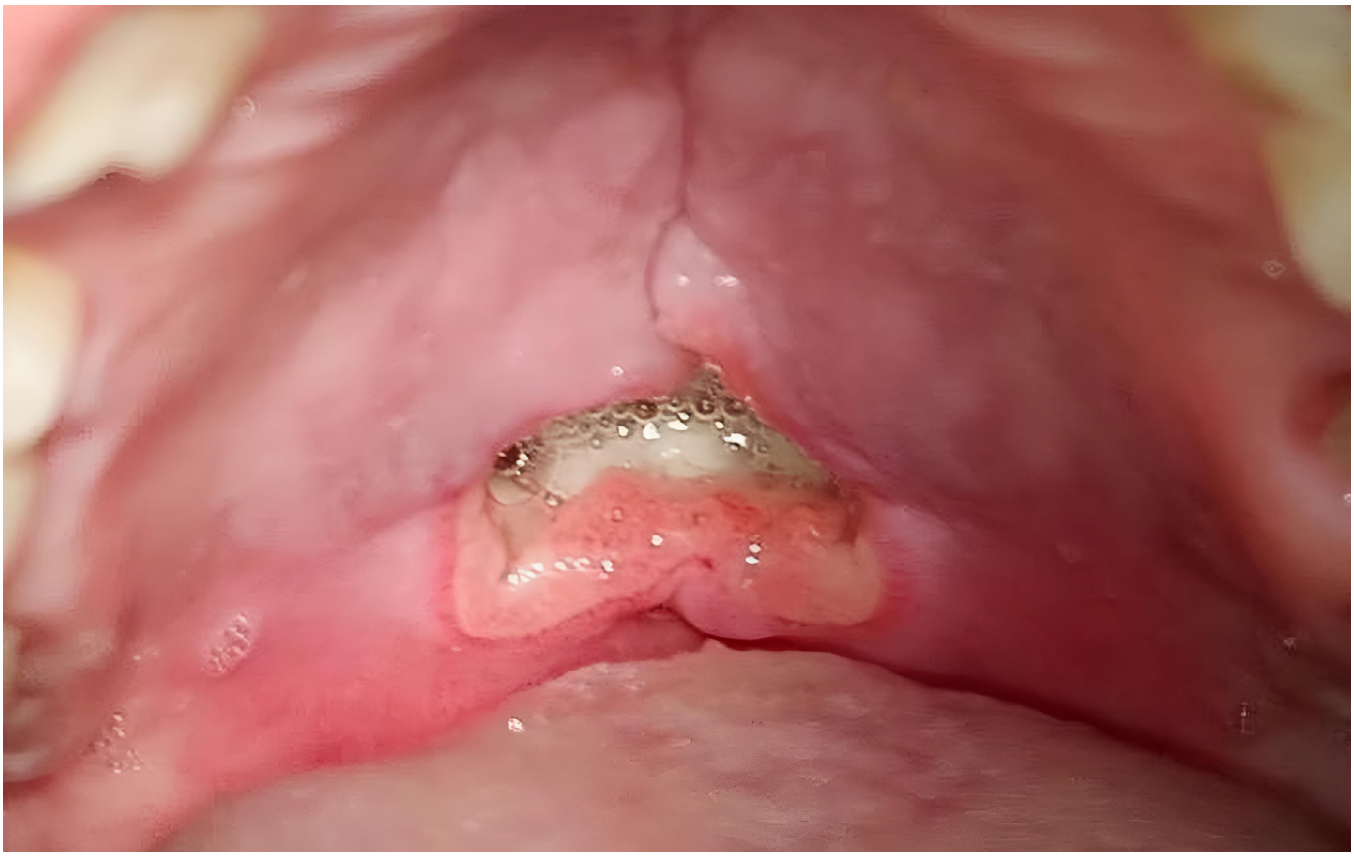

Figure 1. Initial clinical presentation. Painless ulcerated lesion on the midline of the soft palate, with necrotic contents and raised, slightly indurated, erythroplastic borders.

The patient underwent a rapid syphilis test (Syphilis Bio/Bioclin® - Quibasa Química Básica Ltda, Belo Horizonte, MG, Brazil), which yielded a negative result. Following debridement of the necrotic tissue and local irrigation, an incisional biopsy was performed.

