

Case Report

Lymphoid-rich lesions of the salivary glands: how not to miss malignancy

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ABSTRACT

Salivary gland lesions with prominent lymphoid components pose a significant diagnostic challenge in cytopathology due to considerable morphological overlap among reactive, benign, and malignant conditions. While fine-needle aspiration cytology (FNAC) is commonly used as a first-line diagnostic tool, its accuracy may be limited by sampling variability and tumor heterogeneity, particularly in lymphoid-rich neoplasms where the epithelial component is minimal or obscured. This report presents three cases that illustrate frequent diagnostic pitfalls in lymphoid-rich salivary gland lesions: acinic cell carcinoma with prominent lymphoid stroma initially misdiagnosed as chronic sialadenitis, adenoid cystic carcinoma of the submandibular gland with cervical lymph node metastasis, and Warthin's tumor mimicking chronic granulomatous sialadenitis on cytology. These cases underscore the importance of meticulous cytomorphological assessment, adequate sampling, and comprehensive clinicoradiological correlation. Histopathological examination remains indispensable for establishing a definitive diagnosis in ambiguous cases. Greater awareness of lymphoid-rich variants of salivary gland tumors and maintaining a low threshold for surgical biopsy are essential to avoid missed or delayed diagnoses of malignancy.

Keywords: FNAC, Acinic cell carcinoma, Adenoid cystic carcinoma, Warthin's tumor, Lymphoid-rich salivary gland lesions, Minor salivary glands

INTRODUCTION

Lymphoid-rich lesions of the salivary glands constitute approximately 2-8% of salivary gland tumors and encompass a broad spectrum of benign and malignant conditions.¹ These lesions pose a diagnostic challenge due to the frequent admixture of epithelial and lymphoid components, resulting in considerable overlap between reactive, benign, and malignant entities. Fine-needle aspiration cytology (FNAC), although widely used as a first-line diagnostic tool, may be limited by sampling error and morphologic heterogeneity.^{1,2}

Lymphocytic infiltration may disrupt normal salivary gland architecture by replacing acini and ducts, encasing nerves, and extending into interlobular connective tissue and adjacent fat. Distinguishing reactive lymphoid

processes from epithelial malignancies and identifying lesions with malignant potential remain critical diagnostic hurdles.³

This case series highlights the cytological pitfalls associated with lymphoid-rich salivary gland lesions and emphasizes histopathological correlation to avoid missed malignancies.

CASE REPORT

Case 1: Acinic cell carcinoma with lymphoid-rich stroma

A 54-year-old woman presented with a slowly progressive right parotid swelling of two years' duration, associated with dull aching pain. Imaging revealed a well-defined heterogeneously enhancing lesion in the deep lobe of the

right parotid gland. FNAC showed sparse salivary epithelial elements with abundant lymphoid cells, suggestive of chronic sialadenitis (Figure 1a).

The patient underwent superficial parotidectomy. Histopathological examination predominantly showed features of chronic sialadenitis with lymphoid aggregates. However, focal areas revealed nests and acinar arrangements of polygonal cells with granular basophilic cytoplasm and microcystic spaces, consistent with acinic cell carcinoma (Figures 1b and c). This case illustrates the masking effect of lymphoid stroma leading to initial cytological under-diagnosis.

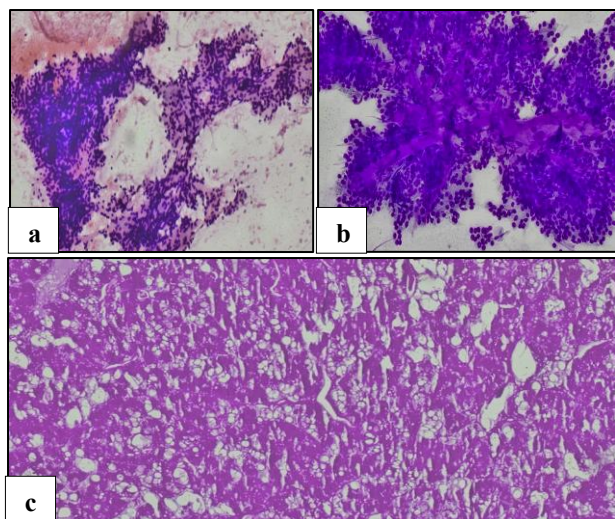


Figure 1: (a) Chronic sialadenitis 10x MGG, (b) acinar pattern 10x MGG, and (c) acinic cell carcinoma HPR 10x H and E stain.

