ORIGINAL RESEARCH PAPER

Rheumatology

KEY WORDS: Autoimmune disease, Sjogren's Syndrome, Sicca, Primary Sjogren's, Dry mouth, SjS

SICCA MANIFESTATIONS IN SJÖGREN'S OVERLAP SYNDROME: A CASE REPORT

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ABSTRACT

Primary Sjögren syndrome (SjS) is a systemic autoimmune disease that primarily affects the exocrine glands and results in the severe dryness of mucosal surfaces, mainly the mouth and eyes due to inflammation and resultant pathology of lacrimal or salivary glands.1,2 This disease predominantly affects middle-aged women, but can also be observed in children, men and the elderly1. One-half of affected individuals also develop extra-glandular involvement implying the occurrence of signs and symptoms in organs other than the salivary and lacrimal glands including the joints, skin, lungs, gastrointestinal (GI) tract, nervous system, and kidneys.3 Sjögren syndrome frequently occurs in conjunction with other autoimmune disorders including rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) which is also known as Secondary Sjögren's or Sjögren's Overlap Syndrome.4 The clinical presentation of SjS is heterogeneous and can vary from sicca symptoms to systemic disease and lymphoma.3,5 The pathophysiology of SjS is the destruction of the epithelium of the exocrine glands, as a consequence of abnormal B cell and T cell responses to the autoantigens such as Ro/SSA and La/SSB, among others.6,7 Diagnostic criteria for SjS include the detection of autoantibodies in patient serum and histological analysis of biopsied salivary gland tissue.4,9 Therapeutic approaches for SjS include both topical and systemic treatments to manage the sicca and systemic symptoms of disease.5,10 SjS is a serious disease with excess mortality, mainly related to the systemic involvement of disease and the development of lymphomas in some patients. Knowledge of SjS has progressed substantially, but this disease is still characterized by sicca symptoms, the systemic involvement of disease, lymphocytic infiltration to exocrine glands, the presence of anti-Ro/SSA and anti-La/SSB autoantibodies and the increased risk of lymphoma in patients with SjS.3,5

CASE REPORT

A 52 year old female presented to the Medicine OPD with the complaints of Dryness of mouth since 6 months. It was insidious in onset and gradually progressive in nature to the point where she cannot finish a sentence without discomfort due to dryness and drinking water in between. She also complaints of dryness of eyes since 7 days with mild redness and no ocular discomfort or visual disturbance. She also complaints of headache since 5 years on and off along with reduced hearing in right ear. She had a healthy lifestyle. She has a past history of multiple joint pain with morning stiffness 2 years back which was relieved by taking medication. Family history was unremarkable.

Physical examination revealed she was conscious, alert and well oriented to time, place and person with all the vitals within normal limits. Her cardiac, abdominal and CNS examination was within normal limits as well. Her respiratory examination revealed expiratory rhonchi with inspiratory fine crepetitions in left lower lobe. Her skin was dry and the skin over the face and forearm showed presence of bluish-black purpura like lesions with tiny skin ulcerations. Furthermore, Schirmer's test was performed and was found to be positive and slit lamp examination was suggestive of Kerato-conjunctivitis Sicca (KCS).

On evaluation, her hemoglobin was found to be 9.8 g/dL with WBC to be 4280 /uL with differential WBC showing lymphopenia. Her ESR at 1st hour was 120 mm/hr. Her RA factor was also positive (454 IU/ml). Her liver function test was normal except for globulin to be 5.12 g/dL. Her CRP, anti CCP, Random blood sugar level, kidney function test and thyroid function test were within normal limits. Her Anti Nuclear Antibody (ANA) level by direct immunofluorescence (IIF) was positive with anti cell code (ICAP) to be AC-4 with estimated titre of 1:1000 with reports as attached below. ANA profile on Immunoblot showed SS-A, SS-B and Ro-52 to be positive. USG whole abdomen showed no abnormalities. HRCT Thorax was suggestive of focal fibronodular and calcific changes at places bilaterally with associated volume loss and traction bronchiectasis(L>R).

