A Rare Case Report of Sjögren’s Syndrome in a Young Female with Clinico-sono graphical Characterization and Literature Review

Bacem AE Ottoman¹* and Rania A. Ali²

Received 5 September 2014; Published online 31 January 2015

© The author(s) 2015. Published with open access at www.uscip.us

Abstract

Gougerot-Sjögren syndrome is an autoimmune disease of idiopathic etiology which has a slew of signs and symptoms all over the body especially within the mucosal surfaces. Epitomical of its cardinal symptoms of the primary type are xerophthalmia, xerostomia and vaginal dryness. For secondary Sjögren syndrome, it involves another connective tissue disorder, mostly rheumatoid arthritis. Malignant transformation into lymphoma and squamous cell carcinoma is well-documented. This report describes a rare case of primary Sjögren’s syndrome in a 27–years-old female that has missed the diagnosis for seven years. Gougerot-Sjögren syndrome is classically seen in women above 50 years so that it was expected to be a post-menopausal disease; thence, the rarity of this case is apparent.

This paper also characterizes some valuable assets both clinically and radiographically that help the average practitioner diagnose the discussed disease much easier. The findings point out some of the multiple norms and mercurial nature of the disease. The drawn conclusion is Sjögren’s syndrome is a multifactorial disease whose diagnosis is not as straightforward as it might appear and it needs a good command of real collaboration between multiple specialties. The progression of the disease is also banking on patient education that proved to be a very powerful investment.

Keywords: Sjögren syndrome; Xerophthalmia; Xerostomia; Parotid ultrasound; Diagnostic biopsies

1. Introduction

Gougerot-Sjögren syndrome or Sjögren's syndrome (SS) has been defined as an autoimmune epithelitis characterized by lymphocytic infiltration of exocrine glands and epithelia in multiple sites. The involvement of lacrimal and salivary glands results in the typical features of xerostomia...
and xerophthalmia. According to Moutsopoulos (1994), it can be seen alone (primary SS) or in association with other autoimmune rheumatic disease (secondary SS). It was first described by Gougerot in 1925 while Henrik S. C. Sjögren, the Swedish ophthalmologist, has gathered the big picture in 1933: a disease that blocks off one's watery pipes by the crowd of lymphocytes. It causes withered mucosa along the gastrointestinal tract, parched lips that cannot be moistened by the dry tongue as well as a slew of annoying symptoms running through shrivel body systems. Immunological, viral, hereditary, environmental and hormonal etiologic factors are controversially supported with no upper hand given. Regezi et al. (2007) believes that a cocktail of diverse predisposing factors hits the susceptible victims of the disease.

The diagnosis of the disease is not straightforward because it displays episodes of remission and activation and requires a good knowledge of the numerous atypical presentations. Neville et al. (2009) describes it classically as a disease of middle-aged and old females (> 50 y) with two forms; primary and secondary. Sjögren’s syndrome is either indolent or aggressive. Voulgarelis et al. (1999) confirms that SS is usually associated with other connective tissue disorders ranging from rheumatoid arthritis, lupus erythematosis, sweet’s syndrome, Hashimoto’s thyroiditis, Grave’s disease or even lymphoma. The propensity of malignant transformation to lymphoma is up to 5% of cases. Follow up is accordingly very mandatory.

2. Case Presentation

![Clinical pictures showing the bilaterally enlarged parotid glands](image)

**Fig. 1.** Clinical pictures showing the bilaterally enlarged parotid glands

After seven years of consulting rheumatologists, otolaryngologists, dentists, radiologists and ophthalmologists, a 27-years-old female visited our unit of sonography, department of radiodiagnosis, Giza hospital with bilateral swelling of parotid glands (figure 1), dryness of mouth, eye and vagina, burning sensation of the tongue and oral mucosa, concomitant pain with swallowing and history of rheumatic fever. The undiagnosed patient reported a regular treatment
for her cardiac condition that is monitored and followed up by scheduled laboratory investigations. She was a mother of two daughters. Consanguineous marriage has been very frequent in her ancestors for three generations according to her narration— a casual or causal finding that votes for inheritance if it plays a vital part in providing a backcloth for the development of Sjögren's syndrome.

For ultrasound study, a linear transducer was used to best visualize the superficial structures of the head and neck. The remarkably conspicuous finding of the ultrasound study was the parotid glands showing parotidomegaly and heterogeneous echopattern. The glandular parenchyma was atrophic with diffuse cystic cavities whose diameter was subcentimetric. The sonographic picture revealed miliary sporadic calcifications. The submandibular glands inclined to recapitulate a similar picture bilaterally while the left submandibular gland was milder. The overall picturesque was giving the impression of the so-called “cribriform” appearance. Cervical lymph nodes were oval in shape; insignificantly enlarged with the largest one measuring 9 mm x 4 mm. Both thyroid lobes and isthmus displayed a normal echopattern and texture (figure 2).

