

Acute Cholestatic Hepatitis Due to EBV Infection-Case Report

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Abstract

Background: Epstein-Barr virus (EBV) is part of the herpes virus family and infects up to 90% of the population. EBV is one of the viruses that persist for life in human organism. During infectious mononucleosis caused by EBV infection, jaundice is distinctly uncommon and may reflect either more severe hepatitis such as cholestatic hepatitis.

Case presentation: A 23-year-old girl with clinical signs of infectious mononucleosis, presented with hyperbilirubinaemia, elevated hepatocellular enzyme levels AST 410U/L, ALT 585U/L, ALP 825U/L, thrombocytopenia; lymphocytosis 67.6% and monocytosis 15.4%. She had history of dental treatment. Serology for Epstein-Barr virus Viral Capsid Antigen

Immunoglobuline M (EBV VCA IgM), was positive. The serological examination for hepatitis A-E as well HIV, CMV and Toxoplasma gondii resulted negative. The patient left the hospital after 19 days in good clinical conditions.

Conclusions: Epstein-Barr virus is associated with a wide variety of clinical manifestations and can present as cholestatic hepatitis with or without features of infectious mononucleosis. Cholestasis is associated with EBV infection, and should be part of the differential diagnosis.

Keywords: Epstein-Barr virus, infectious mononucleosis, cholestatic hepatitis, liver enzyme.

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INTRODUCTION

EBV is a member of the human herpes virus family. It is a double-stranded DNA virus belonging to the Herpes family and the primary cause of infectious mononucleosis (1). The Epstein-Barr virus was named after Michael Anthony Epstein and Yvonne Barr who discovered together the virus and in 1964 published its existence (2). The virus replicates in the epithelial cells of the oropharynx and in β lymphocytes. Nearly all seropositive persons actively shed the virus in the saliva (3). EBV can also spread through blood and semen during sexual contact, blood transfusions, organ transplantations and it can also spread by using objects, such as a toothbrush or drinking glass from an infected person. The incubation period from the time of infection to the development of clinical symptoms is 4 to 7 weeks in young adults, but may be considerably shorter in young children (4). EBV causes a number of cancers, such as Burkitt's, Hodgkin's and T-cells lymphomas, gastric and nasopharyngeal carcinomas (5,6). Infection from EBV may present as a mild infectious illness in young children, but in adults it can cause a type of infection known as the Pfeiffer's Drüsenfieber (glandular fever). Symptomatic disease most commonly presents in young adults with the classic triad of fever, sore throat and lymphadenopathy. Abnormal liver blood tests are common in Epstein-Barr virus infection, but symptomatic hepatitis is rare (7,8,9,10). Jaundice is distinctly uncommon and may reflect either a

more severe hepatitis or an associated hemolytic anemia. Cholestatic hepatitis due to EBV infection is infrequently reported and may pose a diagnostic quandary (11,12,13). Infectious mononucleosis caused by Epstein-Barr virus usually resolves over a period of weeks or months without sequelae but may occasionally be complicated by a wide variety of neurologic, hematologic, hepatic, respiratory, and psychological complications (3,5,6,7,9,12). The aim of this paper is to present a female patient with cholestatic hepatitis due to mononucleosis.

CASE PRESENTATION

A 23-year-old girl patient presented at the emergency service at University Clinic of Infectious Diseases, Tirana, Albania, complaining of sore throat, myalgia, high fever, anorexia, nausea, vomiting, and fatigue for 8 days. She had a history of dental treatment and was clinically healthy before. She had no liver disease and she had not received any immunosuppressive treatment. On clinical presentation she had a temperature of 39°C, blood pressure of was 95/60 mmHg, heart rate 97 beat/min and respirations rate was 19 /min. Sclera jaundice was prominent. Physical findings included bilateral cervical lymph node enlargement, pharyngeal erythema and hepatosplenomegaly. Laboratory findings showed decrease in hemoglobin level, platelet count, albumin level, prothrombin time; increase in lymphocytes and monocytes count, AST, ALT, ALP, GGT and total bilirubin levels. See table 1.

