*Case Report*
*Internal Medicine*
DOI: 10.56016/dahudermj.1634106

DAHUDER
Medical Journal
e-ISSN: 2791-9250

# Cholestatic hepatitis in a patient with primary Epstein-Barr virus infection: A case report

**Ali Erol[1], Ayse Gokce[2], Feridun Gurlek[3], Neslihan Baykara Erol[4],**

*[1].Department of Internal Medicine, Health Sciences University Bursa Yüksek Ihtisas Training and Research Hospital, Bursa, Türkiye*
*[2].Department of Radiology, Health Sciences University Bursa Yüksek Ihtisas Training and Research Hospital, Bursa, Türkiye*
*[3] Department of Allergy and Immunology, Health Sciences University Bursa Yüksek Ihtisas Training and Research Hospital, Bursa, Türkiye*
*[4] Department of Pulmonology, Health Sciences University Bursa Yüksek Ihtisas Training and Research Hospital, Bursa, Türkiye*

## ABSTRACT

Primary Epstein-Barr virus (EBV) infection is a herpes virus characterized by sore throat, fever, and lymphadenopathy. Liver involvement is characterized by moderate elevation of aminotransferases and hepatosplenomegaly, which regresses spontaneously. Cholestatic hepatitis in patients is a rare presentation of primary EBV infection. A 19-year-old male patient presented to the emergency department with complaints of nausea, vomiting, right upper quadrant pain, and mild sore throat for 2 days. Acute EBV infection was diagnosed based on serology results and no dilating lesions detected on radiological imaging. Healthcare professionals should keep in mind that EBV may also be involved in the etiology of cholestatic hepatitis.

***Keywords***: Epstein-Barr virus, cholestasis, hepatitis

## INTRODUCTION

EBV is a member of the Herpesviridae family that causes infectious mononucleosis (EM), characterized by sore throat, fever, and lymphadenopathy. EM is a self-limiting disease that is common worldwide and usually seen in young adults.[1] Liver involvement is characterized by moderate elevations in aminotransferases and regresses spontaneously. Cholestatic hepatitis, characterized by elevations in alkaline phosphatase and bilirubin, is less common.[2] A case of cholestatic hepatitis, presented to the emergency department with nausea, vomiting, and mild sore throat, and treated with conservative methods was planned to be presented.

## CASE REPORT

A 19-year-old male patient was admitted to the emergency department with complaints of nausea, vomiting, and a sore throat for the last 2 days. He had no previous medical history. On admission, his body temperature was 36.5 °C, pulse rate was 90/min, and respiratory rate was 18/min. Blood pressure was 120/70 mmHg. Tonsillitis was detected in the pharynx, and a palpable lymph node was found in the submandibular area of the neck. On abdominal examination, the right upper quadrant was tender and painful, and the spleen was found to be enlarged two finger widths below the costal margin. Laboratory findings; alanine aminotransferase (ALT): 389 (15-

***Received:*** *February 5, 2025;* ***Accepted:*** *March 3, 2025;* ***Published Online:*** *Julyl 29, 2025*

***How to cite this article:*** *Erol A, Gokce A, Gurlek F, Baykara Erol N. Cholestatic hepatitis in a patient with primary Epstein-Barr virus infection: A case report. DAHUDER MJ 2025,5(3):109-112. DOI: 10.56016/dahudermj.1634106*

***Address for correspondence:*** *Ali Erol, University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Türkiye*
*E-mail: alierol625@gmail.com*

Available at http://dergipark.org.tr/en/pub/dahudermj

55) U/L, aspartate aminotransferase (AST): 384 (10-45 ) U/L, alkaline phosphatase (ALP): 555 (40-150) U/L, gamma glutamyl transferase (GGT): 252 (12-64) U/L, lactate dehydrogenase (LDH): 811 (125-220) U/L, total bilirubin: 1.92 (0.2-1.1) mg/dL and direct bilirubin: 1.22 (0.0-0.5) mg/dL, erythrocyte sedimentation rate (ESR): 20 (0-15) mm/h, C-reactive protein (CRP): 44 (0-5) mg/L, procalcitonin 0.09 (0-0.5) ng/ml, white blood cell (WBC) 17.17 × 10 3 (3.5–10.5 × 10 3 )/mm 3, neutrophil (NEU) 3.09 × 10 3 (1.9–8 × 10 3 )/mm 3, lymphocyte (LYM) 13.44 × 10 3 (0.9–2.9 × 10 3 )/mm, hemoglobin (Hb): 13.2 (13.5–17.5) g/dL, platelet: 176 × 10 3 (150–450 × 10 3 )/mm 3. Blood and urine cultures were negative. No pathology was detected on the postero-anterior chest radiograph. Hepatitis B and C, anti-HIV, rheumatoid factor, anti-nuclear antibody, C3, C4, anti-Toxoplasma IgM, anti-Rubella IgM, Parvovirus B19 IgM, and direct Coombs test were negative. Anti-CMV IgM 11.3 (< 0.85) was positive, CMV PCR was negative (31.2-156000000 IU/ML), EBV VCA IgM 47.78 ( < 0.5) S/CO, EBV DNA PCR 392, EBV VCA IgG, EBV EA, EBV EBNA IgG, HAV IgM, Brucella tube agglutination was negative.