Anti Nuclear Antibody (ANA)
Indirect immunofluorescence (IIF)

Parameters	Result
ANA Result :	**Positive**
Anti Cell Code (ICAP) :	**AC-4**
Pattern Details :	
Nuclear :	**- Fine speckled**
Cytoplasmic :	- Negative
Mitotic :	- Negative
Fluorescence Intensity :	**+++ : Strong**
Estimated Titer :	**1:1000**
Antigen Association :	**SS-A/Ro, SS-B/La, Mi-2, TIF1γ, TIF1δ, Ku**
Clinical Relevance :	**AC-4 Present in a varying degree in distinct SARD, in particular SjS, SLE, subacute cutaneous lupus erythematosus, neonatal lupus erythematosus, congenital heart block, DM, SSc, and SSc-ANA overlap syndrome;**
Medical Remark :	Kindly correlate with clinical findings. Adv. ANA (ENA) Profile immunoblot test. If SSc, AIM, or to a lesser extent SLE, is clinically suspected, it is recommended to perform a follow-up test ("Myositis Profile Immunoblot test") for detecting autoantibodies to Mi-2, TIF1γ, and Ku.

Anti Nuclear Antibody (ANA) Profile, Immunoblot

Parameters	Result	Index/ Intensity	Bio. Reference Range	Autoimmune disease association
Mi-2	Negative	0	Negative	DM
Ku	Negative	2	Negative	SLE, Myositis, Systemic sclerosis (SSc)
nRNP/Sm	Negative	0	Negative	MCTD (Sharp Syndromes)
Sm	Negative	1	Negative	SLE
SS-A	**Positive**	21	Negative	SS or SLE, Neonatal lupus erythematosus
Ro-52	**Positive**	37	Negative	SS or SLE, SSc or Idiopathic inflammatory myopathy
SS-B	**Positive**	16	Negative	SS or SLE, Neonatal lupus erythematosus
Scl-70	Negative	0	Negative	Diffuse or limited form of SSc
PM-Scl100	Negative	0	Negative	Overlap syndrome (Polymyositis, Dermatomyositis& Systemic sclerosis)
Jo-1	Negative	0	Negative	Myositis (Poly/Dermatomyositis)
CENP B	Negative	0	Negative	SSc - limited form or diffuse form, Primary Biliary Cholangitis (PBC)
PCNA	Negative	0	Negative	SLE
dsDNA	Negative	0	Negative	SLE
Nucleosomes	Negative	1	Negative	SLE
Histones	Negative	0	Negative	Drug-induced SLE, RA
Ribosomal P-protein	Negative	0	Negative	SLE
AMA-M2	Negative	2	Negative	PBC or other chronic liver diseases, SSc
DFS70	Negative	0	Negative	Atopic dermatitis, Rheumatic diseases

She was diagnosed with primary Sjögren's Syndrome sicca predominant with bronchiectasis with hypergammaglobulinemia and was prescribed with Hydroxychloroquine 300 mg PO once daily along with Pilocarpine 5 mg PO twice daily along with CarboxyMethyl Cellulose Drops LA and was asked to follow-up in the OPD every month.

DISCUSSION

Sicca manifestations, characterized by dryness of the eyes (xerophthalmia) and mouth (xerostomia), are hallmark symptoms of secondary Sjögren's syndrome (SjS).[3,5] These manifestations significantly impact patients' quality of life, often leading to difficulties in swallowing, speaking, and maintaining oral hygiene.[5] The pathophysiology involves autoimmune processes where lymphocytic infiltration leads to glandular dysfunction, particularly affecting the salivary and lacrimal glands.[6,7]

In secondary SjS, sicca symptoms may be exacerbated by the underlying autoimmune condition, commonly rheumatoid arthritis or systemic lupus erythematosus. The interplay between these disorders can complicate the clinical picture,[4] making diagnosis and management more challenging.[3] Early recognition of sicca manifestations is crucial for implementing appropriate therapeutic strategies, which may include symptomatic relief with artificial tears, saliva substitutes, and, in some cases, systemic immunosuppressive

therapies.[5,10]

Recent studies indicate that the severity of sicca symptoms correlates with the degree of glandular involvement observed through imaging and histopathological analysis.[9] Biomarkers and objective measures, such as Schirmer's test and salivary flow rates, provide valuable insights into the extent of dryness, aiding in more personalized treatment approaches.[4,9]

Sicca manifestations in secondary Sjögren's syndrome represent a complex interaction between autoimmune processes and glandular dysfunction. Effective management requires a multidisciplinary approach, focusing on symptom relief and addressing the underlying conditions.[10] Continued research is essential to better understand the mechanisms behind sicca symptoms and to develop targeted therapies that can improve the quality of life for affected individuals.[3,6] Comprehensive patient education and regular follow-ups are vital in optimizing management and enhancing patient outcomes.[10]

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