Case Report

A Rare Case of Acute Hepatitis with Concomitant Infections with Epstein-Barr Virus, Cytomegalovirus and Hepatitis C

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Abstract

Acute hepatitis due to concomitant infections with Epstein-Barr virus (EBV), cytomegalovirus (CMV) and hepatitis C causing symptomatic icteric hepatitis in immunocompetent individuals is extremely rare. The typical presentation of CMV and EBV infectious mononucleosis is often self-limiting characterized by lymphadenopathy, fever and pharyngitis. EBV and CMV like viral hepatitis can cause transaminitis but is usually asymptomatic and found incidentally on blood works, but in rare cases coinfection of EBV and CMV can cause asymptomatic transaminitis with jaundice with an incidence of 0.5-6.6% [1]. Nonetheless, to the best of our knowledge, the coinfections of triple viral infections with EBV, CMV and hepatitis C in an immunocompetent individual leading to acute hepatitis have rarely been reported. Herein, we presented a female patient with icteric acute hepatitis due to coinfection with EBV, CMV and hepatitis C.

Introduction

An Epstein-Barr virus is a human dsDNA herpes simplex. More than 90% of the population are seropositive for the infection **[**2**]**. Like other members of the herpes virus family, it has a latency phase. Affected patients usually have peripheral blood lymphocytosis, with atypical lymphocytes. It causes infectious mononucleosis with the triad of fever, sore throat and lymphadenopathy. Hepato-splenomegaly, maculopapular rash, transaminitis are also common but are self-limited **[**3**]**.

Cytomegalovirus is a human dsDNA herpes simplex virus 5. In immunocompetent hosts, it is generally asymptomatic or present as a mononucleosis syndrome **[**4**]**. However, in immunodeficient hosts especially transplant and HIV patients, it causes severe diseases such as retinitis, pneumonitis, encephalitis, hepatitis, or gastrointestinal tract ulceration **[**5**]**. Rare sporadic cases of fatal fulminant hepatitis and cholestatic jaundice have also been reported.

Hepatitis C is an RNA virus of the family Flaviviridae. Transmitted through contact with blood, also crosses the placenta **[**8**]**. The infection is one of the most common chronic liver diseases 50 to 80% will develop chronic liver disease and of those 5 to 30 % will develop cirrhosis and even fewer develop hepatocellular carcinoma. Most cases of hepatitis C are anicteric and asymptomatic and less than 25% are apparent, fulminant hepatitis C is rare **[**9,10**]**.

Testing for chronic HCV infection should be performed in patients who have evidence of liver disease (increase ALT/ AST, cirrhosis). Hepatitis C virus infection can also have extrahepatic presentation such as porphyria cutanea tarda, mixed cryoglobulinemia, lichen planus, necrolytic acral erythema, unexplained arthritis or false-positive rheumatoid factor, sjögren syndrome/sicca symptoms, membranoproliferative glomerulonephritis, idiopathic thrombocytopenic purpura.

In Patients with superimposed infection with EBV, CMV and hepatitis C subclinical transaminitis are the most common finding in immunocompetent patients; elevations of alkaline phosphatase and total bilirubin are less typical **[**6,7**]**.

Case report

A 30-year-old Hispanic woman with no significant past medical history presented to the ED with the chief complaint of abdominal pain for the past month. The patient reported that the pain was graded at 6/10 in intensity, located to the lower abdominal region, radiating to the back and was associated with nausea and non-bloody non-bilious vomiting on multiple episodes after meals. The patient denies fever, chills, constipation, diarrhea, hematochezia, blood in stool, sick contact, alcohol/ pain medication use, dark-colored urine or any urinary changes.

She reported recent travel to Puerto Rico in the past 3 months, she is sexually active with one male partner since December 2019, does not use contraceptives, rents a room in a house with her boyfriend and shares utensils, and has three kids who live in Puerto Rico, her last gynecologic visit was in Puerto Rico and was without any abnormality. She denies alcohol or IV drug use.

On admission, the patient was afebrile with a Temperature of 98.5 F, Blood Pressure 95/53 mmHg, Heart Rate 95/min, Respiratory rate16/min, Spo2 100% on Room air, BMI 27.3, she had slight tenderness of the epigastric and lower abdominal region on palpation, the abdomen was soft, negative for murphy sign, and normal bowel sounds. Cervical lymphadenopathy, exudative tonsillitis, buccal mucosa exanthema and skin rash were not detected on examination.

