CASE REPORT

Acute hepatitis E presenting with clinical feature of autoimmune hepatitis

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A 32-year-old immigrant man presented with new onset jaundice. His past medical history was significant for type 2 diabetes mellitus, hypertension, and hyperlipidemia. His initial laboratory finding and liver biopsy were suggestive of autoimmune hepatitis (AIH). The plan was to start steroids pending negative results for viral serology, but it came back positive for hepatitis E virus. The patient's liver function test and clinical condition improved significantly on conservative management over a period of 1 month. Therefore, we suggest testing for hepatitis E especially in immigrants or recent travelers to endemic areas who presents with clinical features suggestive of AIH.

Keywords: *hepatitis E*; *autoimmune hepatitis*; *transaminitis*; *IAIHG*; *hepatitis serologies*

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Acute hepatitis has a broad range of etiologies that consist of viral infection, autoimmune disease, toxic, and metabolic disorders. Hepatitis E virus (HEV) is the second most common cause of sporadic hepatitis in the Middle East and North Africa with the highest incidence in Asia, Africa, Middle East, and Central America (1, 2). HEV is an icosahedral, non-enveloped single-stranded RNA virus, that is, approximately 27–34 nm in diameter. HEV has four genotypes. In developed countries, sporadic cases of HEV genotype 3 have occurred following consumption of uncooked/undercooked pork or deer meat (2), whereas in developing countries like India and Bangladesh, the burden of HEV infection is from HEV genotype 1 and 2 (3). Diagnosis of acute hepatitis E is made based on detection of HEV RNA by polymerase chain reaction (PCR) and/or anti-HEV IgM. During the resolution phase of the infection, serum is positive for anti-HEV IgG. HEV infection is usually a self-limiting disease in immunocompetent patients. HEV is associated with acute liver failure (4) and in some cases is thought to trigger possibly an immune response that can ultimately develop into autoimmune hepatitis (AIH) (5). We present a case of new onset jaundice and markedly elevated transaminases suggestive of AIH but found to be acute HEV infection.

Case presentation

A 32-year-old overweight non-alcoholic non-smoker Bengali man was admitted to our hospital with jaundice, nausea, non-bilious, non-bloody vomiting, and worsening malaise for 3 days. His past medical history was significant for type 2 diabetes mellitus, hypertension, and hyperlipidemia. He denied any sick contacts, use of herbs, or recent change in medications. His physical examination was significant for normal vital signs, scleral icterus, and without stigmata for chronic liver disease. Laboratory values on admission and during the hospital course are shown in Table 1. In our patient, initial workup revealed alkaline phosphatase (ALP)/ aspartate transaminase (AST) with ratio <1.5, more than twofold increase in IgG, antinuclear antibody (ANA), and anti-smooth muscle antibody (ASMA) titer >1:80, anti-mitochondrial antibody (AMA) positive, negative drug history, and no alcohol intake. A liver biopsy performed showed lymphoplasmacytic portal inflammation with significant interface hepatitis and cholestasis (Figs. 1 and 2). These clinical findings added up to an International Autoimmune Hepatitis Group (IAIHG) score of 13 points. Because the patient emigrated from an endemic area for hepatitis E about 1 month prior to presentation, HEV IgM was checked, which subsequently returned positive. The test was performed by Focus Diagnostics, Inc. based out

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Table 1. Laboratory values

	Day 1	Day 2	Day 8	Day 9	Day 11	Day 27
WBC (K/mcl)	7.9		8.6			5.3
Platelets (K/mcl)	168		276			214
AST (U/L)	642	573	346	227	97	33
ALT (U/L)	1,249	1,096	1,082	797	378	38
ALP	152	148	138	121	94	76
GGT	235	203	109	93	74	45
LDH	419	396	221	160	126	155
Albumin	4.0	3.6	4.1	3.7	3.2	4.1
Total bilirubin	5.1	5.4	12.1	10.9	8.0	1.2
Conj. bilirubin	3.1	3.2	7.2	6.7	4.5	0.6
INR		1.2	1.1			
PT		13.3	11.6			
IgG				3,590		2,330
IgA				318		233
IgM				199		148
HAV IgM	Negative					
HBsAg	Negative					
HBsAb	Negative					
HBcAb	Negative					
HEV IgM			Positive			
HCV RNA PCR	Not detectable					
HSV DNA PCR			Not detectable			
CMV DNA PCR			Not detectable			
HIV	Negative					
ANA	1:1,280					
ASMA	1:160					
AMA	1:40					

