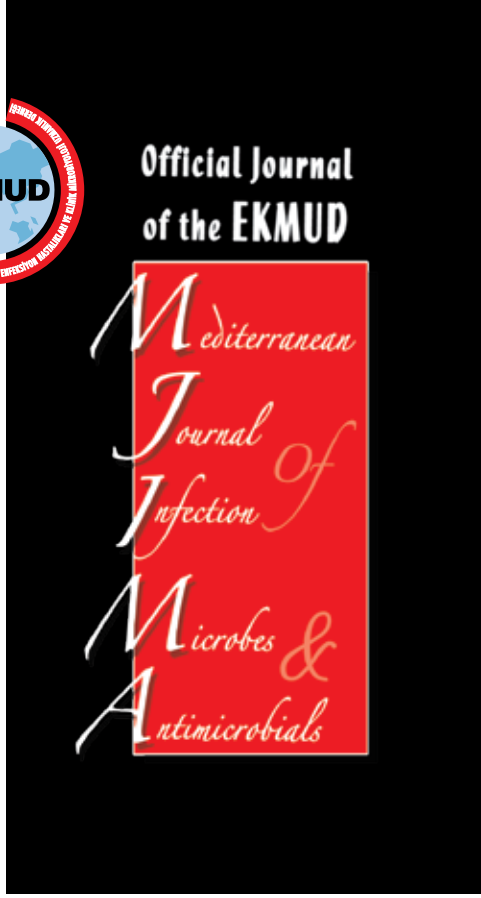
URL: http://www.mjima.org/

OLGU SUNUMU ● CASE REPORT



A Case of Infectious Mononucleosis Presenting with Cholestatic Hepatitis

Kolestatik Hepatit ile Başvuran Bir Enfeksiyöz Mononükleoz Olgusu

Mesut YILMAZ[1], Özlem ALICI[2]

[1] Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, University of Istanbul Medipol, Istanbul, Turkey

[1] *İstanbul Medipol Üniversitesi Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, İstanbul, Türkiye*

[2] Clinic of Infectious Diseases and Clinical Microbiology, Istanbul Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey

[2] *İstanbul Fatih Sultan Mehmet Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, İstanbul, Türkiye*

ABSTRACT

Although mild liver involvement is common in patients with Epstein-Barr virus (EBV) infection-induced infectious mononucleosis, acute cholestatic hepatitis is rare. In this report, we describe a 21-year-old previously healthy man with EBV-induced infectious mononucleosis presenting with acute cholestatic hepatitis. Serological tests for EBV infection were consistent with acute infection (EBV capsid antigen was reactive with IgM and IgG antibodies) and the Monospot test was positive. The patient was managed supportively and his condition improved. Acute EBV infection should be considered in the differential diagnosis of patients presenting with cholestatic hepatitis.

Key words: Cholestatic hepatitis, infectious mononucleosis, Epstein-Barr virus

Received: 01.06.2012 • ***Accepted:*** 24.07.2012 • ***Published:*** 15.09.2012

ÖZET

Epstein-Barr virüs (EBV)'ün neden olduğu enfeksiyöz mononükleoz klinik tablosunda hafif karaciğer tutulumu alışıldık bir bulgu olsa da, akut kolestatik hepatit nadir görülür. Bu makalede akut kolestatik hepatit ile başvuran, öncesinden sağlıklı 21 yaşında bir erkek hastada gelişen EBV'ye bağlı enfeksiyöz mononükleoz olgusu sunulmuştur. EBV enfeksiyonu için yapılan serolojik testler akut enfeksiyon ile uyumlu (EBV kapsid antijeni IgM ve IgG antikorları ile reaktif) ve Monospot testi pozitif saptanmıştır. Hastanın genel durumu destek tedaviyle düzelmiştir. Kolestatik hepatit ile başvuran hastalarda akut EBV enfeksiyonu ayırıcı tanıda akılda tutulmalıdır.

Anahtar kelimeler: Kolestatik hepatit, enfeksiyöz mononükleoz, Epstein-Barr virüs

Geliş Tarihi: 01.06.2012 • ***Kabul Ediliş Tarihi:*** 24.07.2012 • ***Yayınlanma Tarihi:*** 15.09.2012

INTRODUCTION

Infectious mononucleosis (IM) caused by Epstein-Barr virus (EBV) is almost always a self-limited disease of young adults. Mild liver enzyme abnormalities are not uncommon and resolve spontaneously[1,2]. Liver involvement is usually consistent with parenchymal injury rather than with decreased bile flow. Although cholestasis has been reported rarely, a recent study of primary EBV infection showed that cholestatic liver disease was more common than initially thought (observed in up to 59% of 41 patients)[3-5]. We describe a young male patient with cholestatic hepatitis secondary to acute EBV infection.

