SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Gastroenterology

Cholestatic Jaundice during Epstein-Barr Virus Primary Infection: A Rare Manifestation

Abdelfettah Touibi[1*], R. Laroussi[1], I. Mouslim[1], S. Hdeyi, S[1]. Berrag, F[1]. Nejjari, T[1]. Adioui, M[1]. Tamzaourte[1]

[1]Department of Gastroenterology I, Mohammed V of the Military Hospital, Rabat, Morocco

DOI: 10.36347/sasjm.2023.v09i06.035 | **Received:** 08.04.2023 | **Accepted:** 12.05.2023 | **Published:** 26.06.2023

***Corresponding author:** Abdelfettah Touibi
Department of Gastroenterology I, Mohammed V of the Military Hospital, Rabat, Morocco

Abstract **Case Report**

Infectious mononucleosis, induced by the Epstein-Barr virus (EBV), is a very frequent infection, affecting mostly young adults. Although liver damage is often mild and self-limiting, only a few cases of severe EBV-induced cholestatic hepatitis and jaundice have been reported in the literature. EBV infection should be considered as part of the differential diagnosis in patients with an obstructive pattern on liver function tests without evidence of biliary obstruction demonstrated on advanced imaging. The diagnosis is usually confirmed only by serology and the evolution is generally favorable. We report the observation of an 16 year old female with no particular medical history, who developed a febrile cholestatic jaundice without signs of hemolysis and without biliary obsruction on imagery.

Keywords: Epstein Barr Virus primary infection, Cholestatic jaundice.

INTRODUCTION

EBV Primary infection usually occurs in childhood. It is often asymptomatic and occurs between 10 and 30 years of age in developed countries [1, 2]. Increasing age seems to raise the likelihood of symptomatic infection. typically the classic triad of infectious mononucleosis (IM) includes fever, tonsillitis, and lymphadenopathy [1, 2].

Although liver involvement is common in acute EBV infection, it usually manifests as transient transaminase elevation in 80-90% of patients [3, 4]. The increase in liver enzymes is usually mild, lower than in typical acute viral hepatitis, and clinical manifestations of hepatitis are rare [5]. Significant cholestasis and jaundice are rare with an estimated incidence below 5% [4, 5].

CASE REPORT

A 16 year old female with no particular personal or family medical history, she was admitted in the emergency department. Her symptoms dated back to one week before her admission with the onset of a dry cough with dyspnea followed two days later by a progressively aggravating jaundice, firstly conjunctival and then frank cutaneous-mucosal, without remission, associated to dark urine and lightly discolored stools without pruritus or abdominal pain, all evolving in a context of fever and asthenia.

The general examination found a patient alert, and oriented to time, place, and person with a fever to 39 degrees Celsius, a tachycardia to 95 beats per minute and a cutaneous-mucosal jaundice. The abdominal examination was normal, especially no sinsibility or hepatosplenomegaly, the neurological examination noted the absence of a meningeal syndrome, The oropharynx was normal, the rest of the physical examination was without particularities.

The initial biological assessment showed a complete blood count with 9600 leukocytes/mcL, 41.1% lymphocytes, a hemoglobin rate of 12.3 g/dL and a platelet count 144,000/mcL at the lower limit of normal. the liver function tests were disturbed with: aspartate aminotransferase (AST) 96 IU/L (3 times normal value), alanine alanine aminotransferase (ALT) 105 IU/L (2.5 times normal value), γ-glutamyl transpeptidase (γ-GT) 165 IU/L (5 times normal value), alkaline phosphatase (ALP) 128 IU/L, lactate dehydrogenase (LDH) 715 IU/L; hyperbilirubinemia (total bilirubin 162 mg/dL, direct bilirubin 115 mg/dL); C-reactive protein 54.34 mg/L and prothrombin time was normal.

For the etiological assessment, the hepatic ultrasound was normal and did not show any obstructive image or dilatation of the bile ducts, the serologies of acute hepatitis A, B and C were normal as well as those for cytomegalovirus and herpes simplex virus. Viral capsid antigen (VCA) Anti-VCA IgM and Anti-VCA IgG were positive and EBV nuclear antigen (EBNA) Antibody IgG was negative. In light of this assessment, the diagnosis of cholestatic jaundice induced by EBV primary infection was retained.

