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Necrotizing Sialometaplasia of the Larynx: A Rare Entity Obscuring a Malignancy

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Introduction: Necrotizing sialometaplasia is a rare, benign, and self-limiting inflammatory lesion that commonly involves minor salivary glands. It is theoretically associated with ischemia. It is commonly found in the palate, and laryngeal presentation is a very unusual entity. Almost half of such cases have an underlying malignancy; therefore, suspicion of a malignant lesion should be high when this entity is found at any laryngeal level.

Case presentation: The present case was a 59-year-old male presenting a necrotizing sialometaplasia in the larynx, which obscured a malignancy, delaying the diagnosis until a positive metastatic cervical lymph node emerged.

Conclusion: Necrotizing sialometaplasia is an extremely rare pathology at the larynx, with only five cases reported in the literature. The current case was the 6th to date. Almost half of such cases presented a malignancy beneath the lesion; therefore, it is crucial to perform a close follow-up in such patients.

INTRODUCTION

Necrotizing sialometaplasia (NS) was first described by Abrams et al., [1] in 1973 as a necrotizing inflammatory affliction of minor salivary glands. This condition may be misdiagnosed as a malignancy, but the misdiagnosis can also happen in the opposite direction. This entity typically involves the seromucous glands located at the palate, buccal mucosa, tongue, tonsil, nasal cavity, trachea, larynx, maxillary sinus, and retromolar trigone. NS is not an uncommon lesion primarily located at the oral cavity, but to the authors` best knowledge, the laryngeal localization is only described in five cases [2-5]. Its etiology is unknown, but ischemia is suspected as the main cause of its pathogenesis. Surgery, systemic diseases, cocaine use, local anesthetics, radiation, and trauma may also be counted as triggers for this entity. The characteristic histology is necrosis of acinar cells and secondary squamous metaplasia. It is a self-limiting condition that resolves

spontaneously within 4 to 90 days, but in some cases, it may present an underlying malignancy within it. Therefore, there should be high suspicion of a malignant disease when presented in the larynx.

CASE PRESENTATION

A 59-year-old male patient referred to the clinic with marked dysphonia over the last month. He denied dyspnea or throat pain. His medical history included chronic obstructive pulmonary disease secondary to tobacco consumption. He denied excessive alcohol consumption. On the fiberoptic exploration, severe Reinke edema and aryepiglottic fold thickening with slight impairment of motility in the right hemilarynx, but no lymphadenopathies, were observed (Figure 1).

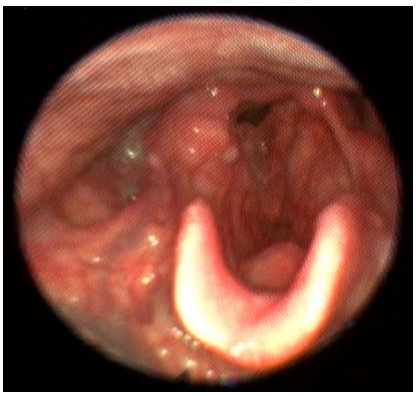

Figure 1: Thickening of the Right Aryepiglottic Fold With a Mild Paralysis of the Right Hemilarynx

Computed tomography (CT) scan images revealed a tumor centered on the right aryepiglottic fold, without impairment of the ipsilateral vocal fold or other laryngeal or thoracic regions. No adenopathies were identified; therefore, the suspected diagnosis was a T3N0M0 tumor. Biopsies were performed under general anesthesia, and the histopathology examination revealed no malignancy but mild dysplasia. Close follow-up was advocated, and since the laryngeal exploration was very suggestive of malignancy, further biopsies were taken under general anesthesia. Results of these biopsies were consistent with the diagnosis of NS without any dysplasia or malignancy suspicion. During the first four months of follow-up, the motility impairment continued to progress until the patient presented a right vocal fold paralysis. Since the pathology was on progression, a positron emission tomography (PET) scan was ordered, revealing a mild FDG uptake (SUVmax 6.7) at a right lymph node and ipsilateral supraglottic area (SUVmax 7.09), but not on other body locations (Figure 2). Since the suspicion of a malignancy augmented, and the laryngeal biopsies were continuously negative, a core needle biopsy of the positive lymph node was performed. The histological study cataloged the samples as a keratinizing squamous cell carcinoma metastasis. Following this diagnosis, further biopsies of the right aryepiglottic fold were taken, but no malignancy at the primary site was ever found.

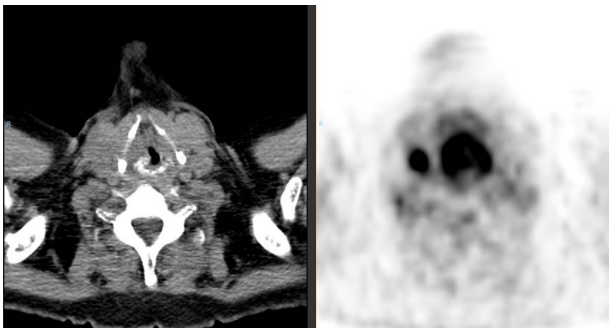

Figure 2: CT Scan and PET Scan of the Pathology
A) CT scan showing a bulging of the right supraglottic area without cartilage invasion; B) PET scan showing a mild FDG uptake at right lymph node and larynx

The stage of the tumor was a suspected T3N1M0 laryngeal neoplasm. Therefore, chemoradiation therapy was advised. The patient was programmed for 33 sessions of radiotherapy and three concomitant doses of 100 mg/m^2 cisplatin, but he was found dead at his home when he was about to end this treatment. The cause of the decease was a myocardial infarction. The surface of the mucosa was partially ulcerated and covered by an irregular acanthotic epithelium. The general architecture of the glands was preserved within pronounced and extensive squamous metaplasia of the salivary gland ducts and acini (Figure 3). In some instances, there was a pseudo-infiltrative pattern and slight inflammation in the surrounding tissue. Some ducts were dilated within mucous or necrotic debris. Immunohistochemistry analysis pointed flattened basal cells at the periphery of epithelial islands; P53 test result was negative (Figure 4).

