AUTOIMMUNE HEPATITIS IN A PATIENT WITH PRIMARY SJOGREN’S SYNDROME: A RARE CLINICAL ASSOCIATION.

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Abstract

Patients of primary Sjogren’s syndrome presents with signs and symptoms of sicca complex and extra glandular features like rash, arthritis, and leucopenia but there is absence of other concomitant connective tissue disorder. Patients of Sjogren’s syndrome both primary and secondary commonly have evidence of liver disease clinically or on biochemical tests. The most prevalent associated condition is Primary biliary cirrhosis. Here we report a rare instance of a patient of primary Sjogren’s syndrome suffering from autoimmune hepatitis also. Although both are autoimmune disorders, the association is quite uncommon in medical literature.

Introduction:

The clinical hallmarks of Sjogren’s syndrome are dryness of the cornea and conjunctiva or keratoconjunctivitis sicca and dry mouth or xerostomia. Primary Sjogren’s patients presents with sicca complex and extraglandular features like rash, arthritis, leucopenia, Raynaud’s phenomenon, lymphadenopathy, vasculitis, peripheral neuropathy etc. There is absence of other connective tissue disorder although the serological and histopathological criterions are fulfilled. Secondary Sjogren’s syndrome is associated with other connective tissue disorders like rheumatoid arthritis, systemic lupus erythematosus, polymyositis, scleroderma, mixed connective tissue disease, primary biliary cirrhosis, and chronic active hepatitis. Apart from exocrinopathy there is involvement of lung, kidney, thyroid and central nervous system. The association of Primary Sjogren’s with liver pathology was first proposed by Christiansson in 1954.¹ But very few cases of primary Sjogren’s with autoimmune liver diseases like Primary Biliary Cirrhosis, Primary Sclerosing Cholangitis, Autoimmune hepatitis etc have been described in scientific literature.

Here we have presented a unique case of Primary Sjogren’s syndrome with autoimmune hepatitis in a 50 years old female.

Case Presentation:

A 50 years old female patient, homemaker by occupation, presented to us with chief complaints of abdominal distension followed by pedal swelling along with persistent heaviness and dragging sensation in left upper abdomen for last three years. About 5-6 months back, she had one episode of fever which was completely relieved by antipyretics, following which she developed arthralgia involving both small and large joints of upper and lower extremities with morning stiffness. She also had persistent sensation of gravel in both eyes for which she had to

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clear her eyes with water for last two years along with dryness of mouth for the same duration which compelled her to take frequent sips of water. For the past few months, she had also pain in the region of both the parotids. There was also h/o progressive generalized weakness, easy fatigability and weight loss as evidenced by loosening of her clothes for last 1 year.

The patient was non diabetic and normotensive. There was no history of hematemesis or melaena. The patient denied any history of cough, hemoptysis and revealed no history of rash or bleeding from any site. She also had no complaints of low back ache or pain abdomen. There was no history of oral ulceration, alopecia, photosensitivity and also no history of analgesic abuse or any recent trauma. She suffered from jaundice 3 years back for which she visited local physician and the symptoms subsided within two weeks. There was no history of similar or any major illness in her family. On personal history, she had no addiction and no promiscuous behavior. Her sleep, bladder bowel habits were normal but appetite was decreased.

On examination, built was average with BMI of 19.1 kg/m². But there was moderate pallor along with presence of bilateral parotid swelling. Clubbing, icterus, cyanosis were absent, pulse was 100 beats /minute, regular, and blood pressure was of 130/70 mm Hg. No significant skin, hair, nail changes were found. Jugular venous pressure was not elevated. No significant lymphadenopathy was detected. Schirmer’s test was positive. There was no sternal tenderness. Liver was enlarged, firm in consistency, sharp border with liver span of 16 cm along with splenic enlargement of 4 cm below left costal margin. Other systemic examinations were also within normal limit. On routine investigations, Hemoglobin was 9.5gm/dl, Total leukocyte count-2,800/dl, Platelet-50,000/dl and on Differential count-Neutrophil 42/Lymphocyte 47/Monocyte 0/Eosinophil 11. ESR was 78mm in 1st hour and MCV/MCH/MCHC was 97.1/30.2/31 respectively. Urea and creatinine were -14mg/dl and 0.8mg/dl. Serum sodium was 140mEq/Lt and potassium-3.4mEq/Lt. Liver function test revealed: Total bilirubin-1.1mg/dl, Direct bilirubin-0.8 mg/dl, AST-78U/, ALT-46U, ALP-802U. Total serum protein-7.5gm/dl along with altered albumin: globulin ratio-3.6:3.9. Prothrombin time was 13.3/11.2(INR-1.18). APTT was 29.4/27.2 sec. Blood for ANA was positive(1:100 dilution)-fine speckled pattern, anti SS-A/anti SS-B was strongly positive; ASMA, AMA, anti LKM was negative. Serum ceruloplasmin was 41.5 mg/dl (within normal limits). Bone marrow aspiration study was done along with trephine biopsy which revealed only hypercellular marrow. Ultrasonography whole abdomen was done and reported as hepatomegaly, coarse and heterogenous echotexture, splenomegaly but no ascites. Upper G.I endoscopy showed presence of 4 columns of oesophageal varices.