![Image of ultrasound view](image)

**Fig. 2.** Sonographic view of parotid (left) and submandibular (right): The view displays the heterogeneous glands whose parenchyma is exhibiting hypoechoic lesions (cystic cavitation) and some calcification foci.

The patient was formally referred to the department of maxillofacial surgery and diagnosis, Shubra hospital for its enviable diagnostic reputation. A tentative diagnosis of Sjögren's syndrome (SS) was made based on the aforementioned signs and symptoms. Under local anesthesia, the surgeon harvested four minor salivary glands from a normally appearing labial mucosa. The extract was immersed immediately in 10% formalin to be submitted for microscopic examination. Meanwhile, some laboratory investigations including complete blood picture, erythrocyte sedimentation rate, antinuclear acid, rheumatoid factor, anti-Sjögren's syndrome-A (SS-A) and anti-Sjögren's
syndrome-B (SS-B) were performed. The clientele was also referred to a gynecologist to treat and check for any pertinent findings other than the vaginal dryness. Lab results revealed an elevated ESR, positive ANA, strong positive SS-A and positive SS-B. The rheumatoid factor was positive and CBC showed lymphocytopenia, absolute neutropenia, hypochromic microcytic anemic and thrombocytopenia. The histologic examinations viewed a confluence of lymphocytic infiltrate replaces most of the glandular parenchyma with acinar degeneration and few epimyoepithelial islands. No germinal centers were observed (figure 3). The histologic picture is consistent with Sjögren's syndrome. All in all, a diagnosis of secondary Sjögren's syndrome was established. An initial treatment of prednisone tablets (20 mg) was prescribed based on consultation of multiple specialists (ophthalmologist, rheumatologist, dentist and cardiologist).

Fig. 3. Micrographs of H&E stained histologic sections. Low magnification (oil) shows confluence of lymphocytic foci that infiltrate most of the architecture of the glandular parenchyma with acinar degeneration and epimyoepithelial proliferations. Higher magnification power (40x) displays the surge of lymphocytes that replace the glandular parenchyma in addition to an epimyoepithelial islet.

3. Discussion

Gougerot-Sjögren's syndrome is a multifactorial disease of idiopathic origin which is characterized by the expression of an autoimmune process that results principally in keratoconjunctivitis sicca, xerostomia secondary to lymphocyte-mediated destruction of lacrimal and salivary gland parenchyma. Polyclonal B-cell hyperactivity reflects lack of regulation by T-cell subpopulations. Antimuscarinic receptor autoantibody production and altered autonomic activity of the affected glands have caused type III receptor dysfunction (Regezi et al. 2007). Moreover, the role for retroviruses has come from the demonstration of antibodies against HIV-associated proteins in a subset of patients with Sjögren's syndrome and from the clinical similarity of HIV-associated salivary gland disease to Sjögren's syndrome (Neville et al. 2009).
Immunogenetic typing studies have indicated statistically significant expression of various histocompatibility antigens in patients with primary and secondary forms of the syndrome. HLA-DR4 antigen is often identified in patients with secondary Sjögren's syndrome; antigens found in patients with the primary form include HLA-B8 and HLA-DR3 types (Regezi et al. 2007).

According to the Consensus report of the revised version of the European criteria, proposed by the American-European Consensus Group, classification criteria for Sjögren's syndrome investigate some items: Ocular involvement with detecting any persistent dryness of the eye for more than 3 months with a sensation of sands or gravel therein. That is to trace ≤ 5mm tears in 5 minutes using Schrimer test without anesthesia and ≥ 4 using Rose Bengal score. Oral involvements include persistent dryness of the mouth for more than 3 months with swelling of the salivary glands: the sine qua non of multiple sips to moisten the oral cavity every few minutes with salivary flow ≤ 1.5ml in 15 minutes. Histologically, salivary gland biopsy specimens must show lymphocytic foci (50 or more lymphocytes is a focus) within the glandular area. More than one focus in 4 mm² is regarded as consistent with the salivary component of Sjögren's syndrome. Serologically, positive ANA and antibodies to SS-A or SS-B or both is a must. Other manifestations include neurological involvements, associated well-defined connective tissue disease without any history of neck radiation, hepatitis C infection, sarcoidosis or use of anticholinergic drugs (Vitali et al 2002).