Anti-CMV IgM positivity was considered as a false positive due to cross-reaction between herpes family members. In the patient's emergency ultrasound, liver parenchymal echogenicity increased as grade 1, spleen size was 15 cm, gallbladder was contracted and no dilatation, stone or space-occupying lesion was detected in the bile ducts. In the ultrasound requested in the ward, right inguinal 22x11 mm and left inguinal 20x12 mm lymph nodes with thickened oval cortices and fatty hilums were detected. In the patient's superficial ultrasound, multiple oval lymph nodes with fatty hilums were detected in the neck, the largest of which was 40x20 mm in the right submandibular localization and the largest of which was 35x17 mm in the left submandibular localization. On the 9th day of his hospitalization, ALT, AST, total bilirubin and direct bilirubin, ALP and GGT, Crp decreased to 84 U/L, 56 U/L, 0.85 mg/dL, 0.37 mg/dL, 170 U/L, 90 U/L, 14 mg/L, respectively. Ampicillin-sulbactam was added to the patient's treatment for simultaneous treatment of cryptic tonsillitis and cholecystitis on his first hospitalization. There was no decrease in hemoglobin during his follow-up. No additional pathology was detected in his peripheral smear except for atypical lymphocytes and leukocytosis. On the 8th day of his hospitalization, abdominal computed tomography was requested for regression control (Figures 1 and 2). The patient did not have any antibiotic-related rash. The patient's clinical condition gradually improved with antibiotic and conservative treatment on the 9th day of his hospitalization, and he was discharged. On the 14th day after discharge, in the outpatient clinic laboratory values, ALT, AST, total bilirubin and direct bilirubin, ALP and GGT values were determined as 23 U/L, 22 U/L, 1.01 mg/dL, 0.65 mg/dL, 127 U/L, 31 U/L, respectively. USG shows no dilatation of the gallbladder and splenomegaly (Figures 3 and 4).

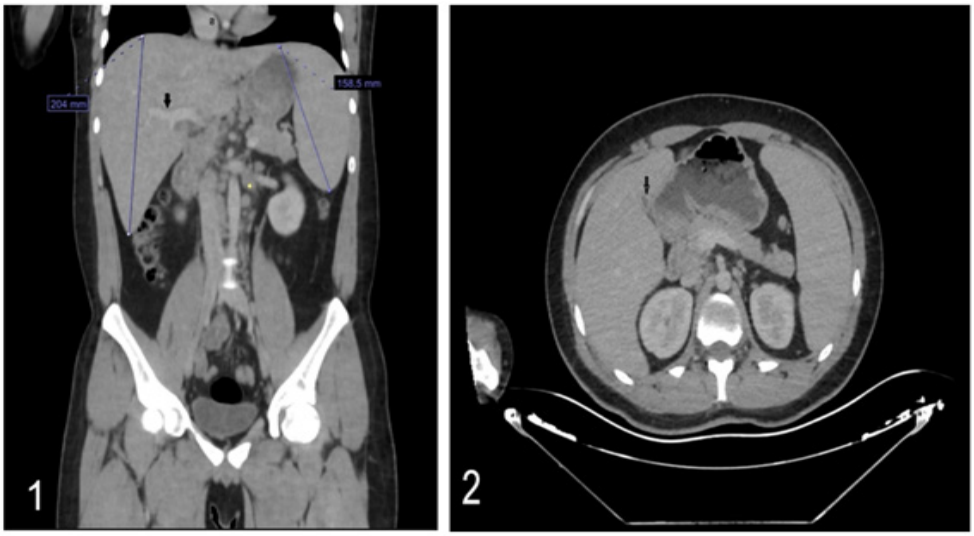


**Figure 1:** Coronal abdominal CT image shows periportal edema (arrow), increased liver and spleen size, minimal heterogeneity in the parenchyma, and multiple moderate lymphadenopathy (stars) in the mesenteric fat tissue.

**Figure 2:** Axial abdomen CT image shows a regressed, thin-walled contracted gallbladder (arrow) on the 8th day after treatment.

