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Acute hepatitis induced by Epstein- Barr virus infection: A case report

Epstein- Barr virus infeksiyonunun yol açtığı kolestatik hepatit: Olgu sunumu

İbrahim DOĞAN, Meltem ERGÜN, Mehmet CİNDORUK, Selahattin ÜNAL

Department of Gastroenterology, Gazi University, School of Medicine, Ankara

Epstein- Barr virus is a causative agent of infectious mononucleosis syndrome, which is commonly seen in young adults and characterized by fever, sore throat and lymphadenopathy. In adults, Epstein- Barr virus infection can cause liver function test abnormalities without pharyngitis or lymphadenopathy. Liver involvement usually causes mild elevation of transaminases and this abnormality resolves spontaneously. Jaundice might develop rarely during the clinical course of Epstein- Barr virus infection. It reflects either more severe hepatitis or Epstein- Barr virus infection-associated hemolytic anemia. Acute hepatitis with icterus is a rare clinical manifestation in primary Epstein- Barr virus infection. Especially in older patients, Epstein- Barr virus infection can cause cholestasis; the diagnosis can be established by elimination of extrahepatic biliary obstruction. Here we report an acute hepatitis in a patient who presented with icterus and was diagnosed as acute Epstein- Barr virus infection.

Key words: Epstein- Barr virus, hepatitis

Epstein- Barr virusu ateş, boğaz ağrısı ve lenfadenopati ile karakterize ve genç erişkinlerde sık olarak görülen enfeksiyöz monocucleosis sendromuna sebep olan virustur. Erişkinlerde Epstein- Barr virusu infeksiyonu farenjit ve lenpadenopati olmaksızın karaciğer enzim anormaliklerine sebep olabilir. Karaciğer tutulumu çoğunlukla hafif transaminaz yüksekliğine sebep olur ve kendiliğinden düzelir. Sarılık Epstein- Barr virusu infeksiyonu klinik seyri sırasında nadir görülebilir. Bu ya daha ciddi bir hepatit ya da Epstein- Barr virusu ilişkili hemolitik aneminin belirtisidir. Sarılığın eşlik ettiği akut hepatit Epstein- Barr virusu infeksiyonunun nadir klinik prezentasyonudur. Özellikle yaşlı hastalarda Epstein- Barr virusu infeksiyonu kolestaza sebep olabilir ve ekstrahepatik biliyer obstruksiyon nedenlerinin dışlanmasıyla tanıya ulaşılır. Biz sarılıkla prezante olan, Epstein- Barr virus infeksiyonunun sebep olduğu, akut hepatit olgusunu sunduk.

Anahtar kelimeler: Epstein- Barr virus, hepatit

CASE REPORT

A 68-year-old male presented with jaundice and pruritus. He had malaise for two weeks and was jaundiced for one week. He had subtotal gastrectomy and Billroth 2 operation for peptic ulcus 30 years ago, cholecystectomy 12 years ago and prostatectomy 7 years ago. He had suffered hypertension for 7 years and was taking perindopril regularly. He denied alcohol consumption. He had blood transfusions during his operations.

On admission to the hospital, he appeared jaundiced; his temperature was 36.5°C and blood pressure 126/85 mmHg. He had moderate hepatomegaly. Initial laboratory studies yielded aspartate transaminase (AST): 1553 U/L (ULN: 40 U/L), alanine transaminase (ALT): 1396 U/L (ULN: 40 U/L), alkaline phosphatase (ALP): 147 U/L (ULN: 120 U/L), and gamma-glutamyl transpeptidase (GGT) 50 U/L (ULN: 50 U/L). Total bilirubin was 34 mg/dl (ULN: 1.2 mg/dl) and direct bilirubin was 25 mg/dl (ULN: 0.5 mg/dl). The white blood cell (WBC) count was 7600 with 40% neutrophils and 60% lymphocytes. Atypical mononuclear cells were seen on the blood film. Virologic tests were negative for HBsAg, HBsAb, Hbc IgM Ab, HCV Ab, HCV RNA, HAV IgM Ab, and HIV Ab. The patient had not received any immunosuppressive treatment or cancer chemotherapy and had no malignancy history that may have caused immunosuppression.

An ultrasound examination revealed absence of gallbladder (due to previous cholecystectomy) and a common bile duct with a diameter of 9 mm.