Histological sections revealed a mucosal fragment partially lined by hyperplastic parakeratinized stratified squamous epithelium, exhibiting exocytosis, drop-shaped rete ridges, and a disorganized basal layer. A large ulcerated area was covered by a fibrinopurulent membrane, with small nests of squamous cells in connective tissue. These squamous cells exhibited eosinophilic cytoplasm, prominent and occasionally multiple nucleoli, mild cellular atypia, and several mitotic figures. Additionally, ducts with squamous metaplasia and acini with PAS-positive mucous cells, without necrosis, were observed. Small clusters containing both mucous and squamous cells were also identified (Figures 2 and 3).

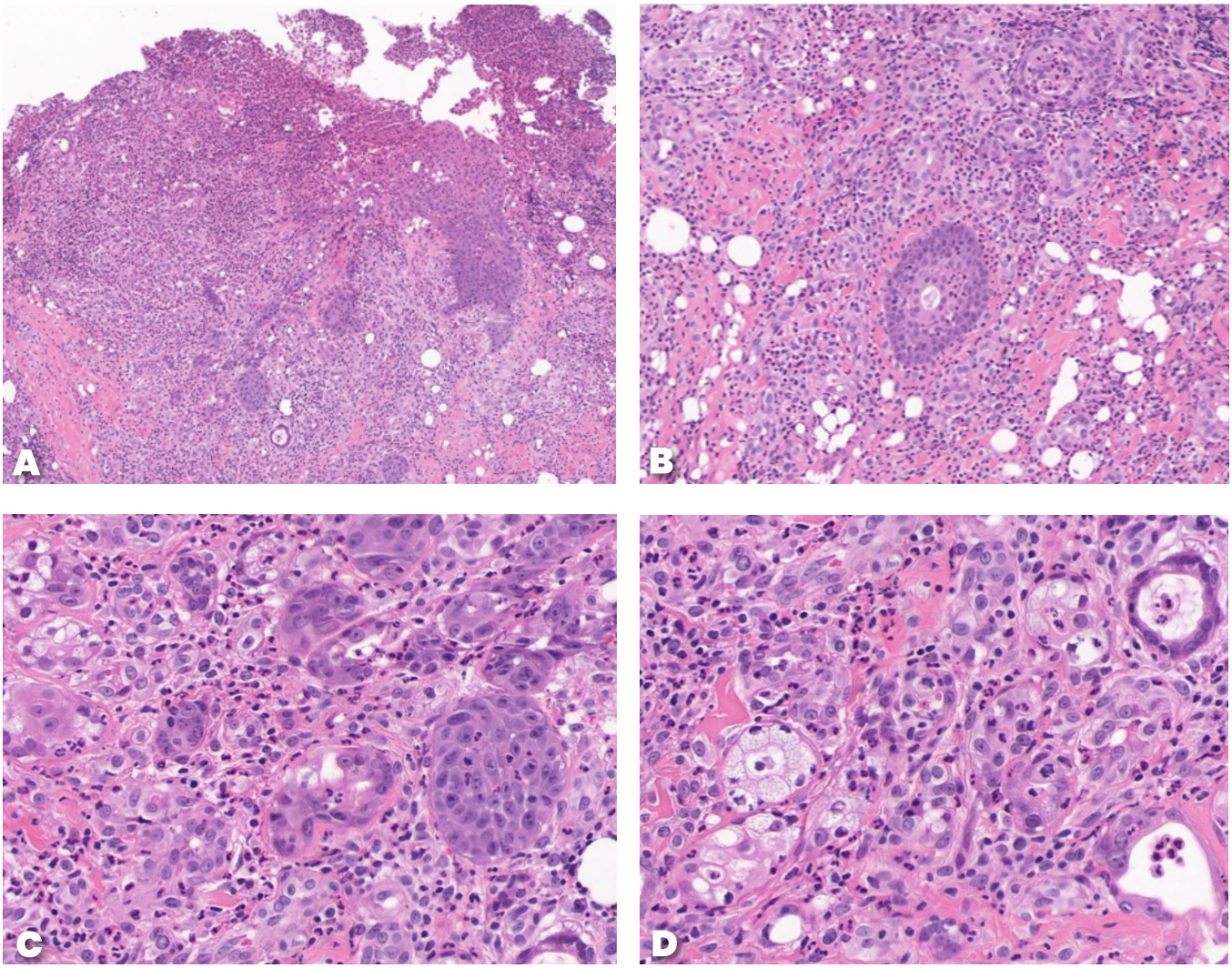

Figure 2. Histological sections (Hematoxylin and eosin).
A. Mucosal fragment partially lined by hyperplastic parakeratinized stratified squamous epithelium with an extensive ulcerated area lined by a fibrinopurulent membrane (original magnification 50x).
B. Duct exhibiting squamous metaplasia (original magnification 100x).
C and **D.** Small nests of mucous and squamous cells characterized by eosinophilic cytoplasm, nuclear hyperchromatism, evident and occasionally multiple nucleoli, cellular atypia, and numerous mitotic figures (original magnification 200x).

Cytoplasmic positivity for AE1/AE3 was detected in all parenchymal cells, whereas only ductal and mucosal cells displayed cytoplasmic positivity for CK7 and CK19. The stroma was composed of fibrous connective tissue, with an intense mixed inflammatory infiltrate and numerous blood vessels with thickened endothelium. Given the histological similarities between MEC and SCC with salivary gland infiltration, immunohistochemistry for calponin and smooth muscle actin was conducted, revealing myoepithelial cells encircling some of the epithelial islands (Figure 3).