CASE REPORT

A 21-year-old man was admitted to our hospital with a 10 day history of high-grade fever, chills, rash extending from the trunk to face and extremities with pruritus, and malaise. Five days prior to admission, he had been diagnosed with upper respiratory tract infection and prescribed an oral beta-lactam antibiotic and a non-steroidal anti-inflammatory drug. His prior medical history was unremarkable. He had no known drug allergies and took no medications. He denied alcohol consumption, blood transfusion, or injection drug use, but reported having a recent intimate contact with his girlfriend.

On admission to the hospital, he was dehydrated and appeared seriously ill; he had a body temperature of 39.1°C, pulse rate of 110 bpm, and respiratory rate of 25 breaths/min. His blood pressure was 128/72 mmHg with no postural changes. He had moderate pharyngeal erythema with bilateral cervical and posterior lymphadenopathy. Physical examination revealed mild jaundice, moderate hepatomegaly, and enlarged spleen (2 cm below the left costal margin) with tenderness to palpation, but no further pathological findings. Initial laboratory tests revealed C-reactive protein (CRP): 25 mg/L (0-5), aspartate aminotransferase (AST): 180 U/L (0-38 U/L), alanine aminotransferase (ALT): 392 U/L (0-41 U/L), gamma-glutamyl transferase: 507 U/L (10-66), and alkaline phosphatase: 373 (40-129) U/L. Total bilirubin was 2.5 mg/dL and direct bilirubin was 1.5 mg/dL. Complete blood count showed a white blood cell count (WBC) of 11.900/mm^3 with 33% neutrophils and 40% lymphocytes, hemoglobin (Hb) of 14 g/dL, hematocrit of 39%, and a normal platelet count of 160.000 platelets/mm^3. Bacterial cultures of urine and blood were negative. Chest X-ray and thorax computed tomography (CT) did not show any pathologic changes. An abdominal ultrasound examination confirmed the liver and spleen to be enlarged to 17 cm and 16 cm, respectively. The gallbladder and intraluminal bile ducts were normal. An abdominal CT also showed hepatosplenomegaly but excluded dilatation of the biliary tree Figure 1. He was treated symptomatically for dehydration and fever. The course of the patient's liver enzymes are given in Figure 2.

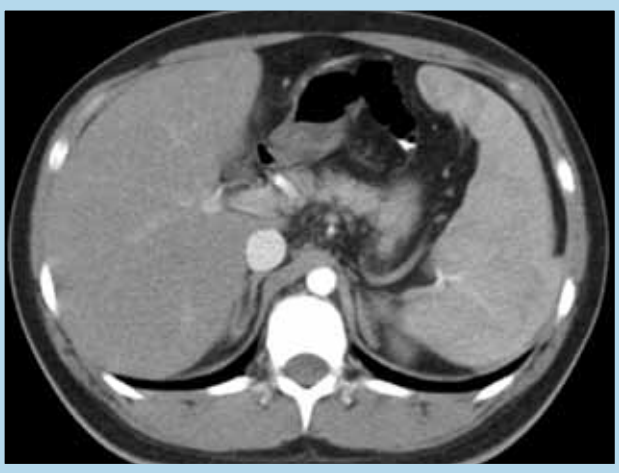
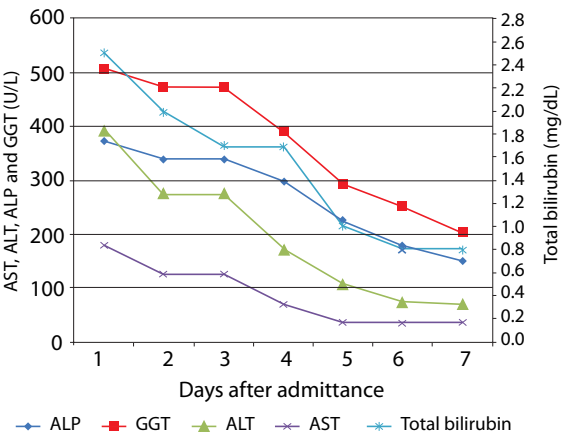


Figure 1

Abdominal computed tomography scan of the patient showing hepatosplenomegaly.

