Case Report

Autoimmune Cholangiopathy with Dacryocystitis

Sepideh Haghazali MD•*, Fatemeh Haj-Manouchehry MD**

Autoimmune liver diseases are different entities that sometimes have overlapping features. They share many of the general characteristics of autoimmune diseases, with systemic involvements. Here, we report a 30-year-old woman with ophthalmic symptoms of conjunctivitis and dacryocystitis who was treated completely. After a few months, the patient presented with autoimmune cholangiopathy. Sequelae of autoimmunity have been considered in different organs in this case.

Archives of Iranian Medicine, Volume 12, Number 1, 2009: 76 – 78.

Keywords: Autoimmune • conjunctivitis • dacryocystitis • hepatitis

Introduction

Autoimmune liver diseases are a group of well-known disorders including autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), and autoimmue cholangiopathy(AIC).

PBC has special characteristics but not specific histologic findings including destruction of small intrahepatic bile ducts, portal inflammation, and progressive scarring.[1] Almost all these patients have circulating antimitochondrial antibody (AMA).

Interface hepatitis and plasma cell infiltration in portal spaces on histologic examination are the characteristics of AIH. Other helpful laboratory abnormalities are hypergammaglobulinemia, and autoantibodies.[2–3]

Those patients with prominent bile duct damage, little parenchymal injury who are negative for AMA and have either antinuclear antibodies or antibodies against smooth muscle are regarded as having AIC. AIC is characterized by classic clinical, biochemical, and histologic features of PBC, but negative serum AMA.[1,4] A wide range of labels for this condition shows the extent of the confusion. They include "mixed types," "overlap syndrome," "immune-cholangitis," "autoimmune cholangitis," and "AIC," as well as "hepatitic form of PBC" and "cholestatic autoimmune hepatitis."[5] Ursode-oxycholic acid (UDCA) is the preferred treatment for PBC or AIC patients. In the latter group systemic corticosteroide may also be effective.

Liver biopsy can change the scenario. Superimposition of AIH on histologic examination suggests the combination of glucocorticoids and UDCA as the treatment.[6–7]

Hemolytic anemia, idiopathic thrombocytopenic purpura, type 1 diabetes mellitus, thyroiditis, celiac sprue, and ulcerative colitis are the common extrahepatic associated disorders. Uveitis, celiac disease, pernicious anemia, Sjögren's syndrome, mixed connective tissue disease, Weber-Christian panniculitis, calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia syndrome are less common associations.

Nonimmunologic diseases, such as thrombotic thrombocytopenic purpura and sickle cell disease have also been described.[8–9]

Herein, we report a case of AIC with dacryocystitis and conjunctivitis.

Authors' affiliations: *Department of Internal Medicine (Gastroenterology and Hepatology Ward), **Department of pathology, Qazvin University of Medical Sciences, Qazvin, Iran.
•Corresponding author and reprints: Sepideh Hghazali MD, Department of Internal Medicine (Gastroenterology and Hepatology Ward), Qazvin University of Medical Sciences, Qazvin, Iran.
Fax: +98-218-8012-992, E-mail: sephagh@ams.ac.ir
Accepted for publication: 10 April 2007

Case Report

A 30-year-old woman was referred to an ophthalmologist with palpebral edema without blurred vision. The ophthalmologist diagnosed a palpebral mass of the lacrimal gland in the supratemporal area and subconjunctival hypertrophy. According to the ophthalmologists' report, refractometry, motility, and alignment had no abnormalities and cornea and intraocular pressure were normal. The patient had no dryness in the mouth and eyes and there were no other complaints and the general physical examination was also normal.

The ophthalmologist obtained a biopsy from conjunctival tissue and lacrimal gland to rule out lymphoma and vasculitis. The specimens showed lymphoplasmatoid infiltration in the conjunctiva and occasional eosinophils and neutrophils (Figure 1). Lacrimal gland specimens showed lymphoepithelial lesions. No granuloma was seen (Figure 2).