Case 2: Adenoid cystic carcinoma with cervical lymph node metastasis

A 53-year-old man presented with a left submandibular swelling and facial nerve involvement. Imaging suggested a malignant salivary gland tumor with regional lymphadenopathy (Figure 2a). FNAC revealed basaloid epithelial cells arranged in cribriform and syncytial patterns with hyaline globules, consistent with adenoid cystic carcinoma.

Surgical excision demonstrated adenoid cystic carcinoma of the submandibular gland with metastatic deposits in cervical lymph nodes and extracapsular extension (Figures 2b and c). Tumor cells showed positivity for CD-117 on immunohistochemistry. This case emphasizes that cervical lymph node metastasis, though uncommon, is a significant prognostic indicator in adenoid cystic carcinoma.

Case 3: Warthin's tumor mimicking chronic sialadenitis

A 69-year-old male smoker presented with a painless parotid swelling. FNAC revealed benign ductal cells with lymphocytes, epithelioid histiocytes, and giant cells,

suggesting chronic sialadenitis with granulomatous reaction (Figure 3a). Superficial parotidectomy revealed a well-circumscribed tumor with cystic and solid areas.

Histopathology showed papillary structures lined by bilayered oncocytic epithelium with dense lymphoid stroma, confirming Warthin's tumor (Figure 3b). This case highlights how inflammation and sampling limitations may obscure classic cytological features.

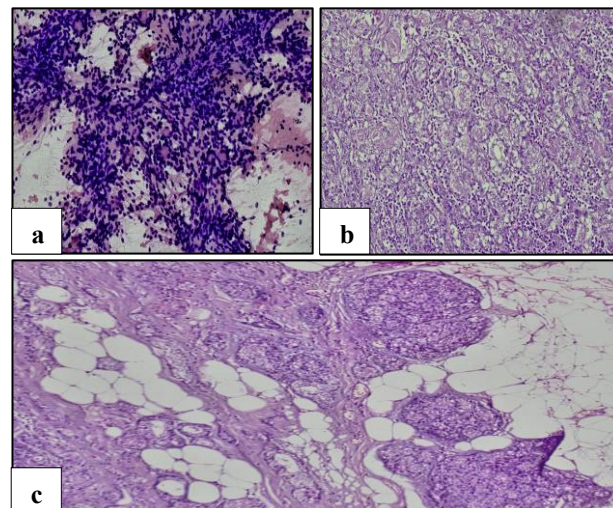


Figure 2: (a) Mets deposits to lymph node, AdCC 10x MGG, (b) Mets deposits to lymph node, AdCC HPR 10x H and E, and (c) extra capsular extension of AdCC HPR 10x H and E.

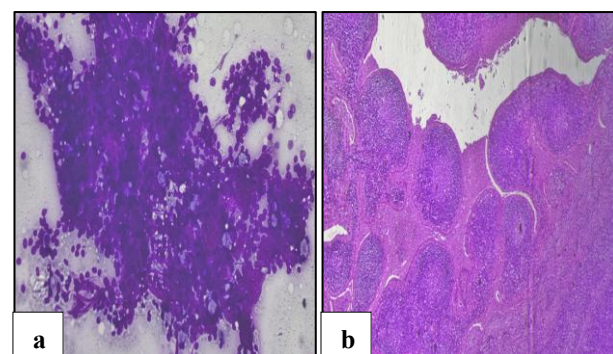


Figure 3: (a) Chronic sialadenitis 10x MGG, and (b) Warthin's tumor HPR 10x H and E.

DISCUSSION

Lymphoid-rich lesions of the salivary glands represent one of the most challenging diagnostic categories in cytopathology due to their marked morphological heterogeneity and frequent overlap between reactive, benign, and malignant entities. The diagnostic complexity is further compounded by the intrinsic limitations of FNAC, particularly sampling error and tumor heterogeneity, which are accentuated in lesions where the lymphoid component predominates over epithelial elements.¹ As demonstrated in the present case series, this

diagnostic pitfall can lead to underdiagnosis or delayed recognition of malignancy.