Figure 2

Course of liver biochemistry results for AST, ALT, ALP, GGT, and total bilirubin. (ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase).



After three days of hospitalization, his course was complicated by several episodes of fever with negative blood cultures. His body temperature was still up to 40°C, and CRP had risen to 92 mg/L. His WBC was 16.000/mm^3 with 68% lymphocytes (20% atypical). Serological studies remained negative for antinuclear antibodies (ANA), antimitochondrial antibodies (AMA), anti-smooth muscle antibody (ASMA), cytomegalovirus (CMV) and Toxoplasma. Further laboratory evaluation ruled out hepatitis A, B, C and human immunodeficiency virus (HIV). The patient had a history of exposure to drugs that could implicate drug-related liver-bile duct injury; however, a liver biopsy was not approved by the patient.

Monospot test was positive, as was his EBV viral capsid antigen (VCA) IgM. IgG for EBV VCA was negative and nuclear EBV Ag was negative, a pattern indicative of an acute EBV infection. The liver enzymes and bilirubin levels improved during his hospitalization. Follow-up tests two months later showed EBV VCA IgM positive and EBV VCA IgG positive, confirming the diagnosis of EBV infection. Hepatosplenomegaly and all liver chemistry abnormalities had resolved.

DISCUSSION

EBV is a ubiquitous human herpesvirus that is usually transmitted through close personal contact among young children and via intimate oral contact among adolescent and young adults. In the developing countries, 80-100% of children are usually seropositive by three to six years of age; however, seropositivity often occurs between the ages of 10 and 30 years in developed countries[6]. The cause of difference in age distribution of primary EBV infection is unclear.

The majority of patients with IM recover uneventfully without any complications, although a wide range of clinical complications including neurologic, hematologic, respiratory, and psychological complications may occur[6]. Hepatic involvement is very common in EBV infection, occurring in 50-80% of cases, with elevated liver enzyme levels that are usually up to four times normal, however, severe hepatocellular liver injury is rare[7,8]. High concentrations of enzyme-inhibiting autoantibodies against the antioxidative enzyme, manganese-superoxide dismutase (MSD), have been postulated to play a role as the mechanism whereby EBV might induce cholestasis; however, the exact mechanism remains undetermined[9]. The liver damage during EBV infection is induced by activated cytotoxic T lymphocytes (CTLs) in the sinusoids directed against B lymphocytes harboring the virus[10,11]. Another contributing factor may be the effect of the virus on systemic and intrahepatic production of pro-inflammatory cytokines, which interfere with the activity of both the sinusoidal and canalicular transporting systems that may lead to cholestasis. Viral infectious processes affecting the biliary tree may have protean clinical and imaging appearances. Abdominal ultrasound evaluations of

EBV hepatitis may show an enlarged liver and/or spleen; however, gallbladder thickening has been reported rarely[12,13]. In Turkey, severe hepatitis in EBV-induced IM has been reported in various age groups, including infants, children, young adults, and the elderly, with a favorable outcome[14-17].

In a great number of patients with drug-induced hepatocellular injury, the cause is idiosyncratic drug reaction. Although it was not possible to rule out drug-induced hepatotoxicity in our patient since a liver biopsy was refused, we believe that cholestatic hepatitis was related to EBV in this patient because idiosyncratic drug reactions occur in only about 0.01-1% of individuals who are taking the drug[18].

Mild EBV-induced hepatitis is a common finding during IM and is usually asymptomatic. This case shows that more significant liver involvement may occur, including mild jaundice and elevations in transaminases and other enzymes indicative of cholestasis. Therefore, EBV infection should be considered in the differential diagnosis of patients with liver abnormalities or diverse hepatic manifestations, increased levels of aminotransferases, or a transitory cholestatic pattern, and the outcome is favorable.