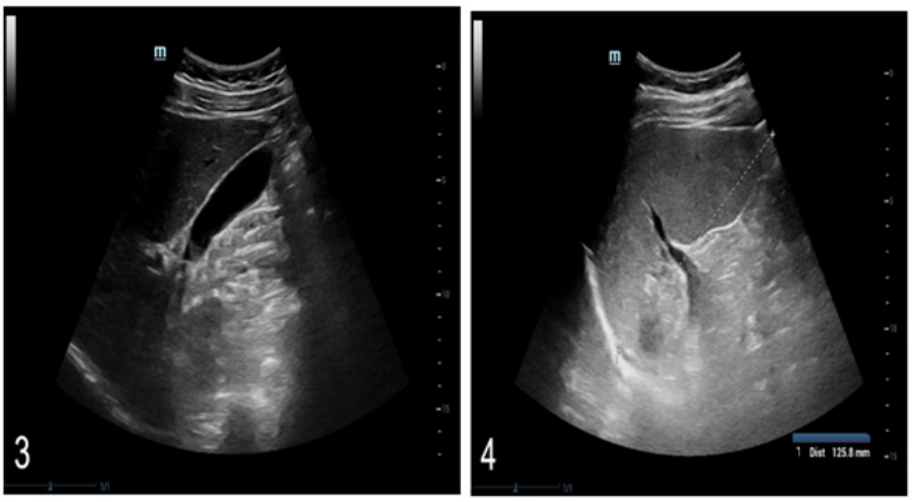


**Figure 3:** Gallbladder transverse diameter and wall thickness are within normal limits, no intraluminal pathology was detected.

**Figure 4:** Spleen long axis was measured at the upper limit of normal as 12.5 cm.

## DISCUSSION

EM is commonly seen in society starting from childhood. In our society, 80-86% seropositivity was detected in the adult age group.[3] The most common findings observed in EBV infection include sore throat, fever, and widespread lymphadenopathy. Although liver involvement is frequently observed, moderate transaminase elevation and hepatomegaly are also detected in 10% of cases, and in 80-90% of cases, liver enzyme elevations regress spontaneously. Cholestatic liver disease, characterized by elevated serum alkaline phosphatase, is seen in less than 5% of cases.[4] The patient's transaminase values were found to be more than 7 times higher, and no positive findings were detected in other etiologies. GGT and ALP values were 3 times higher, and bilirubin values were borderline higher, suggesting cholestatic hepatitis. In the patient's follow-up, laboratory values decreased to normal levels on the ninth day. Information on the pathophysiology of cholestasis in EBV infection is limited. It is thought that the effect of EBV is not through direct cytotoxic effect but through inhibition of antioxidative enzymes.[5] There are several possible mechanisms that can be associated with EBV infection in cholestatic hepatitis. EBV can lead to activation of T-lymphocytes. This can trigger an inflammatory response in the liver related to the infection, leading to damage to hepatocytes and the development of cholestatic symptoms. In addition, EBV can directly attack hepatocytes and cause damage to these cells. Damaged hepatocytes can contribute to the development of cholestasis by causing disruptions in bile production and flow. In addition, the epithelial cells in the bile ducts affected during EBV infection can lead to cholestatic hepatitis by impairing bile flow as a result of the virus attacking these cells. Reactive autoimmunity that develops after the virus can also target liver tissue and trigger cholestatic processes. In addition, high viral load and replication can contribute to the development of cholestatic hepatitis by increasing inflammation of the liver.[6]

Among the EM laboratory findings, leukopenia or leukocytosis can be detected, and atypical lymphocytes are seen at a rate of 25%.[7] In our patient, atypical lymphocytosis was detected in the peripheral smear. Laboratory findings of EBV infection include Early antigen (EA), Epstein-Barr nuclear antigen (EBNA), Viral Capsid Antigen (VCA), or heterophile antibody test, and IgM type antibodies against VCA (anti-VCA IGM).[8] In our case, EBV infection was diagnosed with tonsillitis clinic and EBV VCA IgM positivity. When a review of 3 different EBV-associated cholestatic hepatitis cases was examined, similar to our case, they were treated with fluid resuscitation and analgesics.[9]

HIV, CMV, Brucella, Hepatitis A, B, and C, and HIV infections are included in the differential diagnosis of EBV. CMV is a member of the herpesvirus family and can also cause infectious mononucleosis. In our patient, hepatitis serologies, anti-HIV, and brucella agglutination tests were found to be negative. Anti-CMV IgM was positive, and

CMV DNA PCR was found to be negative. With the current findings, concomitant acute CMV infection was not considered in our case. In addition, CMV IgM antibodies investigated with the ELISA method can cross-react with other herpes family members, and false-positive results can be obtained.[10] Cervical lymphadenopathy is present in approximately 70% of patients with primary EBV infection.[11] In our case, 2 lymph nodes measuring 3 cm in size were detected in the right and left submandibular regions. In addition, hepatosplenomegaly occurred in 30% of the cases and was also detected in our case.[12] Patients usually recover spontaneously within 2-3 weeks. Infectious mononucleosis can cause complications such as neurological, hepatic, and splenic rupture. Treatment is supportive. Antiviral treatment can be used in severe cases. Our patient's clinical and laboratory findings showed regression as a result of supportive treatment.