Local corticosteroid with 5 mg oral prednisolone for six weeks were administered. The mass regressed and the patient did well in the next three months. After six months, the patient became icteric with fatigue, pruritus, and weight loss of about 5%. General physical and abdominal examinations were normal.

Laboratory data showed increment of alkaline phosphatase up to 14 times normal along side with elevation of gamma glutamyl transpeptidase (GGT) up to 10 times normal. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) had risen up to four to five times of upper normal limit (Table 1). Ceruloplasmin was increased up to one and a half times normal. Viral markers for HBV, HCV as well as ANA, anti-SMA, anti-LKM, AMA, and ANCA were negative.

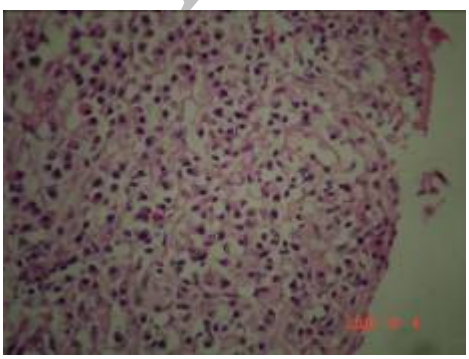

Figure 1. Conjunctival lymphoplasma cell infiltration (H&E, ×100).

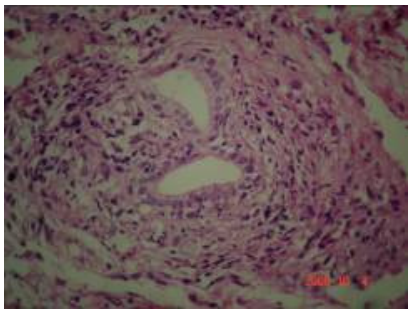

Figure 2. Inflammation around the lacrimal gland (H&E, ×100).

Mild hypergammaglobulinemia was detected by serum protein electrophoresis (Table 2). Thyroid function tests were within normal limits.

Ultrasonagraphy of the liver and biliary system and magnetic resonance cholangiopancreatography findings were normal.

Needle liver biopsy revealed chronic hepatitis, grade 8/18 and stage 3/6 in modified histologic activity index (HAI) scoring system with foci of piecemeal necrosis, portal tract expansion with predominance of lymphocytes, ductopenia, and mild bile duct proliferation without granulomas (Figures 3 and 4).

A diagnosis of AIC was made and she received prednisolone, azathioprine, and UDCA. After treatment, jaundice and pruritus resolved. Liver function tests showed about 50% decrement in ALT, AST, and alkaline phosphatase after three to four weeks (Table 1). Xanthelasmas appeared after two months of treatment. The patient received immunosuppressives and UDCA and she was followed six months later, who was in favorable condition.

Discussion

Autoimmune liver diseases are associated with

Table 1. Liver function test changes with treatment.

Liver function tests (normal ranges)	Before treatment	After treatment
ALT (0 – 40) U/L*	229	104
AST (0 – 40) U/L**	173	100
Alkaline phosphatase (64 – 306) (IU/L)	4153	2540
GGT (0 – 32) IU/L***	348	Not available
Total bilirubin (up to 1) mg/dL	3.53	1.1
Direct bilirubin (up to 0.25) mg/dL	1.92	0.4
ESR (1st hour)	57	51

*ALT=alanine aminotransferase; **AST=aspartate aminotransferase; ***GGT=gamma glutamyl transpeptidase.

Table 2. Serum protein electrophoresis.

SPEP*	g/dL	Percentage
Total protein	9	6.2 – 8.8
Albumin	3.3	35.7 (45 – 55)
Gamma globulin	2.3	26.1 (15 – 23)

*Serum protein electrophoresis.

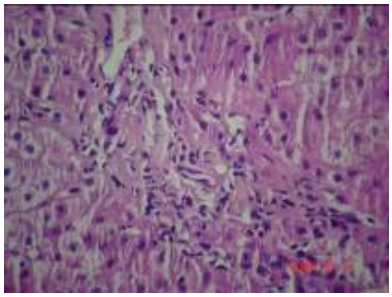

Figure 3. Portal fibrosis and ductopenia (H&E, ×100).

