Review Article

Review on Diagnosis and Management of Necrotizing Sialometaplasia

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ABSTRACT

Necrotizing Sialometaplasia is defined as a benign, self-limiting inflammatory condition of tissues related to salivary gland. It accounts for less than 1percent of total of biopsied oral lesions. NS (NS) has a very good prognosis. Ischemia owing to trauma is the most common cause of NS, which is a perfectly benign lesion. With or without biopsy, the lesions heal on their own. The goal of a biopsy is to rule out cancer as the cause of their troubling clinical symptoms. The majority of cases of NS are thought to be caused by vascular ischemia. Management of NS doesn't necessates surgery or medications as the disease is self-healed one, surgery is only applied when cellular masses are massive. This article aims to overview epidemiology, diagnosis and management of NS.

Keyword: Necrotizing Sialometaplasia, inflammation, Ischemia, salivary gland.

Introduction

Necrotizing Sialometaplasia (NS) is defined as a benign, self-limiting inflammatory condition of tissues related to salivary gland that can clinically and histologically resemble carcinoma of squamous cells or mucoepidermoid carcinoma, resulting in unnecessary invasive surgery [1]. Abrams et al. described this pathological condition as a responsive necrotizing inflammatory disease that include salivary glands of the hard palate in 1973 [1, 2]. It accounts for less than 1percent of total of biopsied oral lesions. It can appear everywhere there is salivary gland tissue. Traditionally, the mucoserous glands of the hard palate are involved. Nasal cavity, trachea, parotid and Sublingual glands, submandibular gland, larynx, buccal mucosa, tongue, and tonsil, are among the other Sites where it has been documented [3-7]. In 1984, Mesa et colleagues evaluated over 10,000 oral biopsy specimens and found just three cases of NS, all of which had been misdiagnosed as other benign entities, accounting for only 0.03 percent of biopsied oral lesions. Shin et al looked at all biopsy materials collected from the oral cavity in a single Korean institution from 2012 to 2018 and discovered four cases of NS out of 726. 5 In 1991, the biggest series of NS patients showed an average age at diagnosis of 45.9 years, with males outnumbering females by a ratio of 1.9:1, and whites outnumbering blacks by a ratio of 4.9:1 [8-10]. The majority of cases of NS are thought to be caused by vascular ischemia. A necrotic myocutaneous reconstruction flap, embolization following carotid endarterectomy, sickle cell anaemia,

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Or Raynaud phenomenon has all been described to produce vascular compression. This pathogenic process is supported by the connection of nearby neoplasia that results in ischemia necrosis of the glandular elements and the histologic characteristics of NS. Local anaesthetic injections caused NS in a rat model in an experiment. Tobacco usage has been proposed as a probable cause of NS [11-13].