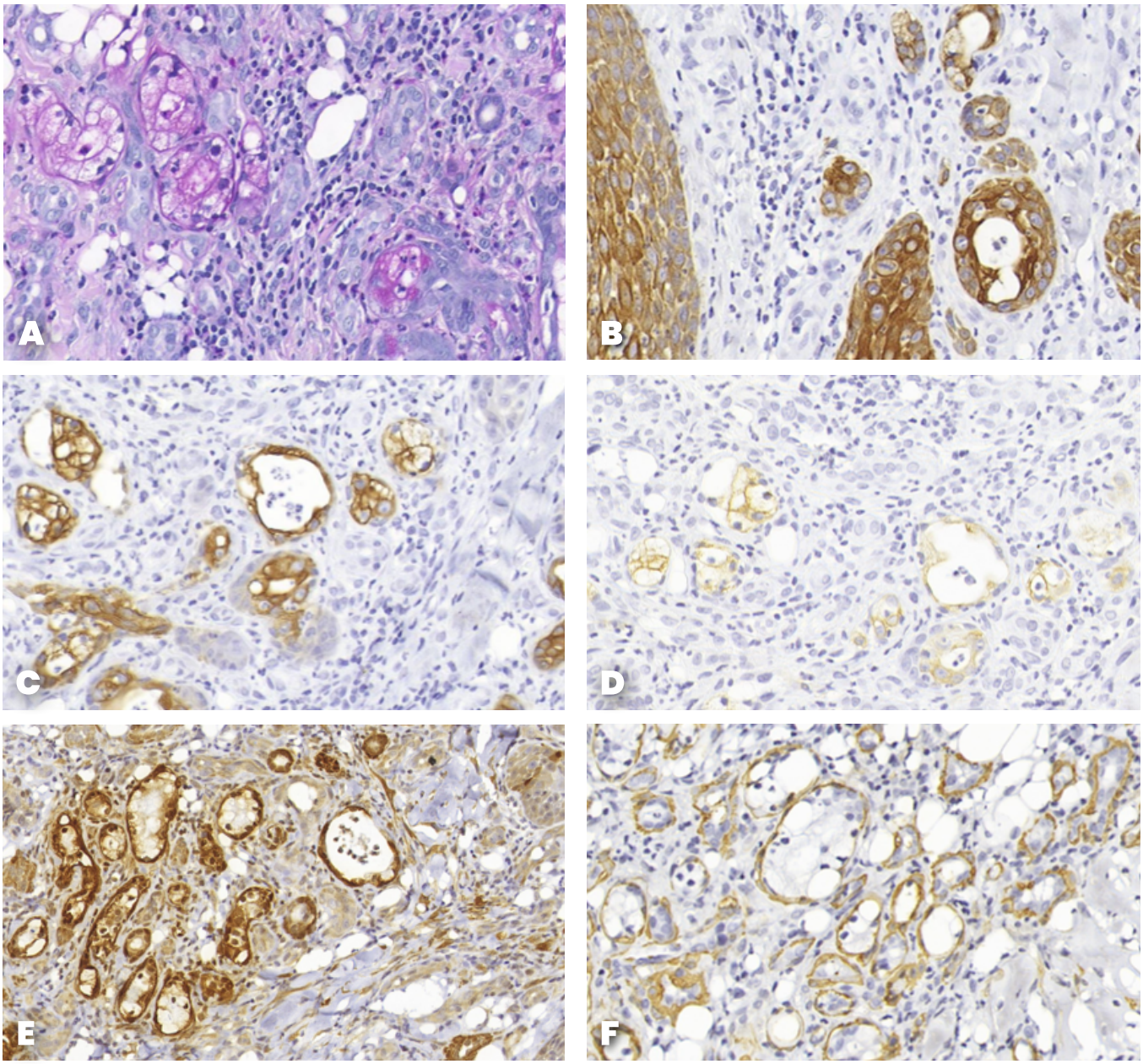

Figure 3: Histological sections (PAS and immunohistochemistry)
A. Acini composed of PAS-positive mucous cells (original magnification 200x).
B. Positive for AE1/AE3 in all parenchymal cells (original magnification 200x).
C. Ductal and mucosal cells displaying cytoplasmic positivity for CK7 (original magnification 200x).
D. Ductal and mucous cells displaying cytoplasmic positivity for CK19 (original magnification 200x).
E. Calponin staining in myoepithelial cells surrounding epithelial islands (original magnification 200x).
F. Smooth muscle actin staining in myoepithelial cells surrounding epithelial islands (original magnification 200x).

Given that the clinical and histologic features of the lesion suggested NS, the patient was monitored with weekly clinical follow-ups, as NS cases typically resolve following an incisional biopsy. No significant clinical changes were noted until the third week of follow-up, when the remission of the lesion began. Complete wound