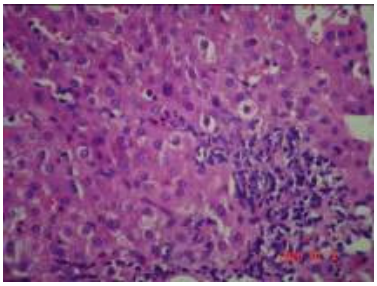

Figure 4. Piecemeal necrosis (H&E, ×100).

extrahepatic autoimmune and nonautoimmune conditions. It seems that autoimmune disorders concurrently seen with AIH caused the inclusion of this feature in the scoring system of international AIH group.[10]

Ophthalmic involvement is not a common association. Recently Romanelli et al. have reported a case of AIH with uveitis.[11]

In 1987, immunocholangitis was first reported in three women. This condition later was named as AIC. All of these patients responded to immunosuppressive treatments. [12]

We have described a lady with dacryocystitis and conjunctivitis who was found to have AIC later on. To the best of our knowledge, this is the first case of AIC associated with dacryocystitis and conjunctivitis that ever reported.

Loss of tolerance against self tissue is one of the most important concepts in autoimmune diseases.

It seems that similarity between eye and liver involvement on histologic specimens defines a wandering and powerful self attack of different tissues in this patient.

Ophthalmologic involvement is not common in autoimmune liver diseases. Considering these cases, it may be justified to assess the liver with simple tests such as AST, ALT, Alkaline phosphatase, and GGT in patients presenting with autoimmune ocular diseases.

References

1 Kaplan MM. Primary biliary cirrhosis. *N Engl J Med*. 1996; **335:** 1570 – 1580.

2 Manns MP, Strassburg CP. Autoimmune hepatitis: clinical challenges. *Gastroenterology*. 2001; **120:** 1502 – 1517.

3 Czaja AJ, Freese DK, American Association for the Study of Liver Disease. Diagnosis and treatment of autoimmune hepatitis. *Hepatology*. 2002; **36:** 479 – 497.

4 Feldman M, Friedman, Lawrence S, Sleisenger, Marvin H. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management*. 8th ed. Philadelphia: Saunders; 2006: 1885 – 1898.

5 Suzuki Y, Arase Y, Ikeda K, Saitoh S, Tsubota A, Suzuki F, et al. Clinical and pathological characteristics of the autoimmune hepatitis and primary biliary cirrhosis overlap syndrome. *J Gastroenterol Hepatol*. 2004; **19:** 699 – 706.

6 Ben-Ari Z, Dhillon AP, Sherlock S. Autoimmune cholangiopathy: part of the spectrum of autoimmune chronic active hepatitis. *Hepatology*. 1993; **18:** 10 – 15.

7 Chazouillères O, Wendum D, Serfaty L, Montembault S, Rosmorduc O, Poupon R. Primary biliary cirrhosis-autoimmune hepatitis overlap syndrome: clinical features and response to therapy. *Hepatology*.1998; **28:** 296 – 301.

8 Krawitt EL. Clinical manifestations and diagnosis of autoimmune hepatitis. Up-To-Date. 2006; NO 14.2.

9 Bloom JN, Rabinowicz IM, Shulman ST. Uveitis complicating autoimmune chronic active hepatitis. *Am J Dis Child*. 1983; **137:** 1175 – 1176.

10 Bittencourt PL, Farias AQ, Porta G, Cançado EL, Miura I, Pugliese R, et al. Frequency of concurrent autoimmune disorders in patients with autoimmune hepatitis: effect of age, gender, and genetic background. *J Clin Gastroenterol*. 2008; **42:** 300 – 305.

11 Romanelli RG, La Villa G, Almerigogna F, Vizzutti F, Di Pietro E, Fedi V, et al. Uveitis in autoimmune hepatitis: a case report. *World J Gastroenterol*. 2006; **12:** 1637 – 1640.

12 Beuersand U, Rust C. Overlap syndromes. *Seminar Liver Dis*. 2005; **25:** 311 – 320.