

Fine needle aspiration cytology in the diagnosis of Sjögren's syndrome

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ABSTRACT

Introduction: Sjögren's syndrome is an autoimmune disease belonging to the group of collagenases. It is characterized by lymphocytic infiltration of the exocrine glands, leading to their impairment or complete dysfunction. The inflammatory process usually involves cells of the salivary or lacrimal glands. However, also other organs and systems can be affected.

Purpose: The presentation of a Sjögren's syndrome case. The pathologist's role in the disease diagnosis.

Case presentation: A 63-year-old female patient with the enlarged left parotid salivary gland and symptoms of xerostomia and xerophthalmia was referred for ultrasound imaging and fine-needle aspiration biopsy (FNAB). Ultrasonography revealed inhomogeneous echostructure of the

salivary gland with multiple tiny, oval, hypoechoic areas, hyperechoic zones of fibrosis and enhanced vascularization of the gland. The pathological analysis of FNA showed a benign lymphoepithelial lesion, and Sjögren's syndrome was suggested. Blood serum analysis found anti Ro-52 (SS-A), anti-La (SS-B) and anti-ANA antibodies at 1:1,000 titer. Sjögren's syndrome was diagnosed based on accessory investigations and the clinical condition of the patient.

Conclusions: The pathomorphological analysis of fine-needle aspiration biopsy of the salivary gland contributed to the diagnosis of Sjögren's syndrome in the patient.

Key words: Fine-needle aspiration biopsy, salivary glands, Sjögren's syndrome

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INTRODUCTION

After rheumatoid arthritis, Sjögren's syndrome is the second most common autoimmune disease belonging to the group of collagenases. The disease occurs predominantly in women at the perimenopausal age (approximately 90%) [1]. The inflammatory process usually involves exocrine glands (lacrimal and salivary), but also other organs and systems can be affected. Microscopically, it is characterized by lymphocytic infiltration of the glands, which results in their impairment or complete dysfunction. Two types of Sjögren's syndrome are distinguished – primary and secondary. The former is idiopathic, whereas the latter accompanies other connective tissue disorders, most frequently rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) [2].

The etiology of Sjögren's syndrome is unknown. A number of factors can be involved, including genetic, environmental and hormonal ones. It is believed that chronic stimulation of the immune system plays a key role in the disease pathogenesis, particularly the involvement of anti-Ro/SS-A and anti-La/SS-B antibodies. Among the environmental factors, such infectious agents as EBV, CMV, *Helicobacter pylori*, rubella virus, herpes virus or toxoplasmosis may play a role. Furthermore, some hormonal disorders, including lower estrogen level and estrogen-to-androgen ratio imbalance can be responsible [1,3,4].

In 95% of cases, Sjögren's syndrome is manifested by dry eyes (xerophthalmia) and dry mouth (xerostomia). Decreased secretion of tears causes gritty sensation under the eyelids, burning eyes and conjunctival hyperemia. Damage to the salivary glands may hinder mastication, swallowing of dry foods and speaking. The disease is also accompanied by some systemic symptoms, namely fatigue, fever, myalgia and arthralgia. Due to its nonspecific symptoms, the diagnosis of Sjögren's syndrome is often difficult. Some drugs, particularly antihistamines, antidepressants, anxiolytics, antihypertensives, anticholinergics or antiemetics may contribute to that difficulty [5-7].

Laboratory findings include hypergammaglobulinemia, ANA antibodies $\geq 1:320$, serum anti-Ro (SS-A) and anti-La (SS-B) antibodies and a positive rheumatoid factor [5]. Ultrasonography, scintigraphy, sialography and biopsy of the salivary glands can also be helpful [7-10].

Symptomatic treatment of Sjögren's syndrome consists mainly in the protection of the eyes, use of artificial saliva and sugar-free chewing gum. Moreover, anti-inflammatory drugs are also applied [11, 12]. Medications stimulating the exocrine glands are administered when the salivary glands are only partially impaired [13]. In secondary Sjögren's syndrome, treatment of the underlying disease is essential. The patient should

be constantly monitored and laboratory investigations have to be repeated to check for the presence of monoclonal protein due to increased risk of lymphomas in these patients [14].