closure was achieved after 5 weeks (Figure 4), confirming the NS diagnosis. Unfortunately, the patient was lost to follow-up after the lesion was resolved.

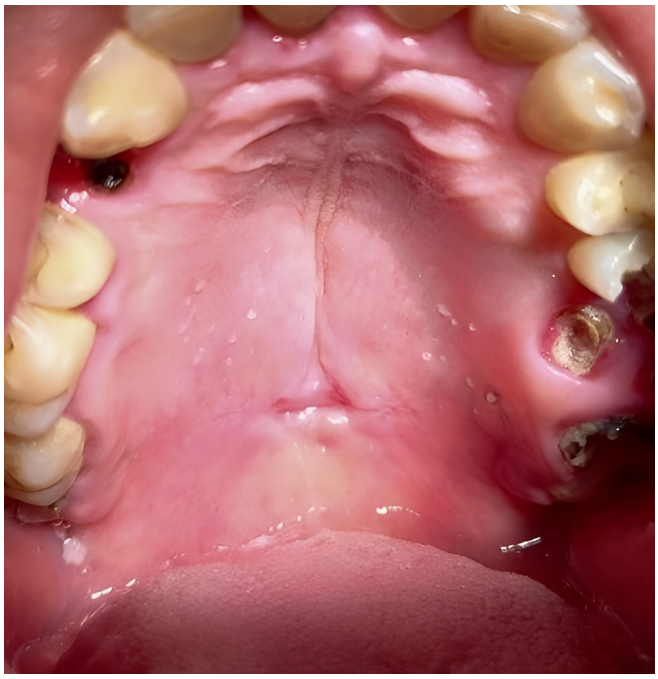

Figure 4: Clinical appearance of the lesion after 5 weeks of follow-up.

Discussion

NS is a rare but benign process affecting salivary gland tissue [15], most commonly observed in white patients, with a male-to-female ratio of approximately 2:1 [16]. While it can occur across a wide age range, from 1.5 to 80 years, it is most frequently reported in individuals over 40 years old, consistent with the epidemiologic profile of the patient described here [17,18]. Medeiros et al. [18], in their literature review on published NS cases, identified a similar profile to that of our patient. They found that NS predominantly affects men between 20 and 68 years old, with a preference for the hard palate. The lesion may present with or without pain, and additional symptoms can include fever, chills, malaise, or swelling [18].

