Histopathology and Its Role in Diagnosing Necrotizing Sialometaplasia: A Report of Three Cases

Indirani VL, Gayathri Ramesh, Gauri Mishra, Amrita Raj

Abstract

Necrotizing sialometaplasia is an uncommon benign, self limiting, inflammatory lesion of salivary gland which can be both clinically and histologically mistaken for mucoepidermoid carcinoma or squamous cell carcinoma. Here we report the three cases of Necrotizing Sialometaplasia which represented with different symptoms and locations. The purpose of this paper is to report three cases of necrotizing sialometaplasia to highlight the potential diagnostic pitfall.

Key words: Necrotizing Sialometaplasia; Palatal Ulcer; Pseudoepitheliomatous Hyperplasia.

Case Report-1

A 24 year old male patient complained of ulcer in the right palatal region associated with pain since 10 days measuring about 1.5x2cm. On inspection an ulcer was observed on the right part of hard palate with erythematous borders. Clinical diagnosis of necrotizing sialometaplasia was given. A biopsy was performed. Histopathology showed hyperplastic epithelium with some areas of pseudoepitheliomatous hyperplasia. Lobular architecture of acini was maintained. Squamous metaplasia of ducts with central residual lumen is evident. Inflammatory infiltrate was evident. On higher magnification sections showed bland epithelial islands. Histopathological diagnosis was confirmative of necrotizing sialometaplasia (Fig 1a & 1b).

Case Report-2

A 29 year old female patient presented with palatal ulcer persisting since two weeks. On inspection, an ulcer measuring approx. 2.0x2.0cm was observed. Ulcer had smooth borders with punched out appearance and erythematous periphery. A clinical diagnosis of carcinoma was made. Histology showed pseudoepitheliomatous hyperplasia of the overlying epithelium. Normal lobular architecture of acini was preserved. Necrosis of acini was noticed. Squamous metaplasia of ducts was seen with inflammatory infiltrate. These features were confirmatory for necrotizing sialometaplasia (Fig 1c).

Case Report-3

A 38 year old male patient gave a history of swelling in upper lip since a month. Swelling was nodular type and confined to right part of the lip which was non tender and was persisting since one week. As there was no history of any trauma, insect bite or related to any etiology, a provisional diagnosis of granulomatous disease was made. Histology revealed preservation of normal lobular architecture with necrosis of acini. Squamous metaplasia of ducts was evident.
No pseudoepitheliomatosus hyperplasia was seen. A histopathological diagnosis of necrotizing sialometaplasia of lip was given (Fig 1d).

<table>
<thead>
<tr>
<th>Case</th>
<th>Age / sex</th>
<th>Clinical presentation</th>
<th>Site</th>
<th>Size</th>
<th>Time to resolve</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>24/ M</td>
<td>Unilateral ulcer with pain</td>
<td>Hard palate</td>
<td>1.5x2 cm</td>
<td>4 weeks</td>
</tr>
<tr>
<td>2.</td>
<td>29/ F</td>
<td>Unilateral ulcer without pain</td>
<td>Hard palate</td>
<td>2x2 cm</td>
<td>No follow up</td>
</tr>
<tr>
<td>3.</td>
<td>38/ M</td>
<td>Nodular swelling without pain</td>
<td>Upper lip</td>
<td>2x2.5 cm</td>
<td>5 weeks</td>
</tr>
</tbody>
</table>

Table 1: Relevant clinical details of the three reported cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudoepitheliomatosus hyperplasia</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Preservation of lobular architecture</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Coagulation necrosis of glandular acini</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Squamous metaplasia of ducts and acini</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Mixed inflammatory infiltrate</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Bland epithelial islands at higher magnification</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Residual lumina</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Ulceration</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2: Histopathologic features seen in individual case

Discussion

Abrams et al. in 1973 defined NSM as a reactive necrotizing inflammatory process involving the minor salivary glands of hard palate. Since then numerous cases have been reported with hard palate being the most common site followed by upper and lower lip, maxillary sinus, floor of mouth, tongue, retro molar area, oral mucosa, tonsillar fossa, major salivary glands, nasal cavity, incisor canal, larynx, soft palate and soft-hard palate junction. According to Brannon et al,\textsuperscript{6} the mean age at the time of diagnosis is 46 years, with predilection for male than females. The most common clinical presentation is a deep seated ulcer over the palate with an indurated and well-delineated border mimicking a carcinoma. The ulcer can be unilateral or bilateral. Rarely, it may present as a swelling or a mass with and without associated with pain or parasthesia.\textsuperscript{6-9}