FNAC remains the first-line diagnostic modality for salivary gland swellings owing to its simplicity, safety, and high specificity. However, its sensitivity is variable, especially in cystic, low-grade, or lymphoid-rich tumors. Several studies have emphasized that salivary gland FNAC is among the most demanding areas in cytopathology, even for experienced cytopathologists, because a single aspirate may not be representative of the entire lesion. In lymphoid-rich lesions, aspirates are often dominated by mature lymphocytes, obscuring subtle epithelial atypia and resulting in false-negative or indeterminate diagnoses.^{1,2}

Acinic cell carcinoma (ACC) is a low-grade malignant salivary gland tumor that typically shows serous acinar differentiation. While classic cytological features include loosely cohesive clusters of cells with granular basophilic cytoplasm and microacinar arrangements, the lymphoid-rich variant of ACC poses a significant diagnostic challenge. In such cases, the dense lymphoid background may closely simulate chronic sialadenitis, Warthin's tumor, or benign lymphoepithelial lesions.² In case 1 of the present series, the overwhelming lymphoid population masked the neoplastic epithelial component, leading to an initial cytological diagnosis of chronic sialadenitis. Only thorough histopathological sampling revealed focal areas diagnostic of ACC. This underscores the importance of maintaining a high index of suspicion when evaluating lymphoid-rich aspirates, especially in long-standing or radiologically suspicious lesions. Even scant epithelial cells with granular cytoplasm should prompt consideration of ACC and warrant repeat aspiration or surgical excision.^{3,4}

Adenoid cystic carcinoma (AdCC) is characterized by slow but aggressive growth, perineural invasion, and a propensity for late local recurrence and distant metastasis. Cytologically, AdCC often exhibits basaloid cells arranged in cribriform or tubular patterns with hyaline globules; however, the presence of stromal hyalinization or accompanying lymphoid elements may complicate diagnosis. Traditionally, AdCC has been considered to have a low incidence of cervical lymph node metastasis. Recent literature, however, suggests that nodal involvement may be under-recognized and carries significant prognostic implications.^{5,6} In case 2, the presence of cervical lymph node metastasis with extracapsular extension highlights an aggressive disease course and reinforces the need for meticulous nodal evaluation. FNAC of suspicious lymph nodes should be actively pursued, and identification of nodal disease should influence staging, surgical planning, and adjuvant therapy decisions.⁷

Warthin's tumor is a benign salivary gland neoplasm classically composed of oncocytic epithelium and dense lymphoid stroma and is strongly associated with smoking.

Although FNAC is generally reliable for diagnosing Warthin's tumor, diagnostic difficulty arises when aspirates are cystic, inflamed, or paucicellular.^{8,9} In case 3, granulomatous inflammation and paucity of oncocytic epithelial cells led to a cytological impression of chronic sialadenitis. This highlights a well-recognized pitfall where inflammatory changes overshadow diagnostic oncocytic features. Such cases reinforce the principle that persistent or enlarging salivary gland masses with inconclusive cytology should not be dismissed as benign inflammatory lesions without adequate histological confirmation.^{10,11}

A unifying theme across all three cases is the predominance of lymphoid elements that masked the underlying epithelial pathology. These cases collectively emphasize several critical diagnostic principles. First, sampling adequacy is paramount—multiple passes and targeted aspiration of solid areas significantly improve diagnostic yield. Second, lymphoid-rich aspirates require heightened vigilance, particularly in older patients and smokers, as they may conceal an underlying neoplasm. Third, clinicoradiological correlation is essential, and any discordance between imaging findings and cytological interpretation should prompt repeat FNAC or biopsy. Ultimately, histopathological examination remains the gold standard for definitive diagnosis, particularly in lesions with marked heterogeneity or deceptive cytomorphological features.

By highlighting these diagnostic pitfalls and reinforcing a systematic, cautious approach, the present case series contributes valuable practical insights for cytopathologists and clinicians alike, aiming to reduce missed or delayed diagnoses of salivary gland malignancies.

CONCLUSION

Lymphoid-rich salivary gland lesions represent a significant diagnostic challenge in cytopathology. FNAC findings must be interpreted cautiously, with awareness of overlapping features and potential pitfalls. Representative sampling, clinicoradiological correlation, and timely histopathological confirmation are critical to avoid misdiagnosis and ensure optimal patient management.

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