

# Sjogrens Syndrome Presenting as Lymphoepithelial Lesion on Cytology: A Case Report

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**Abstract:** Fine needle aspiration cytology (FNAC) is an important modality in the diagnosis of various salivary gland pathologies. Our patient eighteen year old unmarried female with gradually increasing swelling in parotid & submandibular region since two years and symptoms of dryness of eyes & mouth and was referred for FNAC which revealed lymphoepithelial picture with features suggestive of Sjogrens syndrome. Blood serum analysis found raised titres for auto antibodies like anti Ro-52 (SS-A), anti-La (SS-B) and anti-ANA antibodies, thus, confirming the cytological diagnosis and establishing the importance of FNAC in salivary gland lesions.

**Keywords:** Fine-needle aspiration cytology, salivary glands, Sjogrens syndrome, Lymphoepithelial lesion

## 1. Introduction

Sjogrens syndrome is an autoimmune disorder presenting with dry eyes (*keratoconjunctivitis sicca*) and dry mouth (*xerostomia*) resulting from immune mediated destruction of the lacrimal and salivary glands. The lacrimal and salivary glands characteristically show dense lymphocytic infiltration consisting mainly of activated CD4+ helper T cells and some B cells, including plasma cells. Serologic studies frequently reveal autoantibodies. Antibodies against two ribonucleoprotein antigens, SS-A (Ro) and SS-B (La) can be detected in as many as 90% of patients by sensitive techniques. Sjögren syndrome occurs most commonly in women at the perimenopausal age (approximately 90%)<sup>1</sup>. As might be expected, symptoms result from inflammatory destruction of the exocrine glands causing xerostomia and keratoconjunctivitis.<sup>2</sup> Cytomorphology of salivary glands in such cases reveals cellular aspirate composed of mixed population of lymphocytes, plasma cells, tingible-body macrophages, germinal centre fragments & lymphoepithelial islands. Differential diagnosis on cytology includes chronic sialadenitis, lymphoepithelial cyst, HIV-associated cystic lymphoepithelial lesions, Warthin tumour and extra nodal marginal zone B-cell lymphoma of Mucosa-Associated Lymphoid Tissue (MALT).

## 2. Case History

We present a case of an eighteen year old female who was unmarried and presented with gradually increasing swelling in parotid & submandibular region since two years (Fig 1, 2) & was referred for FNAC. She had symptoms of dryness of eyes & mouth since six months along with multiple joint pains e.g. knee & elbow since three months. Ultrasonography revealed bilateral bulky parotid & submandibular gland with multiple round to oval well marginated & heterogeneous hypoechoic lesions within parotid glands with increased vascularity (Fig 3). FNAC revealed cellular aspirates composed of mature lymphocytes, plasma cells, tingible-body macrophages, germinal centre fragments along with frequent lymphoepithelial islands. The ductal cells showed reactive changes and acinar cells were sparsely present suggestive of a benign lymphoepithelial lesion (Fig 4, 5). In

extended investigations, blood serum analysis found anti Ro (SS-A) titres of 184.12(positive > 20), anti La titres of 196.13 (positive > 20) (SS-B) and anti-ANA antibodies titre of 1:320 with fine speckled ANA pattern. Rheumatoid factor was also positive in serum analysis.