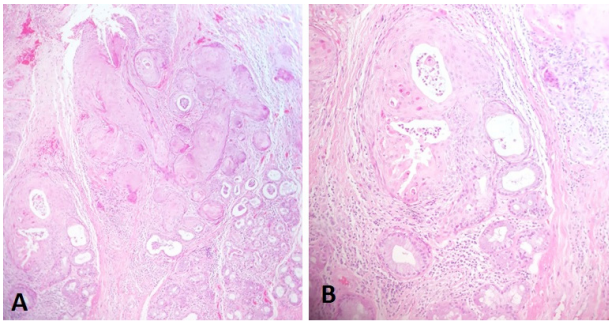

Figure 3: Histopathology Images of the Lesion
A) Squamous metaplasia of ducts and acini with preservation of the architectural pattern; B) Necrosis and inflammation within the specimen

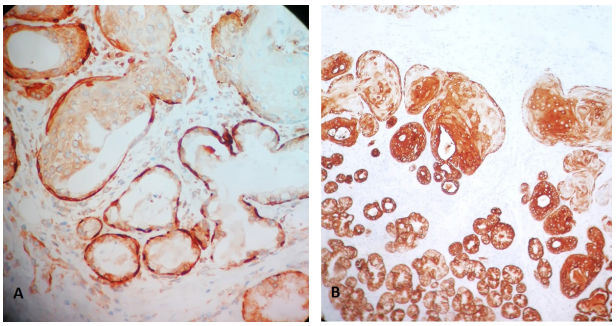

Figure 4: Histopathology Images of the Lesion
A) Calponin, immunoreactivity of basal cells at the periphery of squamous islands, scarce staining on the stromal cells; B) Cytokeratin 7; focally positive staining at the upper part of the image in the squamous islands, strong and diffuse staining of the secretory glands

DISCUSSION

NS is a benign, reactive inflammatory process that affects minor salivary glands. Hence, it can affect any location where minor salivary glands can be found, but it mainly affects the palate, accounting for 77% of the cases. Following this location, the oral cavity is the second most common location, 10%, and major salivary glands are the location of 9% of the cases. The remaining 4% of the cases are localized at miscellaneous sites of the upper aerodigestive tract, such as the larynx [6]. This location is described in scarce publications, with only five cases reported in the literature [2-5]. No NS is ever described at glottal level; it is not expected to occur at this location since seromucous glands are only localized at supraglottic and subglottic submucosa. This condition is known to affect males more than females and the mean age of presentation ranges between the 5th and 6th decades of life [6]. Generally, this entity is asymptomatic, but it may present with pain, numbness, or burning sensation. Its most typical clinical manifestation is a deep ulcerative lesion but can also present as a submucosal nodular swelling. Histopathological criteria to diagnose NS, as first described by Abrams et al., [1] are: coagulation necrosis of glandular acini, squamous metaplasia of salivary ductal epithelium, pseudoepitheliomatous hyperplasia of the overlying epithelium, granulomatous, inflammatory response, and maintenance of the overall lobular morphology. In the current case, all criteria were present. The histopathogenesis of this condition is composed of five stages: infarction, sequestration, ulceration, reparation, and healing [7]. The duration of this sequence varies considerably, but the ranges between 4 and 90 days are accepted, and it is uncommon to describe all the stages at any given biopsy specimen. The differential diagnosis is malignancy, principally mucoepidermoid carcinoma [2], but also includes adenosquamous carcinoma [4] or invasive squamous cell carcinoma [6, 8]. Nevertheless, as described in the current case, this entity can be associated with a malignancy, which obscures underlying disease diagnosis. In addition, if there was a lack of coherence between clinical behavior and histopathology, a more aggressive approach is suggested in the diagnostic efforts, including magnetic resonance imaging (MRI), CT scan, or even positron emission tomography (PET) to rule out an underlying malignancy. Association of NS and a laryngeal malignancy was described twice previously [2, 4], and it is supposed to occur as a compromise of the vascular supply to the tissue caused by a rapid growth pattern of the tumor, implying the consequent ischemia deriving into NS. This basis is suspected to be the one causing the obscurity of the laryngeal malignancy in the current case secondary to the covering of the true malignant process by NS. This theory takes even more significance due to the lack of other known risk factors, such as trauma, surgery, or radiation in the reported patient's larynx. Therefore, it is believed that when NS presents in the larynx, it takes extreme importance to rule out a malignancy within the lesion. Rizkalla et al., [5]reported the utilization of immunohistochemistry to distinguish NS from squamous cell and mucoepidermoid

carcinomas by identifying myoepithelial cells and cytokeratin expression.

NS is a benign condition that is extremely rare at the larynx level. To the authors` best knowledge, the current case was the 6th ever described in the literature, half of which presented a malignancy obscured by NS. It emphasizes the importance of close follow-up and highly malignant suspicion until proven otherwise in patients presenting a laryngeal NS.

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CONFLICTS OF INTEREST

The authors declared no conflict of interest.

ETHICS APPROVAL

This study was conducted according to the principles stated in the Declaration of Helsinki of 1983.

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