A CASE REPORT

Simultaneous Detection of IgM Anti-Hepatitis E Virus and Anti-Epstein-Barr Virus in Acute Hepatitis

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Worldwide, hepatitis E virus (HEV), the diagnosis established by antibody and HEV RNA detection, is a major cause of acute viral hepatitis. This case describes a 39-year-old Indian male with recent onset of anorexia, weight loss and jaundice after traveling to India. Laboratory data showed a positive serology for hepatitis E immunoglobulin M (IgM) and Epstein-Barr virus (EBV) viral capsid antigen (VCA) Antibody (Ab) IgM thus establishing the diagnosis of acute hepatitis E (likely infected via fecal-oral transmission during a trip to India). During his admission he received supportive treatment and was asymptomatic at the time of discharge two weeks later. These results demonstrate the need for caution and careful evaluation of the serological results utilized in the diagnosis of EBV and HEV, as lack of awareness of the cross reactivity of the tests may result in misdiagnosis.

BACKGROUND

Worldwide, viral infection is the most common cause of hepatitis. In areas with tropical or subtropical climate and poor sanitary conditions, hepatitis E virus (HEV) is the major cause of enterically transmitted non-A, non-B hepatitis and is responsible for both water-borne outbreaks and sporadic cases of acute hepatitis. In the Indian subcontinent, HEV accounts for 30-60% of sporadic hepatitis; however, it is no longer confined to Asia and developing countries, and it appears to be an emerging disease in industrialized countries.[1]

Although relatively uncommon, primary Epstein-Barr virus (EBV) infection may also result in hepatitis. If primary infection occurs in adolescence or in adulthood, the most common manifestation is acute infectious mononucleosis. The confirmation of acute infectious mononucleosis is made by viral and serologic tests, and the most important evidence of acute primary EBV infection includes IgM class antibodies detected using EBV virus-capsid-antigen (EBV VCA). It has been documented that false-positive EBV detection can occur due to cross-reactivity with IgM against other viruses such as cytomegalovirus, adenovirus, rubella virus and human immunodeficiency virus (HIV).[2] A false positive may also be the result of the reappearance of EBV specific IgM due to polyclonal activation induced by pathogens that produce an infectious mononucleosis-like syndrome.[3]

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CASE REPORT

A previously healthy, 39 year-old Indian male presented to the emergency department (ED) with one week of jaundice and pruritus. He reported anorexia, malaise and asthenia for about 15 days associated with five pounds of weight loss. Three months prior to his arrival in the ED, he had traveled to India. The patient's partner, who had traveled with him and shared the same food, had not developed any symptoms. He had no previous vaccination for Hepatitis A or B. On examination, the patient had scleral icterus and jaundice. There was no fever, diarrhea, abdominal pain, sore throat, nausea or vomiting. Cardiopulmonary examination was normal and there was no lymphadenopathy or abdominal organomegaly.

His initial laboratory evaluation revealed: aspartate aminotransferase (AST) 1734 U/L, alanine aminotransferase (ALT) 2125 U/L, alkaline phosphatase 215 U/L, total bilirubin 14.9 mg/dl, prothrombin time 13.7 seconds and ferritin 2768 ug/L. Acute hepatitis panel (hepatitis A Ab IgM, hepatitis B core Ab IgM, hepatitis B surface Ab, hepatitis C Ab and RNA qualitative PCR) was negative. A right upper-quadrant ultrasound exhibited a normally sized liver that was heterogeneous in appearance. Given the markedly elevated liver enzymes without a clear etiology, a core needle biopsy was performed. Pathology reported moderate to severe hepatitis of uncertain chronicity and uncertain etiology with mixed hepatocellular and reticuloendothelial siderosis.