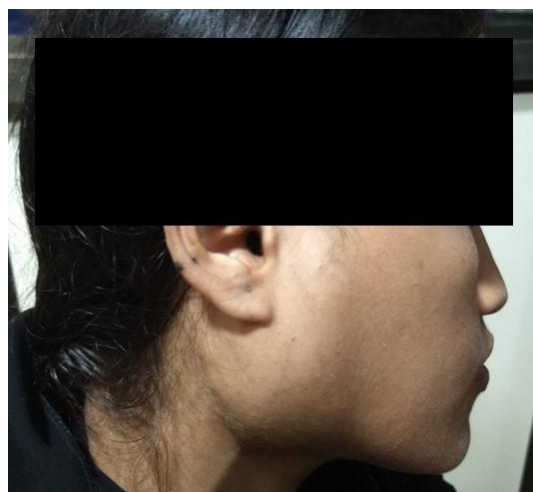
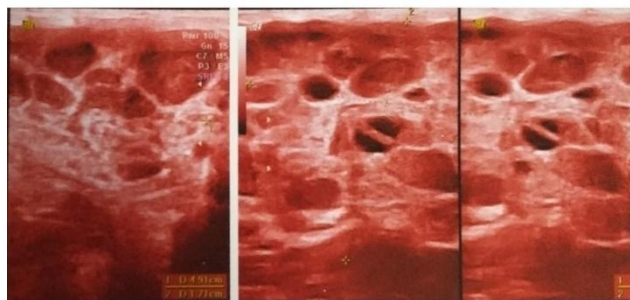


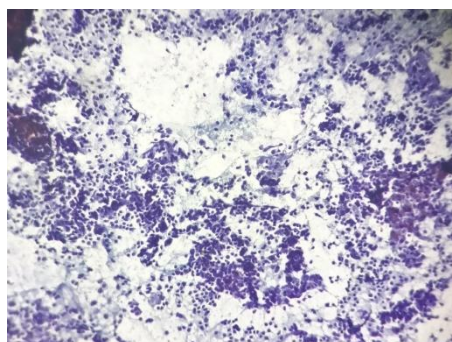
Figure 1: Fine-needle aspiration cytology, salivary glands, Sjogrens syndrome



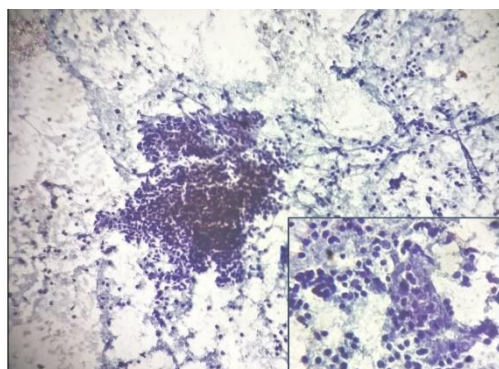
Figure 2: Figure showing bilateral parotid enlargement



**Figure 3:** Ultrasonography of parotid region revealed heterogeneous hypoechoic lesions within parotid glands with increased vascularity



**Figure 4:** FNAC of parotid swelling showing cellular aspirates with a mixed population of mature lymphocytes, plasma cells, tingible-body macrophages, germinal centre fragments and lymphoepithelial islands.



**Figure 5:** Cellular aspirates showing mixed lymphocytic infiltrate along with ductal cells showing reactive changes and sparse acinar cells suggestive of a benign lymphoepithelial lesion

### 3. Discussion

Sjögren's syndrome is an immunologically mediated chronic disease characterised by destruction of the lacrimal as well as salivary glands. Primary Sjögren's syndrome (pSS) presents alone, also known as the *sicca syndrome*, and secondary SS (sSS) occurs in connection with other autoimmune rheumatic disease. This diversity of symptomatic expression adds to the difficulty in the initial diagnosis, and to the identification of homogenous group of patients with a uniform etiopathogenesis or prognosis.<sup>3</sup> As might be expected, symptoms result from inflammatory destruction of the exocrine glands which include keratoconjunctivitis causing blurred vision, burning, and itching, and thick secretions that accumulate in the conjunctival sac as well as xerostomia (dryness of the buccal

mucosa) resulting in difficulty in swallowing solid foods, a decrease in taste, cracks and fissures in the mouth.<sup>2</sup> The **San Diego diagnostic criteria** for primary Sjögren's syndrome are as follows:

- Keratoconjunctivitis sicca,
- Xerostomia,
- Extensive lymphocytic infiltrate on minor salivary gland biopsy,
- Laboratory evidence of a systemic autoimmune disorder.