of San Juan Capistrano, CA, using enzyme linked immunosorbent assay method. The patient was treated with supportive care and closely monitored in an outpatient clinic. He improved clinically with significant improvement of his liver function tests over the next month.
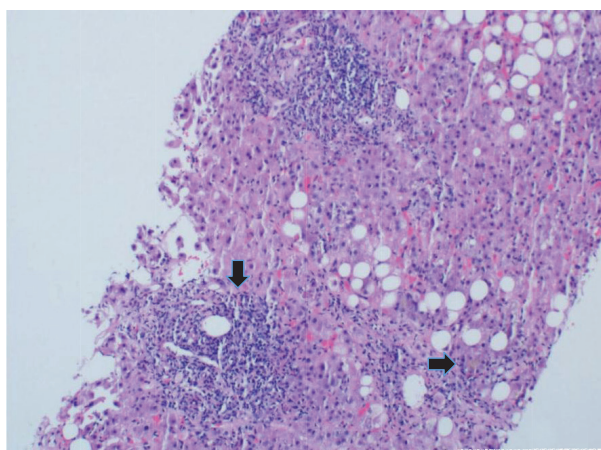
Discussion

IAIHG developed a diagnostic scoring system, which outlined 13 criteria for the diagnosis of AIH in a majority of the patients. It included gender; ALP to AST or alanine transaminase (ALT) ratio; serum globulins or
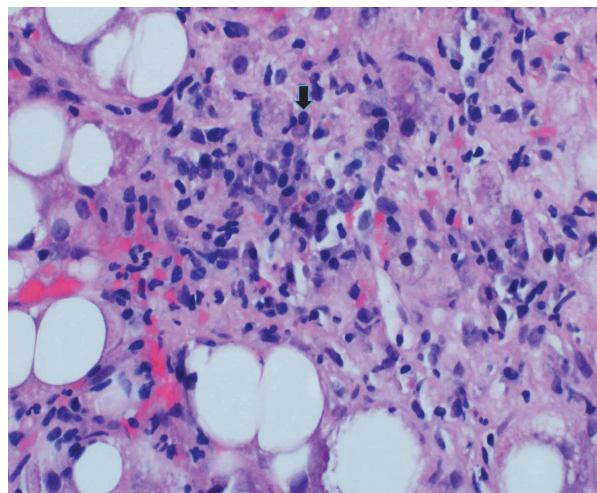

Fig. 1. Portal inflammation (vertical arrow) with interphase hepatitis and cholestasis (horizontal arrow).

Fig. 2. Portal inflammation containing plasma cell (arrow).

IgG levels; ANA, ASMA, or anti-liver-kidney microsome antibodies; AMA; hepatitis viral markers; drug history; average alcohol intake; liver histology; other autoimmune diseases; seropositivity for other defined autoantibodies; HLA DR3 or DR4; and response to therapy (6).

In our case, the IAIHG score of 13 points meets the criteria for 'probable AIH'. Concomitantly, he was positive for anti-HEV IgM and IgG antibodies suggesting acute HEV infection. The pathophysiology of these concomitant presentations of AIH and HEV seroprevalence is not well understood. Several studies have reported the presence of anti-HEV IgG antibodies in patients with AIH suggesting that HEV infection may act as a possible trigger or hapten for the development of AIH (5). Similar to our case, AMA is found to be present in sera of patients with AIH more frequently than expected. However, the clinical significance of it remains unclear (7).

Several observations in our case suggest that HEV may have triggered an AIH response. Resolution of abnormal liver function test and clinical recovery in a short period of 6–8 weeks without any intervention is unlikely in patient with AIH (8). Liver biopsy showing signs of portal inflammation and cholestasis is characteristic of viral etiology. Serology tests were positive for HEV. Patient clinically improved and returned to his home country. Due to that, we were not able to send HEV PCR. HEV PCR is considered to be the most sensitive test for diagnosing acute HEV infection. However, a recent investigation showed a variable sensitivity for different HEV PCR assays (9). Similar cases with a concomitant presentation of HEV and autoimmune mimicry have been reported in the literature (10, 11).

This case illustrates the importance of excluding acute HEV in patients with criteria for 'probable AIH' from an endemic area. Empiric therapy for AIH may lead to protracted and unnecessary therapy. Effect of steroids in such cases, beneficial or harmful, is unclear given the paucity of data in the literature.

In conclusion, our case is unique as it shows that inpatients who are clinically stable and improving with conservative management, treatment with steroids should be delayed until HEV is appropriately ruled out.

Conflict of interest and funding

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