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Case report

A Case of Autoimmune Hepatitis and Thyroiditis Associated with Sjögren's Syndrome

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Abstract

Sjögren's Syndrome is a chronic autoimmune disorder with unknown cause and usually secondary to other autoimmune connective tissue disorders. Associations with extra-glandular organ involvements have previously been reported. Herein, we report a patient with autoimmune hepatitis and thyroiditis associated with Sjögren's Syndrome presenting with iron deficiency anemia.

Keywords: Sjögren's Syndrome, renal involvement, autoimmune thyroiditis, autoimmune hepatitis

Introduction

Autoimmune disorders usually affect women and tend to be together with two or more disorders in one patient. Moreover; patients with any autoimmune disease are prone to develop other diseases [1]. Increased titers of serum autoantibodies which target specific tissues and hypergammaglobulinemia determine disease characteristics. Therefore; symptoms can range between slight fatigues to severe tissue damage. During the diagnostic procedures multidisciplinary approach is helpful. In this paper we present a patient who has Sjögren's Syndrome (SS), autoimmune hepatitis (AIH) and thyroiditis with iron deficiency anemia.

Case report

A 32 year old woman was admitted to our clinic with severe fatigue and malaise. Initially she was evaluated in the out patient clinic and was hospitalized for splenomegaly, anemia (iron deficiency) and hyperglobulinemia. She had fatigue since her last baby miscarriage which was 9 years ago. Then she has initiated to use iron tablets irregularly. During the last 2 months her symptoms worsened. Past medical history was unremarkable other than cholecystolithiasis and insertion of an intrauterine device. She quitted smoking for the last 3 months after smoking 14 pack-years.

On admission she was pale and had hepatosplenomegaly. On auscultation of the cardiac apex, a 2/6 systolic murmur was heard. A standard 12 derivation electrocardiogram showed normal sinus rhythm. Chest X-Ray showed no abnormality. Laboratory evaluations are presented in the Table1.

Her urine analysis was normal. The other laboratory results were as follows; IgG >49,1 g/L (normal 6,5-16); IgA 4,89 g/L (normal 0,4-3,5); IgM 5,04 g/L (normal 0,5-3); antinuclear antibody (Ab) positive; anti-double stranded DNA Ab positive; anti-SS-A Ab positive; anti-SS-B Ab negative; anti-Jo-1 Ab negative; anti Sm Ab negative; anti-ribonucleoprotein Ab positive; rheumatoid factor 11300 IU/ml (normal 0-20); anti liver-kidney microsome-1 Ab negative; anti-mitochondrial Ab 17.4 (normal <15); anti-thyroglobulin Ab 1702 IU/ml (normal 0-40); anti-thyroid peroksidase Ab 39,6 IU/ml (0-35). Serum protein electrophoresis showed a marked polyclonal increase on the γ-globulin fraction {γ-globulin 7,32 g/dL (normal 1,5-3,7)}. Serological markers of hepatitis were all negative except Anti HBc IgM. Ultrasonography of the abdomen and the thyroid gland revealed splenomegaly, cholecystolithiasis and thyroiditis. Schirmer's test showed no abnormality. Minor salivary gland biopsy showed subdermal lymphocyte aggregations. Gastroscopy and biopsy were performed, but patient refused to have liver biopsy. The gastroscopy showed pangastritis and the duodenal biopsy did not correlate with celiac disease. The patient's score for autoimmune hepatitis according to international autoimmune hepatitis group scoring system was 18 [2,3].

10 mg day prednisolone was administered and the patient's signs were relieved with this therapy. Her levels of ALT and AST decreased to 57 and 37 U/L respectively. 200 mg/day hydroxychloroquine was added to the steroid after consultation with rheumatologist. Vaginal hemorrhage caused by intrauterine device was found which may responsible for the deep anemia. Having started oral iron replacement treatment, the patient was

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discharged from our clinic on the fourteenth day of hospitalization with relief of most of her symptoms.