The exact etiology of NS remains unclear, but it is thought to be related to physicochemical or biological injury that reduces local blood supply, leading to infarction of the salivary gland acini, followed by inflammation and tissue repair. This process results in ductal metaplasia and eventual scarring. Various factors can trigger this sequence of events, including local anesthesia, surgical procedures, ill-fitting prostheses, tobacco or cocaine use, alcohol consumption, upper respiratory tract infections, radiotherapy, intubation, violent or induced vomiting (e.g., in bulimic patients), and systemic diseases [7-9].

In this case, the primary associated factor was chronic alcohol use, which may have contributed to the development of NS. Although the patient mentioned previous cocaine use, we do not consider this a causal factor for NS, as the patient ceased using cocaine 7 years ago.

Clinically, NS typically manifests as deep ulcers with raised edges, although non-ulcerated masses or swellings have also been reported [1,6,9]. Palatal lesions are usually single and unilateral, located on the posterior hard palate or at the junction of the hard and soft palate, with or without bone involvement [13]. The clinical presentation of NS shares similarities with various infectious diseases, such as histoplasmosis, tuberculosis, paracoccidioidomycosis, and syphilis. Therefore, these infectious diseases should be considered as potential differential diagnoses [8]. In our case, syphilis was initially suspected but ruled out through serologic testing, and under the suspicion of SCC, an incisional biopsy was performed.

Anneroth and Hansen [19] describe the histopathogenesis of NS as involving five histological stages: infarction, sequestration, ulceration, repair, and healing. Accordingly, a spectrum of histopathological findings can be observed, including ulceration, vascular proliferation, lobular coagulative necrosis of the salivary glands, sequestration of necrotic acini, pseudoepitheliomatous hyperplasia of the lining epithelium with squamous metaplasia of the adjacent ducts and acini, along with mucin accumulations [2,3,8,10].

Although NS is a self-limiting lesion, it is crucial to note that its clinical and microscopic features closely resemble those of malignant neoplasms, which can lead to misdiagnoses and incorrect treatments by pathologists and surgeons [4,14]. Pseudoepitheliomatous hyperplasia, prominent squamous metaplasia of the salivary duct epithelium, and the presence of residual mucous cells in salivary gland lobules may result in a misdiagnosis as SCC or MEC [12]. This misidentification can lead to unnecessary treatments, such as radical surgery, with mutilating effects [14]. In a retrospective study of 69 NS cases, Brannon et al. [13] reported that 8 patients were misdiagnosed and subsequently received inappropriate therapy, ranging from wide excision to total maxillectomy.

Histologic differentiation between NS and neoplastic lesions is based on the preservation of the lobular architecture of the glands, a cytologic appearance of squamous islands without dysplastic features, and the presence of residual ducts within these islands [4,10,12]. Although histologic differentiation seems straightforward, in this report, mild atypia was observed, with multiple prominent nucleoli, several mitotic figures, and an absence of necrotic areas, which can complicate the diagnosis.

However, in cases where the diagnosis with HE

staining is uncertain, particularly in small biopsy specimens, incorporating an antibody panel can provide additional support, though it may not be conclusive [14]. Myoepithelial markers, such as calponin and smooth muscle actin, may highlight residual myoepithelial cells at the periphery of squamous islands present in NS but absent in MEC and SCC [14]. Additionally, CK7 positivity is expected only in the glandular epithelium, aiding in the differentiation of MEC and SCC [20].

Once diagnosed, NS is mostly self-limiting and typically requires supportive care, including lesion debridement, pain management, and local antiseptics. Spontaneous healing generally occurs within weeks, as observed in this case report [6,10,15]. Although NS rarely recurs, careful follow-up is crucial. In cases of late self-limited healing, reevaluation and repeat biopsy may be needed to rule out other potential lesions [3].

Conclusion

NS is a rare lesion that most commonly affects the minor salivary glands. Despite being self-limiting, it can present clinical and histopathologic features suggestive of a malignant neoplasm, leading to potential misdiagnosis and aggressive treatments. Immunohistochemistry can offer additional support for diagnosing NS, which is treated with debridement, pain management, and local antiseptics. Moreover, NS typically heals within a few weeks.