REFERENCES

1. *Barlow G, Kilding R, Green ST. Epstein-Barr virus infection mimicking extrahepatic biliary obstruction. J R Soc Med 2000; 93: 316-8.*
2. *Johannsen EC, Schooley RT, Kaye KM. Epstein-Barr virus (infectious mononucleosis). In: Mandell GL, Douglas RG, Bennett JE, Dolin R (eds). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 6th ed. Philadelphia: Elsevier/Churchill Livingstone, 2005: 1801-20.*
3. *Edoute Y, Baruch Y, Lachter J, Furman E, Bassan L, Assy N. Severe cholestatic jaundice induced by Epstein-Barr virus infection in the elderly. J Gastroenterol Hepatol 1998; 13: 821-4.*
4. *Kofteridis DP, Koulentaki M, Valachis A, Christofaki M, Mazokopakis E, Papazoglou G, Samonis G. Epstein Barr virus hepatitis. Eur J Intern Med 2011; 22: 73-6.*
5. *Hinedi TB, Koff RS. Cholestatic hepatitis induced by Epstein-Barr virus infection in an adult. Dig Dis Sci 2003; 48: 539-41.*
6. *Tsai MH, Hsu CY, Yen MH, Yan DC, Chiu CH, Huang YC, Lin SJ, Lin TY. Epstein-Barr virus-associated infectious mononucleosis and risk factor analysis for complications in hospitalized children. J Microbiol Immunol Infect 2005; 38: 255-61.*
7. *Fuhrman SA, Gill R, Horwitz CA, Henle W, Henle G, Kravitz G, Baldwin J, Tombers J. Marked hyperbilirubinemia in infectious mononucleosis: analysis of laboratory data in seven patients. Arch Intern Med 1987; 147: 850-3.*
8. *Mendez-Sanchez N, Aguilar-Dominguez C, Chavez-Tapia NC, Uribe M. Hepatic manifestations of Epstein-Barr viral infection. Ann Hepatol 2005; 4: 205-9.*
9. *Juttner HU, Ralls PW, Quinn MF, Jenney JM. Thickening of the gallbladder wall in acute hepatitis: ultrasound demonstration. Radiology 1982; 142: 465-6.*
10. *Drebber U, Kasper HU, Krupacz J, Haferkamp K, Kern MA, Steffen HM, Quasdorff M, Zur Hausen A, Odenthal M, Dienes HP. The role of Epstein-Barr virus in acute and chronic hepatitis. J Hepatol 2006; 44: 879-85.*
11. *Dienes HP, Drebber U. Pathology of immune-mediated liver injury. Dig Dis 2010; 28: 57-62.*
12. *Crum NF. Epstein Barr virus hepatitis: case series and review. South Med J 2006; 99: 544-7.*
13. *Sainsbury R, Smith PK, LeQuesne G, Davidson GP, Jureidini KF, Moore DJ. Gallbladder wall thickening with infectious mononucleosis hepatitis in an immunosuppressed adolescent. J Pediatr Gastroenterol Nutr 1994; 19: 123-5.*
14. *Tutar E, Cihan MK, Uysal G, Şaylı T. Epstein-Barr virus-induced severe hepatitis in an immunocompetent infant. Turk J Gastroenterol 2009; 20: 154-5.*
15. *Çelik C, Küçükuğurluoğlu Y, Balcı DB, Öner N, Duran R, Karasalihoğlu S. Elevation of clinical and laboratory features of Epstein-Barr virus-associated acute infectious mononucleosis in children. Trakya Univ Tıp Fak Derg 2008; 25: 221-7.*
16. *Uluğ M, Celen MK, Ayaz C, Geyik MF, Hoşoğlu S. Acute hepatitis: a rare complication of Epstein-Barr virus (EBV) infection. J Infect Dev Ctries 2010; 4: 668-73.*
17. *Tahan V, Ozaras R, Uzunismail H, Mert A, Tabak F, Ozturk R, Aktuglu Y, Ozbay G. Infectious mononucleosis presenting with severe cholestatic liver disease in the elderly. J Clin Gastroenterol 2001; 33: 88-9.*
18. *Kaplan MM. Enzymatic measures of cholestasis (eg, alkaline phosphatase, 5'-nucleotidase, gamma-glutamyl transpeptidase). In: Basow DS (ed). Waltham, MA: UpToDate, 2011.*

Yazışma Adresi /Address for Correspondence

Yrd. Doç. Dr. Mesut YILMAZ

İstanbul Medipol Üniversitesi Tıp Fakültesi,

Enfeksiyon Hastalıkları ve

Klinik Mikrobiyoloji Anabilim Dalı,

İstanbul-Türkiye

E-posta: myilmaz@medipol.edu.tr