

Acute Acalculous Cholecystitis due to EBV Infection Presenting as Acute Abdomen

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ABSTRACT

Epstein-Barr Virus (EBV) is a herpes virus with a high seropositivity rate among the adult population throughout the world. Primary EBV infection is usually asymptomatic among young children. As age increases, it begins to manifest as infectious mononucleosis. Gastrointestinal involvement is often mild and elevations in liver function tests are common in most cases. Here, we report a case of acute acalculous cholecystitis in a 15-year girl during the course of a primary EBV infection which is a very rare presentation in the pediatric population. Our patient recovered without any antibiotic or surgical treatment – parallel to the clinical improvement of the primary disease.

Key Words: Epstein-barr virus (EBV) infection, Acute acalculous cholecystitis, Children, Antibiotics.

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INTRODUCTION

Epstein-Barr Virus (EBV) is a herpes virus that is common in children and often transmitted through saliva from asymptomatic persons. It presents with symptoms mimicking subclinical or viral upper respiratory tract infections in early childhood.¹ In adolescents and early adulthood, EBV infection can lead to infectious mononucleosis syndrome with the typical features including fever, pharyngitis, and lymphadenopathy. Mild to moderately elevated liver enzymes and hepatosplenomegaly are seen in most cases. Other organ system involvements including pneumonia, thrombocytopenia, myositis, pancreatitis and meningoencephalitis may develop during the course of the disease.²

Acute acalculous cholecystitis (ACC), an inflammation of the gallbladder, in the absence of gallstones, is mostly seen during severe infections, trauma, shock, burns, total parenteral nutrition and rarely with surgical procedures.³ Although it constitutes 5-10% of all cases of cholecystitis in adults, it is known to result in more severe morbidity and mortality than calculus cholecystitis (CC).³ ACC has been rarely described in the pediatric population in the literature.

Here, we describe a case of a 15-year girl with ACC associated with acute EBV infection which is an uncommon complication of primary EBV infection in children to emphasize that recovery can be achieved without requiring antibiotic treatment and surgical intervention.

CASE REPORT

A 15-year girl was admitted to the emergency department (ED) with a 2-day history of vomiting, fever (low-grade, 38°C), and periumbilical pain. She had several emergency visits and acute gastroenteritis was considered due to ongoing nausea and vomiting. On the day of admission to ED, the patient was evaluated. She was thought to have acute abdomen and pediatric infectious diseases consultation was requested due to persistent fever. She looked sick on physical examination and was jaundiced. Vital signs showed temperature, 38.3; blood pressure, 120/60 mmHg; heart rate, 97 bpm; respiratory rate, 18 breaths per minute and oxygen saturation, 98%. Periorbital edema and tonsillopharyngitis were observed. Abdominal examination revealed palpable liver with a positive Murphy's sign and a palpable spleen. She did not have any lymphadenopathy. Laboratory findings revealed leukocytes, 11,900/mm³; lymphocytes, 9000/mm³; monocyte, 2100/mm³; neutrophils, 710/mm³; hemoglobin, 12.6 g/dl; and platelets, 136,000/mm³. Transaminases were elevated with aspartate aminotransferase (AST), 178 U/L; alanine aminotransferase (ALT), 268 U/L, alkaline phosphatase (ALP), 233 U/L, gamma glutamyl transferase (GGT), 203 U/L, total bilirubin, 2.5 mg/dL, and direct bilirubin 1.96 mg/dL. Lactate dehydrogenase (LDH), serum albumin, and coagulation parameters were within normal limits. C reactive protein (CRP) was 1.57 mg/dl (Normal: 0-0.8). Ultrasound abdomen showed hepatomegaly with no focal lesions and splenomegaly. The gallbladder revealed an evident