Epidemiology and Prognosis

Based on observations from 10,000 oral biopsy specimens, Mesa and colleagues observed a 0.03 percent incidence. However, they point out that this figure excludes cases of NS that recover without the need for biopsy. Cases of NS in whites exceeded cases in blacks by a ratio of 4.9:1 according to Brannon and colleagues. Given the white-to-black ratio in the United States, no major racial preference appears to exist. The ratio of men to women is roughly 2:1. The average age of patients with NS is 47.9 years, with a range of 17 to 80 years. Female patients are on average 43.1 years old, while male patients are on average 50.3 years old. An 18-month-old infant was diagnosed with NS [14, 15]. Because the first reports occurred in groups of closely residing military men, an infectious, most likely viral, origin has been suggested, although multiple ultrastructural tests have failed to discover viral particles. Because several cases of NSM developed following maxillary tooth extractions, mechanical trauma has been identified as a predisposing factor. In these instances, administering a local anaesthetic into the hard palate could cause ischemia by two mechanisms: pharmacologic vasoconstrictor action and tissue resistance. While lidocaine alone has a vasodilator effect, adrenaline or noradrenaline are frequently coupled with lidocaine for their vasoconstrictive qualities, which can cause tissue ischemia. The hard palate's unique mechanical qualities, combined with its tight tissues, may also be considered as a causative agent. Extreme pressure on the submucosal arteries during injection may be caused by tissue resistance to local infiltration. Animal investigations using palatal lidocaine and epinephrine injections in NSM in rats have partially validated this idea. [16-19]. Because smoking and the use of some medicines might reduce blood circulation to the mucosa, they are classified as predisposing factors for NSM. Other substances, such as cocaine, are known to cause ischemia and necrosis of the nasal mucosa, as well as palatal perforation, when applied to the nasal or oral mucosa. Following general anesthesia GA, several occurrences of NSM have been reported, which could be a kind of local trauma caused by an inadvertent traumatic event during intubation or extubating, or by prolonged local pressure. The drugs used to produce GA have a peripheral vasodilatory impact; however, their action on the palate has not been studied. Chemical irritation from vomiting, gastrointestinal disorders are other probable predisposing variables. Bulimic individuals frequently use their fingers to force themselves to vomit. As a result, these individuals may be affected by a mix of mechanical and chemical variables. A primary etiologic component is thought to be the low pH of gastric contents contacting the oral mucosa [20-22]. NS (NS) has a very good prognosis. Ischemia owing to trauma is the most common cause of NS, which is a perfectly benign lesion. With or without biopsy, the lesions heal on their own. The goal of a biopsy is to rule out cancer as the cause of their troubling clinical symptoms. The NS of the small salivary glands of the hard and soft palates takes around 5 weeks to recover on average. Clinical criteria that may influence healing time include the extent of the lesion and whether or not bone perforation has occurred. The NS lesions are normally painless; however they can also produce pain and numbness. This lesion's most notable trait is its clinical appearance, which signals cancer. The clinical images depict a patient with a suspected cancerous tumor who underwent biopsy and was observed for nine weeks. The lesion appears to be regressing with time [14, 15]. The majority of palatal lesions are unilateral, although there are also midline, bilateral synchronous, and metachronous lesions. The presence of ischemic lobular necrosis of seromucous glands, squamous metaplasia of ducts and acini, preservation of intact lobular architecture despite necrosis and inflammation, and accumulation of necrotic debris in adjacent lobules are the histological criteria proposed by Abrams et al,1 1973. Clinical characteristics and histological analysis are used to make the diagnosis. In prior studies, squamous cell carcinoma and mucoepidermoid carcinoma were included as differential diagnoses. Because the lesion is self-limiting and cures in 6 to 8 weeks, no special treatment is necessary. This self-limiting illness has yet to be recorded in Nepal, which prompted us to investigate [23-25].

Diagnosis

Although it is widely recognized that practically all NSM patients evaluated did not show radiographic changes, saucerization of the adjacent bone was seen in 4 cases reported. Magnetic resonance (MR) study of the characteristics of NSM revealed that this lesion was hyperintense on T2 and hypointense on T1. According to Lee et al, an MRI scan revealed a widespread infiltrating image indicative of a cancerous lesion in an NSM case linked with an adenoid cystic carcinoma, while a multislice computed tomographic analysis revealed no bone alterations. The lesion is frequently covered by hyperplastic squamous stratified epithelium with elongated epithelial ridges when examined under the microscope

Acinar necrosis is characterised by the collapse of mucus-secreting acinar cells with the preservation of acinar outlines, as well as areas packed with mucin, cellular debris, and inflammatory infiltrate of different intensities composed of polymorphonuclear neutrophilic leukocytes, plasma cells, macrophages, and multiple eosinophils [26-29]. The development of ductal squamous metaplasia is the most obvious and significant diagnostic characteristic. A squamous alteration in the cell covering the gland ducts distinguishes it. These squamous cells multiply, obliterating the lumen and changing the ducts into solid masses of squamous stratified epithelial cells with eosinophilic cytoplasm and homogeneous, bland nuclei. It's worth noting that mitotic cells are sparse and appear normal, with no abnormal traits [30]. The expanded rete page of the superficial epithelium is frequently seen near to these solid epithelial masses. This result is indicative of cancer and can lead to a squamous cell carcinoma misdiagnosis. These epithelial solid masses come in a variety of dimensions and densities, have smooth contours, and are occasionally accompanied by areas of fibrosis. Microscopic characteristics of NSM can sometimes lead to the misdiagnosis of r degenerative changes due to age. Lesions in diabetic individuals who have poor control over their disease with mucormycosis can occasionally mirror NSM, but they should not be confused with sialometaplasia [31-35]. Sub acute necrotizing sialadenitis, syphilis, and tb all require microscopic examination for differential diagnosis. Immunohistochemistry may aid in the differentiation of mucoepidermoid carcinoma from NSM lesions. Non-neoplastic breast parenchyma, bronchial mucosa, lung, and sweat gland lesions with similar microscopic appearance have been reported, and there have been multiple instances of malignant and benign tumors associated with NSM lesions, indicating that NSM could emerge as secondary phenomena [36-37]. Squamous cell carcinoma and mucoepidermoid carcinoma are the two most important differential diagnosis. The histology and clinical appearance of nicotinic stomatitis, which is related with cigarette smoking, is relatively comparable in the dentistry literature. With many foci localized to the palate, it tends to be multifocal and substantially more punctate. These latter lesions are not preneoplastic and will go away once you stop smoking. Although not all cases of NSM will be linked to an identifiable causative event, clinical history can assist identify it. However, interpreting these lesions in the appropriate clinical settings is extremely useful when possible. Single-cell necrosis and hyperchromatic, angulated cells can cause serious cytologic atypia. A multiplication of tissue culture such as fibroblasts and granulation tissue may be found in a major salivary gland, such as the parotid. The best histologic indication is the preservation of lobular architecture, which is best visible at low magnification [38]. The application of immunohistochemistry as an adjuvant to diagnosis has been studied and suggested because squamous epithelium can appear startlingly abnormal, with single-cell necrosis. Myoepithelial markers (smooth muscle antibody, p63, calponin), basement membrane markers (laminin, collagen type IV), E-cadherin, and several cytokeratins (CK5, CK6, CK7, CAM 5.2) have been also used for diagnosis. These tests could be useful when the basal layer is malignant the aforementioned antibodies may be supportive of a diagnosis of NSM if hematoxylin-eosin staining is ambiguous, but they are not pathognomonic. All test results must be evaluated in context, both within and outside of the therapeutic situation. As a result, many serial sections and a properly orientated tissue section remain the gold standard for diagnosing NSM at the moment [39, 40].