Address for correspondence: İbrahim DOĞAN
Department of Gastroenterology, Gazi University School of Medicine, Ankara, Turkey
Phone: +90 202 58 16 • Fax: +90 223 63 65
E-mail: ibrahimdogan@gazi.edu.tr

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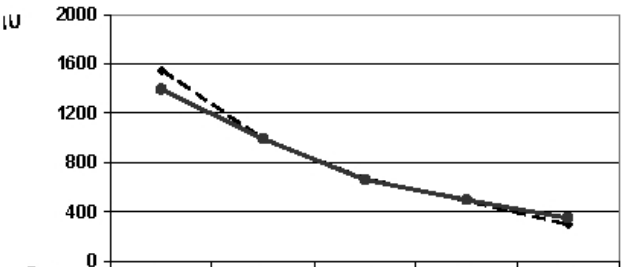
A four-phase computerized tomography (CT) of the abdomen was normal. Endoscopic retrograde cholangiography (ERC) showed no abnormality.

Other virologic and serologic examinations including antinuclear antibody, smooth muscle antibody, cytomegalovirus (CMV) and *Toxoplasma* were negative. Epstein- Barr virus viral capsid antigen (EBV VCA) IgM was positive and Epstein-Barr nuclear antigen (EBNA) IgG was negative, which are indicators of acute EBV infection. The most important evidence of primary EBV infection includes IgM class antibodies detected using EBV VCA, which appears at the beginning of the illness and usually lasts one to two months. EBV DNA measurement was not tested because of unavailability in our center at that time. A liver biopsy for definitive diagnosis was offered to the patient but was not accepted. During the hospitalization period, jaundice resolved spontaneously and the patient's clinical condition improved. On day 22, the patient's liver function tests were within normal limits (Figure 1, 2). During the follow-up period, IgG against EBNA was found to be positive at the eighth week, which supports our diagnosis.



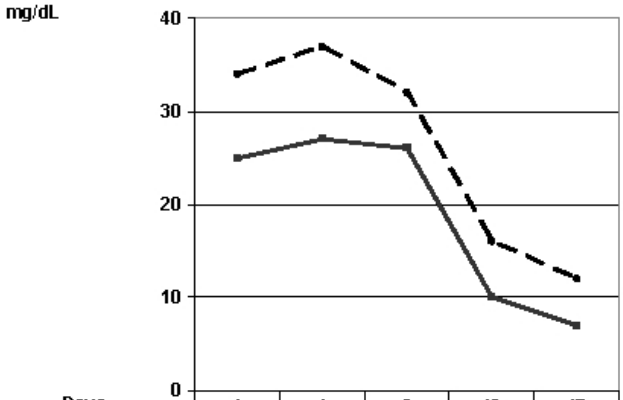
Days	1	4	9	13	17
AST	1550	990	670	490	300
ALT	1390	990	660	500	350

Figure 1. Transaminases during the course of EBV infection

DISCUSSION

EBV is a member of the human herpes virus family. EBV infection causes mononucleosis syndrome, which is common in young adults and transmitted with close personal contact (1). EBV is also a causative agent in Hodgkin lymphoma, Burkitt lymphoma and nasopharyngeal carcinoma (2).

During the course of EBV infection, mild liver enzyme abnormalities may be observed; however,



Days	1	4	9	13	17
Total Bilirubin	34	37	32	16	12
Direct Bilirubin	25	27	26	10	7

Figure 2. Bilirubin levels (total and direct) during the course of EBV infection

overt clinical hepatitis is rarely encountered (3). Fewer than 10% of patients become icteric. Rarely, EBV can cause severe cholestatic hepatitis (4). Abdominal ultrasound, CT and ERC studies can be used to rule out extrahepatic biliary obstruction. Liver biopsy was undertaken in two patients and revealed lymphocytic infiltration in both portal tracts, sinusoids and focal hepatocyte necrosis (5-8). In one biopsy material, lymphocytes stained positively with EBV antibody (8). All of the patient's clinical conditions resolved spontaneously.

Especially in elderly patients, EBV can cause jaundice. Diagnosis is based on exclusion of the extrahepatic biliary obstruction together with virologic and serologic studies. Although it is rare, after exclusion of extrahepatic causes, EBV infection should be included in the differential diagnosis of jaundice in adults.

This patient was considered as EBV-induced acute hepatitis, since ALT and AST levels were markedly higher than ALP and GGT levels; however, there was no histopathological information which could help in the differential diagnosis in this case.

In conclusion, although mild elevation of transaminases during the course of EBV infection is not a rare condition, acute hepatitis with jaundice is rare. EBV should be considered as a possible causative agent if there is no other reason for acute hepatitis with jaundice.

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