## Conclusion

EBV causes infectious mononucleosis, characterized by fever, sore throat, and lymphadenopathy. Hepatic involvement in EBV is usually mild and resolves spontaneously. Although cholestatic hepatitis is a rare complication of EBV, EBV should be considered in the differential diagnosis of patients presenting with cholestatic hepatitis.

*Author Contributions*:

CStudy Conception: AE, AG, FG, NBE; Study Design: AE, AG, FG, NBE; Supervision: AE, AG, FG, NBE; Funding: AE, AG; Materials: AE, AG; Data Collection and/or Processing: AE, FG; Analysis and/or Data Interpretation: AE; Literature Review: AE, NBE; Critical Review: AE, FG; Manuscript preparation: AE, AG.

*Conflict of Interest*

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

*Funding Sources*

The author(s) received no financial support for the research, authorship, and/or publication of this article.

*Ethical Statement*

In accordance with ethical standards, all patient information was anonymized, and no formal ethics approval was necessary.

## REFERENCES

1. Shaw N, Evans J. Liver failure and Epstein-Barr virus infection. Arch Dis Child. 1988;63:432–3. doi: 10.1136/adc.63.4.432
2. Primary Ebstain-Barr Virüs hepatitis complicated by ascites with Ebstein Barr Virüs reactivation during primary Cytomegalovirüs infection. J of Pediatric Gastroenterology 2003;37:87-90. doi: 10.1097/00005176-200307000-00016
3. Kofteridis D, Koulentaki M, Valachis A, Christofaki M, Mazokopakis E, Papazoglou G, et al. Eur J Intern Med. 2011;22(1):73–6. doi: 10.1016/j.ejim.2010.07.016
4. Ebstein-Barr Virüs virüs: an unusual cause of cholestatic hepatitis in older adults.Gastroenterology Hepatology 2007;3(2):101-105.
5. Cameron B, Flamand L, Juwana H, Middeldorp J, Naing Z, Rawlinson W, et al. Serological and virological investigation of the role of the herpesviruses EBV, CMV and HHV-6 in post-infective fatigue syndrome. J Med Virol. 2010;82(10):1684–8. doi: 10.1002/jmv.21873
6. Levitskaya J, Coram M, Levitsky V, Imreh S, Steigerwald-Mullen PM, Klein G, Kurilla MG, Masucci MG. Inhibition of antigen processing by the internal repeat region of the Epstein-Barr virus nuclear antigen-1. Nature. 1995 Jun 22;375(6533):685-8. doi: 10.1038/375685a0.
7. Epstein Barr virus hepatitis. Kofteridis DP, Koulentaki M, Valachis A, Christofaki M, Mazokopakis E, Papazoglou G, Samonis G. Eur J Intern Med. 2011;22:73–76. doi: 10.1016/j.ejim.2010.07.016.
8. Markin R. Manifestations of Epstein-Barr virus-associated disorders in liver. Liver. 1994;14(1):1–13. doi: 10.1111/j.1600-0676.1994.tb00001.x
9. Joshi A, Jha D, Wari E, Saeed M, Hussain M, Hiatt TK. Cholestatic hepatitis in acute Epstein–Barr virus infection: A case report. Clin Case Rep. 2024; 12:e9357. doi:10.1002/ccr3.9357
10. Mellinger J, Rossaro L, Naugler W, Nadig S, Appelman H, Lee W, et al. Epstein-Barr virus (EBV) related acute liver failure: a case series from the US Acute Liver Failure Study Group. Dig Dis Sci. 2014;59(7):1630–7. doi: 10.1007/s10620-014-3029-2
11. M Abdel-Aziz, H El-Hoshy, M Rashed, M Qotb, S Awad, N Naguib. Epstein–Barr virus infection as a cause of cervical lymphadenopathy in children. Int J Paediatr Otorhinolaryngol. 2011;75(4):564–67. doi: 10.1016/j.ijporl.2011.01.020.
12. Womack J, Jimenez M. Common questions about infectious mononucleosis. Am Fam Physician. 2015;91(6):372-376