Autoimmune Hepatitis: Diagnostic Dilemma When It Is Disguised as Iron Overload Syndrome

Gyanendra K. Acharya*, Hung-I Liao†, Simona Frunza-Stefan†, Ronakkumar Patel†, Moe Khaing†

*The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, USA and †Wyckoff Heights Medical Center, 374 Stockholm Street, Brooklyn, NY 11237, USA

Elevated serum ferritin level is a common finding in iron overload syndrome, autoimmune and viral hepatitis, alcoholic and nonalcoholic fatty liver diseases. High transferrin saturation is not a common finding in above diseases except for iron overload syndrome. We encountered a challenging case of 73-year-old female who presented with yellowish discoloration of skin, dark color urine and dull abdominal pain. Initial laboratory tests reported mild anemia; elevated bilirubin, liver enzymes, and transferrin saturation. We came to the final diagnosis of autoimmune hepatitis after extensive workups. Autoimmune hepatitis is a rare disease, and the diagnosis can be further complicated by a similar presentation of iron overload syndrome. Markedly elevated transferrin saturation can simulate iron overload syndrome, but a liver biopsy can guide physicians to navigate the diagnosis. (J Clin Exp Hepatol 2017;7:269–273)

Autoimmune hepatitis (AIH) is a chronic progressive necroinflammatory liver disease of unknown cause associated with circulating autoantibodies and a high serum globulin level.[1] Clinical manifestations range from merely elevated transaminases to liver cirrhosis and/or fulminant liver failure requiring liver transplantation. Here we describe a rare presentation of AIH disguised as iron overload syndrome.

CASE PRESENTATION

A 73-year-old female presented with chief complaint of progressive dark colored urine for 2 weeks, associated with dull abdominal pain, yellowish discoloration of the skin, and increased fatigability. She denied fever. She had a history of hypertension, hypothyroidism, and cholecystectomy. She denied any family history of liver diseases, recent travels, any form of complementary medicine, smoking, alcohol, or any illicit drug use.

On physical examination, the patient was alert and oriented with normal range vitals. She was moderately icteric without pallor. Systemic examinations were unremarkable except for a mild tenderness in the right upper quadrant of the abdomen. Her initial laboratory analysis (Table 1) revealed markedly elevated alanine aminotransferase 829 U/L, aspartate aminotransferase 909 U/L, and total bilirubin 10.9 mg/dl with direct bilirubin 7.8 mg/dl. Viral and alcoholic hepatitis were ruled out with a negative hepatitis viral panel and negative history of alcohol consumption respectively. Cytomegalovirus (CMV) culture and Epstein–Barr virus (EBV) immunoglobulin M (IgM) were negative. Serum free T4, free T3, TSH and serum copper levels were within normal range. Urine toxicology including salicylate was negative. Anti-mitochondrial, anti-smooth muscle, and kidney-liver antibodies were negative but antinuclear antibody (ANA) was only positive with a low titer of 1:160. Therefore, AIH was considered low probability in the initial differential diagnosis. Ultrasound and computed tomography (CT) scan of abdomen reported normal findings except status post cholecystectomy. Iron profile showed a significantly elevated transferrin saturation of 91% [iron of 215 μg/dl/total iron binding capacity (TIBC) of 236 mg/dL] (Table 2), which was confirmed with a repeat test. The patient denied the history of diabetes mellitus, blood transfusion and family history of hemochromatosis. 2D echocardiogram and serum hemoglobin A1c were within normal limits. Magnetic resonance imaging (MRI) of the liver showed no evidence of iron overload (hemochromatosis) (Figure 1). Genetic testing for HFE gene was not carried out.

Keywords: Autoimmune hepatitis, Transferrin saturation, Iron overload syndrome, Autoimmune disease, Diagnostic dilemma
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Address for correspondence: Gyanendra Kumar Acharya, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, USA.
E-mail: achgyanen@hotmail.com
Abbreviations: AIH: autoimmune hepatitis; ALP: alkaline phosphatase; ALT: alanine aminotransferase; AMA: antimicrosomal antibody; ANA: antinuclear antibody; anti-LKM: anti-liver kidney microsomal; anti-SMA: anti-smooth muscle antibody; AST: aspartate aminotransferase; BUN: blood urea nitrogen; CMV: cytomegalovirus; CT: computed tomography; EBV: Epstein–Barr virus; ESR: erythrocyte sedimentation rate; HHC: hereditary hemochromatosis; HLA: human leukocyte antigen; Ig: immunoglobulin; INR: international normalized ratio; LDH: lactate dehydrogenase; LFT: liver function test; MRI: magnetic resonance imaging; PT: prothrombin time; PTT: partial thromboplastin time; PTU: propylthiouracil; RBC: red blood cell; TIBC: total iron binding capacity; WBC: white blood cell
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Table 1 Basic Laboratory Data on Admission.

S. no.	Tests	Values	Reference
1.	CBCD		
	WBC	6.79 × 103/mm^3	4.50–10.9
	RBC	4.91 × 10^3/mm^3	3.8–5.2
	Hemoglobin	15.6 g%	12.2–15
	Platelets	180 × 10^3/mm^3	130–400
	ESR	**44 mm/h**	0–35
2.	Chemistry		
	Sodium	137 mmol/L	136–145
	Potassium	4.6 mmol/L	3.5–5.1
	BUN	11 mg/dL	6–20
	Creatinine	0.7 mg/dL	0.6–1.1
	T. bilirubin	**10.9 mg/dL**	0.3–1.2
	D. bilirubin	**7.8 mg/dL**	0.0–0.2
	AST	**909 IU/L**	13–40
	ALT	**826 IU/L**	7–35
	ALP	**289 IU/L**	25–100
	LDH	**464 IU/L**	100–190
	Total protein	**8.7 g/dL**	6.4–8.3
	Albumin	3.5 g/dL	3.4–4.8
	Amylase	134 U/L	20–104
3.	Basic coagulation profile		
	PT	**13.8 s**	9.70–13.20
	INR	**1.21 ratio**	0.86–1.16
	PTT	35.3 s	20.30–36.0

Table 2 Other Specific Laboratory Data.

S. no.	Tests	Values	Reference
1.	Serology/immunology tests		
	IgG	**2611 mg/dL**	694–1618
	IgA	**492 mg/dL**	81–463
	IgM	**317 mg/dL**	48–271
	Immunofixation screen	**Detected**	Not-detected
	ANA screen	**Positive**	Negative
	ANA titer	**1:160**	1:40
	Anti-mitochondrial Ab	Negative	Negative
	Anti-smooth muscle Ab	Negative	Negative
	Cycl citrul peptide IgG	<16 units	<20
	Double strand DNA ab	1 IU/ml	≤4
	Liver/kid. microsom. tit.	≤20 units	≤20
	Hepatitis (A, B, C, E)	Non-reactive	Non-reactive
2.	Other biochemical test		
	Iron	215 µg/dL	50–170
	TIBC	236 µg/dL	240–450
	Transferrin	163 mg/dL	215–380
	Ferritin	**2463 ng/ml**	10–291
	Transferrin saturation	**91%**	<55%
	Hemoglobin A1c	5.4%	3.9–6.0