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wall thickening with a collection of 15 mm pericholecystic fluid. Oral feeding was stopped and intravenous cefotaxime, analgesics, and fluid therapy were started due to cholecystitis. In serological tests, Hepatitis A, B, and C virus infections were excluded but there was the positivity of IgM and borderline positive IgG against EBV capsid antigen (VCA) supporting primary EBV infection. We were unable to perform the IgG-EBNA test because of non-availability. Cytomegalovirus (CMV) serology was in favor of past infection and toxoplasmosis IgM was negative. Blood and urine cultures were also negative. A diagnosis of ACC due to primary EBV infection was made and antibiotic treatment was terminated on day 2. Ursodeoxycholic acid (UDCA) was added to the treatment. Murphy's sign and fever disappeared on day 3. Control ultrasonography showed significant regression in previous pathological findings and no surgical intervention was required. Liver function tests started showing improvement on day 7 (AST 55 U/L, ALT 169 U/L, ALP 211 U/L, GGT 162 U/L, bilirubin 0.69 mg/dL) and she was discharged without any complication. During a follow-up at 6 months, the patient had no complaints, and liver tests normalised completely over 2 months. EBV VCA IgM became negative and EBV VCA IgG reached high levels showing seroconversion.

DISCUSSION

We report a case of primary EBV infection presenting with ACC, which is rarely reported in the pediatric population. EBV infection is ubiquitous and is often asymptomatic in immunocompetent individuals. In developed countries, primary EBV infection is seen in adolescents and adults while in developing countries, serologic positivity is detected at a much earlier age (3-6 years). The most common clinical manifestation of the infection is infectious mononucleosis with a sore throat, fatigue, cervical lymphadenopathy, and fever.³ Hepatosplenomegaly and elevated transaminases are frequently seen with the initial infection. Primary infection can be complicated by prolonged malaise, upper airway obstruction, and rarely myocarditis, cranial nerve palsies, encephalitis but the development of ACC is an atypical presentation of primary EBV infection in childhood.⁴

ACC accounts for about 5 to 10% of all acute cholecystitis cases in adults and is less often diagnosed in children.⁵ It is most common in patients with major cardiac and abdominal surgery, severe trauma, burns, and in those with a long history of parenteral nutrition. Kawasaki disease and polyarthritis nodosa are among the other systemic causes of the condition.

AAC has been reported to occur during infectious diseases in children including sepsis, gastroenteritis (Salmonella, Shigella, Giardia lamblia, Vibrio cholerae), pneumonia (especially with Mycoplasma pneumoniae), primary cytomegalovirus infection, and hepatitis A virus infections. Non-tuberculosis mycobacteria, leptospirosis, Q-fever, Candida, malaria and human immunodeficiency virus (HIV) are other rarely seen conditions.⁶

In literature, when children with EBV-related ACC are examined, it is seen that it develops most frequently in the 4-18 year age group and in females.⁷ The clinical presentation is nonspecific.

The most common clinical symptoms are fever, abdominal pain, malaise, and vomiting which can also be confused with conditions such as acute appendicitis, as in this case. Hyperbilirubinemia and moderate elevation of transaminases are the common laboratory findings. The wall thickness of the gallbladder has been reported to be 4.2-19 mm with ultrasonographic imaging.⁸

The pathogenesis of EBV-related ACC is unclear; direct invasion of the gallbladder by EBV is undefined but proinflammatory cytokines released by EBV are supposed to cause damage to the biliary epithelial ducts.⁹

Abdominal ultrasonography findings are diagnostic for ACC. The specificity and sensitivity of the gallbladder wall thickness over 3.5 mm has been reported to be 98.5% and 100%, respectively.¹⁰ Pericholecystic fluid, intramural gas, and sonolucent halo are other supportive findings. The ultrasound findings of this patient were also compatible with ACC.

Non-surgical supportive treatment and close ultrasonographic follow-up are recommended for ACC treatment in childhood. Surgical treatment comes to the fore in patients with impaired ultrasonographic findings or in cases without improvement. It has been reported in many case reports that improvement with symptomatic treatment was achieved in EBV-related ACC.¹¹ The antibiotics were discontinued after the diagnosis of primary EBV infection in most of the cases, as in this patient.

In conclusion, it should be kept in mind that viral agents, although rare, may be involved in ACC etiology and that EBV is also among these agents in childhood. In order to prevent unnecessary surgical intervention and the use of antibiotics, primary EBV infection, which can completely recover with conservative treatment, should be considered in pediatric patients diagnosed with ACC.

PATIENT'S CONSENT:

Written informed consent was not received due to the retrospective nature of this study.

COMPETING INTEREST:

The author declared no conflict of interest.

AUTHOR'S CONTRIBUTION:

GA: Concept, design, supervision, data collection and / or processing, literature review, and writing.

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