Table 1. Laboratory data of biochemical and clinical tests

Laboratory data	Reference range	D0	D1	D4	D8	D14	D18
^a AST	0-40 U/L	302	410	408	366	219	156
^b ALT	0-40 U/L	325	430	585	375	137	98
^c Total Bl.	<1.2mg/dl	7.6	7.8	6.8	5.5	3.2	2.1
^d PTHS	70-120%	44.7	53.9	66.7	70.2	74	80.3
^e ALP	30-120U/L	825	470	398	452	249	158
^f GGT	0-55U/L	443	327	287	268	219	189
^g LDH	125-250 U/L	415	335	280	260	200	180
Albumin level	3.5-5.1 mmol/L	2.6	2.6	2.9	3.2	3.4	3.6
Lymphocytes	17-48%	67.6	68	56	52.5	51	51
Monocytes	4-10%	15.4	14.2	13.6	11.9	10.2	10
Platelet cells count	150- 400x10 ³ /mm ³	59	87	134	168	210	230

^a AST: aspartate-aminotrasferase.

^bALT: alanine-aminotrasferase.

^c Bl: bilirubine

^d PTHS: prothrombin time,

^e ALP: alkaline-phosphatase.

^f GGT: γ -glutamyltransferase.

^g LDH: lactate dehydrogenase

Blood cultures (three samples) resulted negative. Cervical ultrasound showed bilateral enlargement of lymph nodules. Abdominal ultrasound showed hepatosplenomegaly and normal gallbladder and biliary tree. Chest radiography was normal. Serological and virological tests for hepatitis A, B, C, E, HIV, CMV, Toxoplasmosis, Rickettsia and Brucella were negative. Direct coombs testing was negative and toxic hepatitis was excluded. The results of antinuclear antibodies (ANA), anti smooth-muscles antibodies (Anti

SMA) were negative and serum protein electrophoresis was normal. EBV viral capsid antigen (VCA) IgM test was positive and EBV VCA IgG was negative. Treatment was based on intravenous fluid, cephalosporin, steroids, support therapy with vitamins and supplements. The patient was hospitalized for 19 days.

DISCUSSION

EBV is best known as the cause of infectious mononucleosis that is characterized by fever,

lymphadenopathy, pharyngitis, and fatigue (5,9,10,12,14). In this presentation the patient was a female student. Shaukat A et al reported predominance of EBV in females with 58% compared with males (14). Cervical ultrasounds of our patient showed bilateral cervical lymphadenopathy. The patient had hepatosplenomegaly and normal gallbladder and biliary tree. Most patients with infectious mononucleosis have leukocytosis with an absolute increase in the number of atypical lymphocytes. Our case also had significantly increased in lymphocytes counts with 67.6% and monocytes count with 15.4%. Abnormal liver function tests occur in up to 80% of patients with EBV infection. Acute hepatitis is mild, clinically undetectable and resolves spontaneously. EBV rarely causes cholestatic hepatitis (8,11,12,13,15). While the pathogenesis of this complication is not well defined, it is thought to be primarily an immune-mediated rather than cytotoxic phenomenon. This idea allowed us to use corticotherapy in this case. Initial laboratory findings in our case showed decrease in albumin level, PTHS also increase in AST, ALT, ALP, GGT, bilirubin and LDH levels. Cacopardo B et al report a rare case of fatal hepatic failure due to Epstein-Barr virus reactivation in a 19-year-old boy who was taking oral steroids (15). The diagnosis of EBV infection is made by suggestive clinical symptoms, laboratory findings, and positive EBV IgM antibody and heterophilic antibodies tests. The primary acute EBV infection is associated with VCA-IgM, VCA-

IgG, and absent Epstein Barr Nuclear Antigen (EBNA) antibodies. The management of EBV cholestasis is focused on supportive therapy. Treatment was based on intravenous fluid, cephalosporin, steroids, fluids, support therapy with vitamins and supplements. Steroids and antiviral medications have been used to treat cases of severe infectious mononucleosis hepatitis. Our case was hospitalized for 19 days. One of limitation of this presentation is the lack of diagnostic procedures such as liver biopsy and endoscopic retrograde cholangiopancreatography, which were not performed due to being particularly invasive and with a high cost.

CONCLUSION

All young people presenting with cholestatic hepatitis in association with other symptoms and signs such as sore throat, fever, myalgia and lymphadenopathy must be tested for Epstein Barr virus.

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Conflict of Interest Disclosure: The authors declare that they have no conflict of interest.

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