Epidemiology of SS is so evident in middle-aged adults with a 9:1 female-to-male ratio. Sjögren's syndrome occurs in all ethnic and racial groups. The peak age of onset is 50 years. Children and teenagers are rarely affected. If so, the juvenile form of SS is self-limiting (Harnsberger et al. 2004). Clinical features of SS include the incidence of xerostomia, keratoconjunctivitis sicca, pharyngolaryngitis sicca, diffuse firm bilateral parotidomegaly, mucosal burning sensation and altered taste, with or without oral candidiasis (Neville et al. 2009). Most extraglandular manifestations, similar to the exocrine gland involvement, can be considered as expression of the so-called ‘autoimmune epithelitis’ because the primary target of the autoimmune response is the epithelial component (Manoussakis et al. 2010). Other manifestations include decreased sweating, dryness and crusting of lips and nasal passages, hearing troubles, vaginal dryness which may cause dyspareunia, vasculitis, glomerulonephritis and peripheral neuropathy. Lymphoma is considered a late development during the course of the syndrome, occurring from 7.5 to 14 years after disease onset (Regezi et al. 2007).

A minor salivary gland biopsy from a normally appearing labial mucosa or a sonar-guided core biopsy from the parotid glands are the most reliable diagnostic tools when incorporated with other clinical, radiological and laboratory studies (Halse et al. (2000) and Kesse et al. (2006).

Sialographic and salivary scintigraphic findings generally are not specific and should be avoided if possible because of the hazard of ionizing radiation upon the radiosensitive salivary glands (Abok1984). Ultrasound examination is the golden choice for diagnosis, management and follow-up. Being a sound wave will neither ionize nor jeopardize the integrity of the glandular parenchyma regardless of its excellent accuracy in describing the disease even in the miliary stage (Harnsberger 2004).
The sonographic image of normal parotid gland shows very clear boundaries homogenous architecture and isoechoic to the thyroid gland. The earliest stage of SS shows very mild features that might be unnoticed by inexperienced sonologist. The punctuate stage displays a miliary pattern of diffuse hypoechoic cystic cavities whose diameter is below 1 cm throughout both parotids (Harnsberger et al. 2004). The cavitation stage reveals multiple cysts within the glandular parenchyma with dots of calcification and increased of vascularity flow on color duplex interrogation. However, lymph nodes show normal size, shape and internal architecture without any evidence of intranodal necrosis and calcification. The advanced stages view large cysts due to the parenchymal destruction and subsequent acinar atrophy that appears as echogenic band. The numerous calcifications, within the regular contour, increase so that it might obstruct many glandular ducts. As the disease progress, the clear boundaries of the major salivary glands become irregular and ill-defined or even invisible. When cervical adenopathy is apparent with loss of hilar architecture, presence of intranodal necrosis and calcification, the disease is potentially transforming into lymphoma or developing a malignancy. The ultrasound is also useful in assessing suspicious cervical lymph nodes (Tan et al., 2010; Wu et al., 2012; Evans et al., 1993; de Kerviler E et al., 2007; and Zinzani et al. 1998).

Treating Sjögren’s syndrome is also problematic and banks heavily on educating patients about their condition. The complications of the sicca component are best managed symptomatically. Artificial saliva and oral lubricants as well as artificial tears are available for this purpose. Preventive oral measures are extremely important relative to xerostomia. Scrupulous oral hygiene, dietary modification, topical fluoride therapy, and remineralizing solutions are important in maintaining oral and dental tissues (Vitali et al. 2010).

The patient must avoid intake of caffeine containing drinks and foods and limit consumption of cariogenic foods and drinks. The patient must not get himself exposed to any ionized radiation, even plain x-ray, unless very necessary. Corticosteroids are conventionally used to mitigate the severity of the disease. Nevertheless, careful follow-up and management by a dentist, ophthalmologist, and rheumatologist, among others, are critically significant (Tan et al., 2010; Wu et al., 2012; and Neville et al. 2009).

4. Conclusion

Gougerot-Sjögren syndrome is a rare disease whose variants and presentations are not conventional and requires real teamwork to promptly diagnose it. Patient education and scheduled ultrasound assessment are very essential. Recently, atypical and rare cases keep hitting. Updated meta-analyses are much recommended.

Acknowledgement

Special thanks are credited to the magnificent professors Dr. Ayman A. Amin, NCI, Egypt and Dr. Brad W. Neville, MUSC, for their ineffable help, support, expert opinions and witty pedagogical attitude toward all their students. We would like to extend our acknowledgement for Mr. Abdel Wahab Ali for teaching us practical lessons of ethics, determination and emotional support.
Conflict of interest: None

Funding source: None

References


http://dx.doi.org/10.1177/1759720X10363246

http://dx.doi.org/10.1259/dmfr/60907848