Management

NSM does not necessates treatment because ulcers or lesions recover within weeks, and it is vital to note that no surgical operation should be performed after the initial biopsy for diagnosis. Recently, 10 mg of intralesional triamcinolone was tried with no success, and most experts think that incisional biopsy is sufficient and that NSM lesions will cure spontaneously by secondary intention during the next 3 - 12 weeks [41-43]. NSM recurrence is extremely uncommon, with only one incidence of new lesions being reported. Nonsteroidal anti-inflammatory medications suppress prostaglandin synthesis to produce anti-inflammatory, analgesic, and antipyretic responses. They primarily compete with cyclooxygenases enzymes that catalyze the formation of cyclic endoperoxides from arachidonic acid to create prostaglandins [44, 45]. Prostaglandins and their derivatives, such as prostacyclin and thromboxane, have a role in physiological activities like protecting the mucosa of the stomata, platelet aggregation, and regulation of the kidney function. They also have a well-known pathophysiological function in inflammation, hyperthermia, and pain. Prostaglandins are powerful inflammatory mediators that cause edema, discomfort, and vasodilation. Analgesia and a reduction in inflammation are linked to the suppression of these substances [44, 45]. Cannon et al [14]. Showed in 2006 that long-term use of systemic nonsteroidal anti-inflammatory medications raises the risk of developing cardiovascular disease. The most developed justification for the cardiovascular potential danger is the inhibition of prostacyclin and prostaglandin E2, which is mediated by this class of drugs; in fact, prostacyclin is a prostanoid that acts as a restraint on

mediators of platelet activation, hypertension, and atherogenesis, including thromboxane A2 [46]. Although surgery is rarely necessary in the treatment of NSM, it can be beneficial in some patients with abnormally large diameters. Finally, the findings of this case and literature study show that NSM can have a wide range of clinical and microscopic symptoms, as well as a number of putative but mainly unproven causative causes. As a result, clinicopathologic correlations are crucial for a conclusive diagnosis. The microscopic findings in the current investigation support the idea of ischemia as an etiologic component. Although NSM is self-limiting and recovers with just minimum supportive care in the vast majority of instances, uncommon cases can grow to be quite large. Surgical debridement followed by flap coverage should be considered as a potential therapy option in these circumstances, as it improves healing conditions while also lowering the risk of sepsis [47, 48].

Conclusion

In necrotizing sialometaplasia patients, vascular ischemia is considered the main causative agent for such a condition; other causes include mechanical trauma and smoking. Diagnosis is an essential step specially to differentiate between NS and tumors as they share having cellular masses. The main diagnostic tool is the microscopic examination. Recently immunohistochemistry is considered as an adjuvant diagnostic tool. Management of NS doesn't necessates surgery or medications as the disease is self-healed one, surgery is only applied when cellular masses are massive.

Conflict of Interest

None

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None

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