With the additional information of the abnormal biopsy pathology, other possible viral causes of acute hepatitis such as EBV, hepatitis E and cytomegalovirus were considered. The new set of laboratory data showed EBV VCA Ab IgM, EBV VCA immunoglobulin G (IgG) and Epstein-Barr nuclear antigen (EBNA) IgG positive and hepatitis E Ab IgM positive. The serologic studies for cytomegalovirus were negative. Overall, a diagnosis of acute hepatitis E was made.

DISCUSSION

We describe herein a case with a positive serology for two viral agents, EBV and HEV, which may be implicated in the etiology of acute hepatitis. Review of three other such documented cases suggests that simultaneous detection of EBV and HEV may be indicative of dual infection. However, the serological tests should be interpreted with caution as there is the possibility for false-positive detection. One possibility includes the presence of an acute infection by HEV with false positivity for EBV detection. Ghinoiu et al. describe a patient with similar serological findings to ours. They concluded that their patient had HEV confirmed by PCR, and the positive serology for EBV and negative EBV PCR was likely related to immune reactivation after hepatic cytolysis caused by the HEV infection.[4] An additional possibility involves an acute infection by EBV resulting in false reactivity for anti-HEV IgM. Fogeda et al. describe a patient with markers of acute primary infection by EBV who also demonstrated positive reactivity to anti-HEV and suggested that it might reflect either a dual infection by HEV and EBV or a false reactivity to anti-HEV by polyclonal B-cell stimulation.[5] Through differential evaluation of the EBNA and VCA IgM and IgG, the authors concluded that the serological findings were more consistent with a diagnosis of EBV infection, however HEV infection could not be excluded. In a recent case, Tappea et al. described a patient with initial negative EBV VCA IgM and HEV positive IgG and IgM. Serology tests performed one week and 4 months later showed positive EBV VCA IgM and loss of HEV IgM reactivity, respectively. They concluded that the patient had an acute EBV infection with an old unrecognized infection by autochthonous HEV.[6]

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Answers to this month's crossword puzzle:

L	C	A	■	■	U	N	I	V	A	R	I	A	T	E
U	■	P	■	H	■	■	I	■	G	■	■	D	■	C
N	U	C	L	E	O	T	I	D	E	■	B	E	A	T
E	■	■	■	A	■	H	■	O	■	■	■	N	■	A
T	U	B	U	L	A	R	■	M	A	S	S	O	N	S
■	S	A	N	E	■	O	N	E	■	B	■	M	■	I
R	E	S	I	D	U	E	■	S	T	O	M	A	T	A
E	■	■	■	■	R	■	A	■	A	■	A	S	A	■
P	L	A	T	E	L	E	T	■	P	S	P	■	I	V
L	■	M	■	B	■	X	E	■	■	Y	■	P	■	A
I	L	E	A	L	■	C	■	C	O	N	T	O	U	R
C	■	B	■	■	G	E	L	■	■	A	■	R	■	I
O	D	O	R	O	U	S	■	H	E	P	A	T	I	C
N	■	M	■	■	T	S	■	D	■	S	■	A	C	E
S	T	A	S	I	S	■	A	L	V	E	O	L	U	S

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In the diagnosis of primary EBV infection, an important piece of evidence is IgM class antibody detection using EBV VCA which appears early in the primary infection and lasts for 1 to 2 months. In our patient, the detection of EBV IgG suggests an older infection, and his recent travel to an endemic area of hepatitis E and the presence of HEV IgM make the diagnosis of hepatitis E with false positive reactivity for EBV most probable. Others have also reported the detection of anti-EBV IgM in patients with other types of hepatitis supporting the theory of a possible false positive anti-EBV during other viral hepatitis syndromes.[7, 8, 9, 10]

CONCLUSION

Immigration from and touristic travel to endemic areas of hepatitis E is a source of introduction of the disease into the United States. This case illustrates the need for primary care physicians to be aware of the presence of HEV in the United States, and should cautiously evaluate serological evidence of EBV infection with an awareness of the possibility of false positive results. Travel advisories and travel health precautions such as safe food and water consumption practices should be emphasized to visitors of endemic regions. ■

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