Treatment was symptomatic. The clinical outcome of the patient was favorable, with resolution of the fever on the 8th day of admission and progressive improvement of the jaundice. She was discharged after 10 days with a clear improvement in the liver function with a total bilrubin level of 17 mg/l, the rest of the assessment was normalized a few months later

DISCUSSION

The EBV virus is one of the most prevalent viruses since, regardless of the geographical area concerned, more than 95% of adults have a serological trace of primary infection. In the vast majority of cases, the infection is inapparent and occurs earlier in life due to poor socio-economic conditions, mainly in children between 1 and 4 years of age. In adults, the infection is manifested by the symptoms of infectious mononucleosis. Reactivations are possible, more frequent in immunocompromised patients. The virus is present in saliva and genital secretions. The transmission is essentially salivary and, although blood transmission has been documented, it remains exceptional. The incubation period is silent and its duration varies between 4 and 7 weeks on average [7, 8].

Cholestatic jaundice is rarely found in EBV primary infection. The diagnosis can only be made after eliminating an obstructive cause of extrahepatic cholestasis by liver ultrasound in the first instance, or more effectively by magnetic resonance cholangiopancreatography. Once excluded, early recognition of potential causes of intrahepatic cholestasis lesions, in which EBV must be considered, is essential for adequate diagnosis and management [9]. Most infections are self-limited and the prognosis is generally excellent; however, in some cases, complications of EBV infection can range from mild hepatitis to lymphoproliferative disorders, hepatosplenomegaly, and, rarely, acute liver failure [10].

The diagnosis of EBV is clinically oriented and is based on laboratory findings. The clinical presentation may include the classic triad of symptoms as well as tonsillar exudates, palatal petechiae, hepatosplenomegaly, and hepatitis [3, 11]. Approximately 5% to 10% of patients may present with jaundice. The hematologic investigation may reveal an absolute lymphocytosis in which more than 10% of the cells are atypical and positive heterophile antibody titers. Heterophilic antibody titers may be falsely negative within the first week and may be consistently negative in approximately 10% of patients. In this case, IgG and IgM antibody tests against EBV viral capsid antigen as well as antibodies against EBV nuclear antigen may help to distinguish the infection [10, 12]. Serum aminotransferase levels are usually elevated by less than five times the upper limit of normal and rarely reach over 1000 U/L. In the reported case EBV specific IgM antibodies were positive, documenting primary infection. No hemolytic anemia was found and other causes were excluded, namely other viruses, drugs, autoimmune and infiltrative diseases [6].

The classic evolution of infectious mononucleosis is towards spontaneous recovery in 3 to 4 weeks and does not require any specific treatment; it usually requires only symptomatic treatment with antipyretics, hydration and rest [13- 15]. Abdominal pain may persist, which in part may be due to splenomegaly [15]. If splenomegaly is present, it is prudent to advise the patient against physical activity to avoid splenic rupture; although rare, the incidence is 0.1-0.2% [16]. Rare complications of EBV may include upper airway obstruction, peritonsillar abscess, encephalitis, myocarditis, or pleural effusion [10, 11, 16]. The patient in this case recovered without serious intervention.

The pathogenesis of cholestatic jaundice in the setting of primary EBV infection is not fully elucidated and several hypotheses have been proposed. It is thought that EBV infection leads to an increase in cytokines with inflammation and disruption of ductal function or direct damage to liver cells by oxidative damage mediated by autoantibodies [17-19]. Once suspected, an appropriate diagnostic approach should be adopted including a medical history, a detailed physical examination and measurement of serological markers [17, 20, 21].

CONCLUSION

Cholestatic jaundice due to EBV primary infection is a rare manifestation that must be suspected in the light of a clinical and biological arguments and confirmed serologically. Treatment is primarily symptomatic and the evolution is mostly favorable, although few cases of severe acute hapatitis have been reported.

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