The typical microscopic features of NSM include ulceration of the overlying epithelium and pseudoepitheliomatosus hyperplasia, with preservation of the lobular architecture of salivary glands, mixed inflammatory reaction and squamous metaplasia of ducts and acini with cells exhibiting uniform nucleus with occasional normal mitosis without cellular atypia. The presences of residual lumina in some metaplastic nests are characteristic of NSM.\textsuperscript{4} Other histopathological finding such as eosinophilic granulocytes in the inflammatory process may be encountered. This feature may indicate an immunologic or allergic mechanism in the pathogenesis of this disease, as emphasized by some authors.\textsuperscript{5,10} The squamous metaplasia of minor salivary gland ducts and acini may contain apoptotic cells and areas of mucin spillage. Older lesions may show reactive fibrosis.\textsuperscript{4,8}

Anneroth and Hansen\textsuperscript{10} proposed five histologic stages in the development and evolution of necrotizing sialometaplasia: infarction, sequestration, ulceration, repair, and healing. They emphasized that these stages could overlap and would be dependent upon the extent and severity of damage. These different stages may occur simultaneously in different areas and the severity and extension of the damage depend on the healing capacity of the host tissues. If the injury is extensive, the sequestration of the necrotic tissues results in ulcer formation with dense inflammatory response, as observed in our patient. 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.\textsuperscript{3,8,10}

When histopathological features of all three cases were compared we observed that, preservation of lobular architecture and squamous metaplasia of ducts and acini are evident in all the three cases. Pseudoepitheliomatous hyperplasia, necrosis, mixed inflammatory infiltrate, bland epithelial islands at higher magnification and residual lumina were seen in two of the cases. Features like ulceration, mucin spillage and apoptotic bodies were absent in all the three cases.

Differential Diagnosis

Clinically, deep ulcer of NSM can be confused with granulomatous diseases such as syphilitic gumma and deep mycosis lesions, which may show a sharp
demarcation. Opportunistic infections are common in patients with poorly controlled diabetes and may mimic necrotizing sialometaplasia and have to be clear and specific about what to be expressed here. For example, clinically, number conditions may simulate NSM such as syphilis, deep fungal diseases, nicotina stomatitis, squamous cell carcinoma and salivary gland tumors. However, the ulcer of syphilis is usually seen in the tertiary stage of syphilis that may present as a clean surfaced ulcer with perforation of the palate, a feature untypical of NSM.3

![Image](image)

**Figure 1:** The photomicrographs of H & E stained section of case 1 under 10X shows pseudoepitheliomatous hyperplasia (a) and under 45X shows bland epithelial islands (b), case 2 under 20X shows coagulation necrosis of glandular acini (c) and case 3 under 45X shows squamous metaplasia of ducts and acini (d).

The second most important differential diagnoses include squamous cell carcinoma and mucoepidermoid carcinoma. An entity described in the dental literature as nicotinic stomatitis, associated with cigar and pipe smoking, has a quite similar clinical presentation. It tends to be multifocal and grossly more punctate, with multiple foci localized to the palate. These latter lesions usually resolve upon cessation of smoking.3

Histopathology plays a key role in diagnosing a case of NSM. Since NSM clinically simulates squamous cell carcinoma and mucoepidermoid carcinoma, histopathology plays a major role in making a conclusive diagnosis of NSM. NSM shows features like bland appearing morphology of metaplastic squamous cells, absence of cellular atypia and preservation of lobular morphology which are absent in squamous cell carcinoma and mucoepidermoid carcinoma. In addition, low-grade mucoepidermoid carcinoma usually has cystic elements partially lined by mucocytes rather than being incorporated into the squamous islands, as in NSM.6

Another lesion which should be histopathologically differentiated from NSM is subacute necrotizing sialadenitis (SANS). SANS clinically presents as nonulcerated nodular lesion on palate usually associated with abrupt onset of pain. Histologically it is characterized by focal acinar cell necrosis secondary to the inflammatory process and
slight atrophy of ductal cells; neither ductal squamous metaplasia nor pseudoepitheliomatosus hyperplasia is observed in SANS.\textsuperscript{7} According Dadfarnia et al.\textsuperscript{11} Ki-67 and p53 staining are generally more intense and are increased in malignancy, and hence these findings may be helpful adjuncts in the differential diagnosis of NS from SCC in appropriate clinical setting.\textsuperscript{11}

**Conclusion**

Considering the self-healing behavior of this pseudo-tumoral condition, the histopathology knowledge of necrotizing sialometaplasia is necessary to make a correct diagnosis in order to avoid mismanagement of affected patients with an inadequate or unnecessary approach. Hence, we emphasize the need for an incisional biopsy to be analyzed by an experienced pathologist to establish a correct diagnosis, since the clinical features of this condition can mimic other diseases, particularly the nodular type may mimic salivary gland tumors.

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**References**


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