Case report

A 63-year-old female patient reported at the ENT Outpatient Clinic with enlarged parotid salivary gland. The medical history revealed dry mouth (xerostomia) and dry eye (xerophthalmia). The ultrasound imaging of the salivary gland showed its enlargement, inhomogeneous parenchymal echostructure, with multiple tiny, oval, hypoechoic areas corresponding to the foci of lymphocytic infiltration and dilated salivary ducts. Ultrasound-controlled FNAB was performed, obtaining a smear rich in mononuclear cells and patches of epithelial cells. FNAB was prescribed again. The patient was referred to a rheumatologist. One month after the first visit, she presented with bilateral enlargement of the parotid salivary glands. The ultrasonography was repeated, additionally showing multiple hyperechoic bands corresponding to fibrotic zones. When the color map was superimposed onto the image and power Doppler was applied, enhanced vascularization of the gland was visualized (Figure 1).

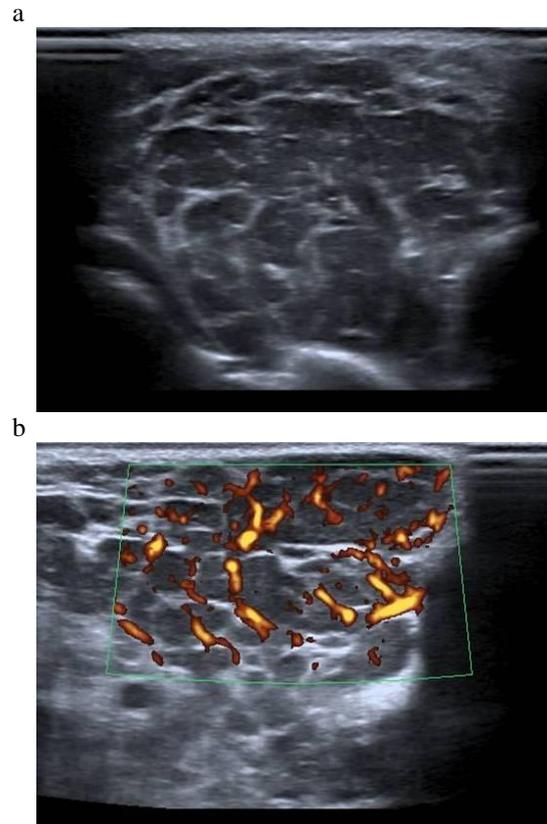


Figure 1. a: Enlarged left parotid salivary gland - inhomogeneous echostructure, with multiple tiny, oval, hypoechoic areas. Numerous hyperechoic bands correspond to fibrotic zones; b: enhanced vascularization of the gland. Authors' photo.

FNAB was repeated with ultrasound imaging and samples were collected from the left and right parotid salivary glands. The smear showed a rich population of lymphocyte type cells with the predominance of small lymphocytes, epithelial cells and macrophages (Fig. 2).

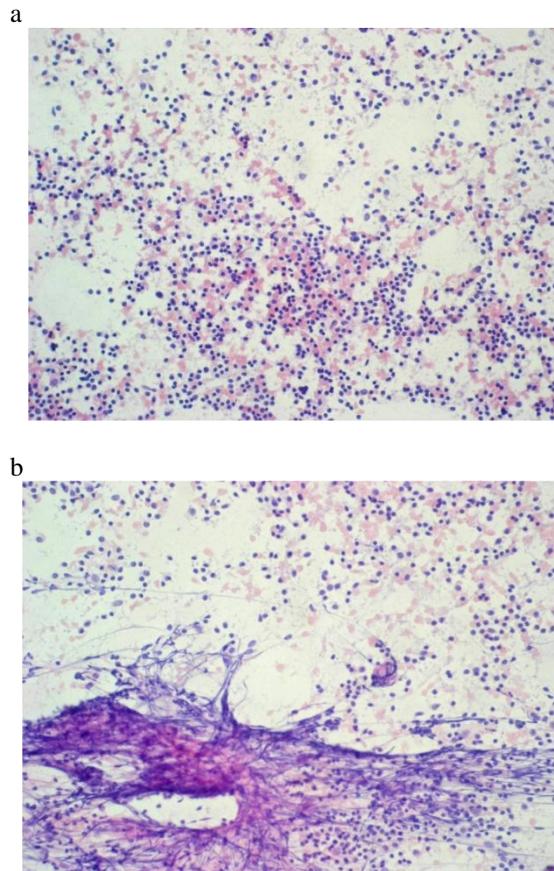


Figure 2. Smear from FNAB with visible abundant population of lymphocytic cells, epithelioid cells and macrophages (HE, magn. 200x) Authors' photo.