As from history, examination and relevant investigations it seemed to be a case of primary Sjogren’s syndrome with features suggestive of chronic liver disease and portal hypertension, we went for liver biopsy to find out the exact histological cause of liver affliction. Microscopical examination of the biopsy specimen showed the normal lobular architecture of liver was maintained. The hepatocytes showed eosinophilic to granular cytoplasm. Some of the hepatocytes showed macro and microvesicular steatosis. Occasional hepatocytes showed dysplastic changes and glycogen vacuolation of nuclei. Necroinflammatory lesions and interface activity were seen. The portal tracts showed increased fibrosis and dense infiltration by lymphoplasmacytic cells. Occasional lymphoid follicles were present. Proliferated bile ductules were also present. No epitheloid granuloma in the portal region was seen. No nodule formation or bridging fibrosis was found. These features were compatible with autoimmune hepatitis. She received prednisolone orally at dose of 1mg/kg body weight initially with slow tapering at rate of 5 mg reduction every 2 weeks. She also received supportive treatment in form of lubricating eye drops. The patient is doing well with treatment regimen and currently receiving corticosteroids at dose of 30 mg daily.
Discussion:
The clinical hallmarks of Sjogren’s syndrome are dryness of the cornea and conjunctiva or keratoconjunctivitis sicca and dry mouth or xerostomia. Primary Sjogren’s patients manifest with signs and symptoms of sicca complex and extraglandular features but there is absence of other connective tissue disorder. The category of secondary Sjogren’s syndrome is reserved for patients with keratoconjunctivitis sicca or xerostomia or both in the setting of another connective tissue disorder like rheumatoid arthritis, systemic lupus erythematosus, polymyositis, systemic sclerosis, scleroderma, vasculitis, mixed connective tissue disorder, primary biliary cirrhosis, and chronic active hepatitis. Apart from exocrinopathy there is involvement of lung, kidney, thyroid, lymphoreticular and central nervous system. The association with liver pathology was first proposed by Christiansson retrospectively in 1954 when he described features of sicca syndrome in a patient with jaundice. 

Subsequent case series in the mid 1970s and early 1980s emphasized the biochemical, serologic, and histologic findings consistent with liver disease and their relationship to primary Sjogren’s Syndrome. Additionally, a large study of 300 primary Sjogren’s Syndrome patients by Skopouli et al concluded that although liver involvement in primary Sjogren’s syndrome was rare, Primary Biliary Cirrhosis accounted for nearly all identified liver disease. Others have noted abnormal liver biochemical profiles more frequently in patients of pSS who had concomitant kidney, lung, or hematological abnormalities.

The definite diagnosis of autoimmune hepatitis requires exclusion of other similar disease, laboratory findings that indicate substantial immunoreactivity and histological features of interface hepatitis. As many as 38% of patients with autoimmune hepatitis have concurrent autoimmune diseases which may mask the underlying liver disease. But the exact prevalence of autoimmune hepatitis with primary Sjogren’s is unclear. Recently in a large retrospective cohort study the prevalence of this association has been found to be 1%.

An aberrant interaction between lymphocytes and different epithelial tissues has been proposed as a mechanism for the damage seen in different organs in primary Sjogren’s. Epithelial cells have been proposed to be the principal target cells for complement mediated destruction as active participants rather than passive bystander effect in the chronic immune response in primary Sjogren’s but further studies are needed to establish the role of liver epithelial cells in the pathogenesis of hepatic damage in this disease, including the analysis of HLA expression and cytokine secretion pattern in these cells.
References:
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