Primary lab data revealed AST 513U/L, ALT 345U/L, Total Bilirubin 1.9mg/dl, Alkaline phosphatase 660U/L, Lipase 146 U/L, GGT 268 U/L, Albumin 2.9 g/dl, Triglycerides 108mg/dL, BUN 11mg/dL, Creatinine 0.7mg/dL, Ethanol level <3 mg/dL, Calcium 8.6mg/dL, Phosphorus 3.4 mg/dL, WBC 6000 U/L, Hemoglobin 11.1 g/dl Platelets 197000 ,PTT 33.7 seconds, INR1.14, CRP 0.5mg/dl, Iron panel: Iron 21 ug/dl, TIBC 426 ug/dl, and Ferritin 29 ng/ml.

Abdominal ultrasonography showed that the liver is mildly enlarged measuring 16.2cm, the echogenic pattern appears to be the upper limit of normal. No definite focal mass. Normal main portal venous flow pattern. There is a slight amount of fluid about the gallbladder. The gallbladder wall measures 2mm within normal limits. There was no sonographic Murphy sign. Spleen appears to be mildly enlarged measuring 10.8cm.

During her inpatient stay, the patient underwent an MRCP on the next day of hospital stay that read hepatomegaly measuring at least 19 cm. No significant loss of signal on out of phase images. No evidence of diffuse liver steatosis. Collapsed gallbladder. Significant gallbladder wall thickening, circumferential. No intrahepatic nor extrahepatic biliary duct dilation. Distal CBD measures 4mm. No choledocholithiasis.

On day 3 of the hospital stay the patient had yellowish discoloration of the skin and sclera, total Bilirubin 4 g/dl peaked at 4.4g/dl on day 6. AST reached 1048 U/L on day 2 and ALT 591U/L on day 3 after which they trended down. The autoimmune workup (ANA and ASMA) was negative, the hepatitis panel for Hep A, E, B was negative. On day 3 EBV IgM > 160 U/ml (0-35.9 U/ml), EBV IgG 80.8 Hepatitis C viral load 24.6 millions and CMV IgM > 240 AU/ml (0-29.9 AU/ml), ceruloplasmin of 43.6 mg/dl IgA level 435 on day 4.

She was assessed with transaminitis due to acute hepatitis secondary to concomitant EBV, CMV and hepatitis C infection. The patient had an episode of diarrhea and vomiting that subsided.

CT abdomen and pelvis read Edematous gallbladder wall thickening to 13mm. This is a new finding compared to 10/21/2020. Hepatosplenomegaly. No intrahepatic ductal dilation.

The patient developed contrast-induced nephropathy on day 4. Creatinine increased within 3 days from 0.8 to 6 to 7.6 mg/dl, urine electrolytes: urine Na 50 mmol/l, urine Creatinine 48.1 mg/dl, renal ultrasound was normal, and she has managed with IV fluid: normal saline 100cc/h sodium bicarbonate then normal saline again at a rate of 80cc/h, the renal function was improving.

Thereafter, the patient improved symptomatically with a decline in transaminitis. Given this improvement, a liver biopsy was not pursued. The patient was discharged on Day 11 of her hospitalization. She later followed up in the clinic where her liver enzymes continued to decline towards normal limits.

Discussion

There are limited reports of simultaneous coinfection with EBV, CMV, and hepatitis C causing transaminitis with acute cholestatic hepatitis in immunocompetent women.

Abnormal liver function tests without symptomatic hepatitis are widely seen with either EBV, CMV, or hepatitis C, however, cholestasis and hepatitis due to co-infection without infectious mononucleosis syndrome is a very rare manifestation of primary infection and only a few reports have introduced cases with acute fulminant hepatitis **[**6,7**]**.

According to previous reports and ours, EBV and CMV-induced hepatitis should be considered in all patients presenting with typical symptoms of acute hepatitis, especially with obstructive jaundice. The mechanism of the obstructive component is not well understood but the accepted hypothesis is due to swelling of the biliary duct rather than an infection of the hepatocytes, biliary, or vascular epithelium **[**12**]**. The same was demonstrated with CMV hepatitis, the virus causes CD8 T cells infiltration of the hepatic duct rather than infection of the biliary tree or hepatocytes **[**12,13**]**.

Any patient with elevated liver enzymes and parameters of cholestasis should be tested for hepatitis A, B and C also further serologic profiles should include HIV, EBV and CMV. Consider Hepatitis C PCR in patients with acute hepatitis with non-reactive hepatitis C antibody in patients **[**11**]**.

EBV and CMV are self-limited diseases therefore in immunocompetent individuals no treatment is needed.

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