The cytological picture confirmed the presence of a benign lymphoepithelial lesion. The diagnosis of Sjögren's syndrome was suggested to the patient's attending physician. In the extended diagnostics, blood serum showed the presence (positive ++) of antinuclear (ANA) antibodies at 1:1,000. The fluorescence pattern of ANA antibodies on h HEP-2 cells was homogenous. The serum showed also the presence of antibodies specific to Sjögren's syndrome: anti Ro-52 (SS-A) and anti La (SS-B) – strongly positive (+++), as well as the presence of antibodies against: RNP/Sm – positive (++), Sm – weakly positive (+) and SS-A – strongly positive (+++). No antibodies were found against Scl-70, PM-Scl, Jo-1, PCNA, dsDNA, centromeres, nucleosomes, histones, ribosomes and type M2 mitochondria. The final diagnosis was Sjögren's syndrome.

DISCUSSION

Until recently, Sjögren's syndrome was diagnosed according to the criteria presented in the year 2002 by the American-European Consensus Group (AECG) [15]. The criteria referred to the symptoms in the oral cavity and eyes, Schirmer's test, histopathology of small salivary glands, involvement of salivary glands (saliva flow, sialography, scintigraphy) and the presence of anti-Ro (SS-A) or/and anti-La (SS-B) autoantibodies. The latest criteria of Sjögren's syndrome were described in 2012 by Sjögren's International Collaborative Clinical Alliance (SICCA) [7]. Only objective parameters remained in the criteria, including histopathology of small salivary glands, presence of anti-Ro (SS-A) or/and anti-La (SS-B) autoantibodies. Blood serum test was extended by ANA antibody titer $\geq 1:320$ and evaluation of eye symptoms was developed. The presence of at least 2 out of 3 points of this classification indicates the diagnosis of Sjögren's syndrome.

Histopathological assessment of tiny salivary glands plays a major role in the diagnosis of Sjögren's syndrome and has been referred to as the golden standard despite little evidence on its usefulness [7]. Material for analysis should be collected at the site of unchanged mucous membrane of the inner lower lip [16]. The histological pattern of Sjögren's syndrome shows chronic periductal inflammation of the salivary glands. The inflammatory infiltrate consists mainly of activated T cells and plasmatic cells. The primary architecture of the organ is under destruction and therefore the inflammatory reaction is accompanied by benign epithelial-myoepithelial lesions. According to the criteria of SICCA, the presence of at least one lymphocyte focus (≥ 50 lymphocytes/ 4mm^2 of glandular tissue adhering to the normal texture of the gland) is a histological indicator of Sjögren's syndrome [7].

In our case, the patient, who was still undiagnosed, had the ultrasound-controlled fine-needle aspiration biopsy. The smear showed an abundant population of lymphocytic cells, epithelioid cells and macrophages, thus indicating a benign lymphoepithelial lesion. The pathomorphological diagnosis guided clinicians towards Sjögren's syndrome. Although FNA method is less invasive than biopsy with histopathological sample collection, it has not been discussed whether FNA can replace biopsy. Ma et al. [17] performed a retrospective study of 11 patients with benign lymphoepithelial lesions diagnosed postoperatively. They found that FNAB, among others, could be useful in the preoperative diagnosis of these lesions, which may eliminate non-surgical patients. However, some problems may arise in the differential diagnosis between a benign lymphoepithelial lesion and a small

lymphocytic lymphoma. Moreover, differential diagnosis should be made of smears with noncancerous and cancerous lesions containing lymphocytic cells, namely chronic inflammation of the salivary gland, reactive inflammation of lymph nodes, lymphoepithelial cyst, lateral cyst of the neck, Warthin's tumor and malignant lymphoma. Experience and skills of the diagnostician are essential, since tumors of the salivary glands are rare [18].

Assessment of lesions observed in the salivary glands in Sjögren's syndrome is still subject to dispute. Apart from applying standard tests, scientists search for new methods to provide useful diagnostic data [6]. Perhaps, FNA of the salivary glands may appear one of them.

CONCLUSIONS

The pathomorphological analysis of fine-needle aspiration biopsy of the salivary gland has contributed to the diagnosis of Sjögren's syndrome in the patient.

Conflicts of interest

The authors declare that they have no competing interests in the publication of the manuscript.

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