Pre-existing lymphoma, graft-versus-host disease (GVHD), acquired immunodeficiency syndrome (AIDS), and sarcoidosis<sup>4</sup> are the specific exclusions.

**Clinically**, parotid gland enlargement is present in half the patients; dryness of the nasal mucosa, epistaxis, recurrent bronchitis and pneumonitis are other symptoms. Manifestations of extraglandular disease are seen in one third of patients which include synovitis, pulmonary fibrosis, and peripheral neuropathy. In contrast to SLE, glomerular lesions are rare in Sjögren syndrome. Defects of tubular function, however, including renal tubular acidosis, uricosuria, and phosphaturia, often are seen and are associated with tubulointerstitial nephritis. About 60% of patients have another accompanying autoimmune disorder, such as rheumatoid arthritis. The patients may develop primary biliary cirrhosis, sclerosing cholangitis, pancreatitis, interstitial nephritis, interstitial lymphocytic pneumonitis and peripheral vasculitis.<sup>2</sup>

The **cytological picture** of a benign lymphoepithelial lesion is characterized by insidious swelling of one or several salivary and lacrimal glands. The aspirates show lymphoid cells with the same morphologic variability noted in reactive hyperplasia of lymph nodes. Small mature lymphocytes are admixed with follicular center cells, plasma cells and histiocytes. This appearance corresponds to the histology of such affected glands, which have abundant lymphoid tissue with large germinal centers. The tissue contains scattered solid epithelial rests, which represent myoepithelial proliferations, but cytologically few, if any; epithelial or epithelioid cells are encountered. A careful cytologic evaluation of the lymphoid infiltrate is needed to preclude a low-grade lymphoma. Low-grade malignant lymphomas can have either a monotonous or a mixed cell pattern, whereas smears from high-grade lymphomas are dominated by blasts. A cytologic diagnosis of malignant lymphoma should always be confirmed using immunocytochemistry to confirm the clonality of the lymphoid cells.<sup>5</sup> **Microscopic examination** of the enlarged salivary glands, both major and minor, may reveal a lymphoepithelial sialadenitis, also known as *benign lymphoepithelial lesion* (BLL). This is characterized by infiltration of the ductal epithelium by marginal zone or monocytoid B-cell type lymphocytes. The result is the formation of cellular aggregates commonly known as epimyoeplithelial islands although the myoepithelial component of these predominantly epithelial structures may be sparse or absent by immunohistochemistry. For a minor salivary gland biopsy to be diagnostic of Sjögren's syndrome it should contain at least four lobules with at least two foci of lymphocytes per 4 mm<sup>2</sup>; a focus is defined as a cluster of 50 or more

lymphocytes. The labial salivary gland biopsy has a sensitivity of 70% to 83%, and it is most useful in patients with partial San Diego criteria, not in patients in whom the index of suspicion is low. The terms *Mikulicz disease* and *Mikulicz syndrome* have been used in the past for salivary or lacrimal gland swellings resulting from Sjogrens syndrome and various other conditions.<sup>4</sup>

In addition, **Serologic studies** frequently reveal autoantibodies against two ribonucleoprotein antigens, SS-A (Ro) and SS-B (La) that can be detected in as many as 90% of patients by sensitive techniques.

It is not clearly established as yet if FNAC can replace histopathological diagnosis in such cases. However, Ma et al.<sup>5</sup> performed a retrospective study of 11 patients with benign lymphoepithelial lesions diagnosed postoperatively. They found that FNAC, among others, could be useful in the preoperative diagnosis of such lesions thus eliminating the need of biopsy/excision in these cases. However, some problems may arise in the differential diagnosis between a benign lymphoepithelial lesion and a small lymphocytic lymphoma which must be confirmed using immunocytochemistry to prove the clonality in cases of lymphoma.

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