REFERENCES

1. Abrams AM, Melrose RJ, Howell FV. Necrotizing sialometaplasia. A disease simulating malignancy. Cancer. 1973;32(1):130-5.

2. El Gaouzi R, Hallab L, Taleb B. A diagnostic error of a necrotizing sialometaplasia: Case report. Ann Med Surg (Lond). 2022;74:103225.

3. Joshi SA, Halli R, Koranne V, Singh S. Necrotizing sialometaplasia: A diagnostic dilemma! J Oral Maxillofac Pathol. 2014;18(3):420-2.

4. Mesa ML, Gertler RS, Schneider LC. Necrotizing sialometaplasia: frequency of histologic misdiagnosis. Oral Surg Oral Med Oral Pathol. 1984 Jan;57(1):71-3.

5. Russo A, Dell'Aquila A, Prota V, Sica GS. Scialometaplasia necrotizzante della ghiandola sottomandibolare. Descrizione di un caso [Necrotizing sialometaplasia of the submandibular gland. Report of a case]. Minerva Stomatol. 1998 Jun;47(6):273-7.

6. Ledesma-Montes C, Garcés-Ortíz M, Salcido-García JF, Hernández-Flores F. Review of the literature on necrotizing sialometaplasia and case presentation. Quintessence Int. 2015;46(1):67-72.

7. Gilowski Ł, Wiench R, Polakiewicz-Gilowska A, Dwornicka K. Necrotizing sialometaplasia of the palatal mucosa in patient with history of anorexia: review and case report. Am J Otolaryngol. 2014;35(3):400-1.

8. Chateaubriand SL, de Amorim Carvalho EJ, Leite AA, da Silva Leonel ACL, Prado JD, da Cruz Perez DE. Necrotizing sialometaplasia: A diagnostic challenge. Oral Oncol. 2021;118:105349.

9. Néri JDSV, Silva VPD, Ramalho LMP, De Castro LP, Santos JND. Necrotizing sialometaplasia: a case report of a non-ulcerated histopathological presentation. Dermatol Online J. 2020;26(12):13030/qt3274n86z.

10. Garcia NG, Oliveira DT, Faustino SE, Azevedo AL. Necrotizing sialometaplasia of palate: a case report. Case Rep Pathol. 2012;2012:679325.

11. Carlson DL. Necrotizing sialometaplasia: a practical approach to the diagnosis. Arch Pathol Lab Med. 2009;133(5):692-8.

12. Dadfarnia T, Mohammed BS, Eltorky MA. Significance of Ki-67 and p53 immunoexpression in the differential diagnosis of oral necrotizing sialometaplasia and squamous cell carcinoma. Ann Diagn Pathol. 2012;16(3):171-6.

13. 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(3):317-25.

14. Rizkalla H, Toner M. Necrotizing sialometaplasia versus invasive carcinoma of the head and neck: the use of myoepithelial markers and keratin subtypes as an adjunct to diagnosis. Histopathology. 2007;51(2):184-9.

15. Gupta A, Priyadarshinee A, Rao LN, Redhu A, Jha KS. Necrotizing sialometaplasia-A self-limiting condition which poses a diagnostic dilemma. Clin Case Rep. 2021;9(4):2019-2022.

16. Penner CR, Thompson LD. Necrotizing sialometaplasia. Ear Nose Throat J. 2003 Jul;82(7):493-4.

17. Solomon LW, Merzianu M, Sullivan M, Rigual NR. Necrotizing sialometaplasia associated with bulimia: case report and literature review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007 Feb;103(2):e39-42.

18. Medeiros MRS, Barros CCDS, Miguel MCDC, da Silveira ÉJD, de Oliveira PT. Necrotizing sialometaplasia: A report of two cases and review of the literature. Stomatologija. 2022;24(2):56-60.

19. Anneroth G, Hansen LS. Necrotizing sialometaplasia. The relationship of its pathogenesis to its clinical characteristics. Int J Oral Surg. 1982;11(5):283-91.

20. Chen S, Peng J, Yuan C, Sun L, Zhang R, Sun Y. Sialadenoma papilliferum: clinicopathologic, Immunohistochemical, molecular analyses of new five cases and review of the literature. Diagn Pathol. 2021 Mar 12;16(1):22.

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Mateus José Dutra			x		x	x	x	x		x			x	x
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