Table 1 The initial and final laboratory values of the patient

	Normal	Presentation	Discharge	Two mouths after
White blood cell ($x10^3/\mu L$)	4300-10300	4940	6670	8100
Red blood cell ($x10^6/\mu L$)	4.38-5.77	4.54	5.02	5.34
Hemoglobin (gr/dL)	13.6-17.2	8.4	10.4	14.8
MCV (fL)	80.7-95.5	63.7	65	76
MCHC (g/dL)	32.7-35.6	29.2	31.7	36.2
RDW (%)	11.8-14.3	18.1	22.6	18.1
Platelet ($x10^3/\mu L$)	156-373	239	271	150
Reticulocyte (%)	1-2	0.95		
Erythrocyte sedimentation rate (mm/hour)		81	46	21
ALT (U/L)	0-34	140	57	32
AST (U/L)	0-34	113	37	23
Alkaline phosphatase (U/L)	35-104	114	101	71
γ-glutamyl transpeptidase (U/L)	0-36	12	11	18
Total bilirubin (mg/dL)	0.0-1.1	0.40		0.78
Urea (mg/dL)	0-50	20	20	30
Creatinine (mg/dL)	0.5-1.1	0.6	0.59	0.92
Iron (ug/dL)	37-145	15		33
Total iron binding capacity (ug/dL)	228-428	464		335
Ferritin (ng/ml)	5-148	4.02		121
Thyroid stimulating hormone (uIU/ml)	0.27-4.2	2.59	1.43	2.22
Free T3 (pg/ml)	2-4.4	2.72	2.18	2.71
Free T4 (ng/ml)	0.9-1.7	1.17	1.13	1.35
Prothrombin time (seconds)	11.9-15.8	15.4		
Total protein (g/dL)	6.6-8.7	10.7	9.9	
Albumin (g/dL)	3.4-4.8	3.38	3.6	

Discussion

Sjögren's Syndrome (SS) is a systemic autoimmune disorder characterized by keratoconjunctivitis sicca and xerostomia. Although SS is an autoimmune exocrinopathy, involvement of non-exocrine organs such as thyroid, hypophysis, kidneys and skin have been reported. At the same time chronic auto-immune hepatitis, digestive disorders, diabetes mellitus, pulmonary disorders, Raynaud's phenomenon, joint and muscle disorders, peripheral neuropathies, and depressive syndromes are reported in the literature [4]. Furthermore, it can be associated with a number of other autoimmune diseases especially autoimmune hepatitis and thyroiditis [5-7].

To our knowledge, this is the first case report for the coexistence of SS, AIH and autoimmune thyroiditis. Our patient presented with completely non-related symptoms of this overlapping autoimmune disorders. She was admitted with iron deficiency anemia caused by excessive bleeding due to intrauterine birth control device. Advanced investigations in the hospital showed that she had Sjögren's Syndrome, autoimmune liver disease and thyroiditis.

The main symptoms of SS are xerostomia and keratoconjunctivitis sicca caused by B lymphocytic infiltration of exocrine glands [8]. In our patient initial main symptom was fatigue. She was carefully questioned for other symptoms because of the presence of hyperglobulinemia. She defined sicca syndrome, oral aphthous ulcers and polyarthritis. Gastroscopy and duodenal biopsy for malabsorptive disorders and liver biopsy for autoimmune hepatitis were recommended. All were performed other than the liver biopsy which the patient refused to have.

Lymphocytic infiltration and hypergammaglobulinemia are commonly found in SS and it is known that the lymphoma frequency among SS patients is higher than the standard population. Presence of a new lymphadenomegaly or seroconversion of Rheumatoid factor from high to low titers should alert the clinician for lymphoma. In our case Rheumatoid factor sharply decreased with treatment, still she was evaluated for lymphoma which was negative.

Liver biopsy has a great role in the diagnosis of AIH. The assessment of liver histology is not only necessary for diagnosis but also for evaluating prognosis of the patient [1]. Our patient did not accept liver biopsy but we used the scoring system for diagnosis and full response to treatment supporting our diagnosis. The patient's score was 18 for autoimmune hepatitis according to international autoimmune hepatitis group scoring system (in this system an aggregate score greater than 15 prior to therapy constitutes a definite diagnosis of AIH. A score of 10-15 is interpreted as probable AIH) [2,3].

The presence of autoantibodies of thyroid and thyroid dysfunctions has previously been reported in the SS. Thyroid autoantibodies can be 28-38 % positive in SS [9]. In our case thyroid hormones were within normal levels but autoantibodies were positive and parenchymal structure of the gland was heterogeneous by the ultrasonography.

Anti HBc IgM may be false positive in patients with high levels of Rheumatoid factor. Similarly as our pa-

tients Rheumatoid factor levels decreased from 11300 to 608 IU/ml, anti HBc IgM became negative with the treatment.

Therapy for SS is planned according to system involvements. If there is only slight exocrine gland involvement, hydroxychloroquine is given. On the other hand if there is severe organ involvement immunosuppressive therapy including steroids should be administered. Hence, our patient's signs and symptoms relieved with steroid, hydroxychloroquine and iron treatment.

In conclusion, it is important to realize that Sjögren's Syndrome may involve many organ systems, thus thoroughly examination is essential in these patients.

Conflict of interest statement. None declared.

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