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Case Report

Acute Alithiasic Cholecystitis Associated with Primary Epstein-Barr Virus Infection in a 30-Year-Old Woman

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Abstract

Acute alithiasic cholecystitis (AAC) during primary Epstein-Barr virus (EBV) infection in adults is rare.

In this paper, we present a case of CAA on primary EBV infection in a young woman. The aim of our work is to describe this clinical picture in order to make clinicians aware of the importance of testing for EBV in CAA.

Keywords: *Acute Acalculous Cholecystitis; Epstein-Barr Virus; Infection*

Abbreviations

AAC: Acute Alithiasic Cholecystitis; EBV: Epstein-Barr Virus; BMI: Body Mass Index; VCA: Viral Capsid Antigen; EBNA: Epstein-Barr Nuclear Antigen

Introduction

Epstein-Barr Virus (EBV) is a herpesvirus that has a tropism for B lymphocytes. It is a ubiquitous virus that is transmitted by saliva. Primary infection usually occurs in childhood, especially in developing countries, at which time EBV infection is non-specific or asymptomatic [1,2]. Infectious mononucleosis is a late form of primary infection in adolescents and young adults, which is mostly seen in developed countries. At this age the clinical picture is most often typical but the infection can present in atypical forms, among these forms is acute alithiasic cholecystitis (AAC) which is an acute inflammation of the gallbladder without identification of gallstones. AAC remains an atypical presentation of primary EBV infection [3,4]. In this paper, we present a case of CAA on primary EBV infection in a young woman. The aim of our work is to describe this clinical picture in order to make clinicians aware of the importance of testing for EBV in CAA.

Case Report

In March 2021, a 30-year-old Caucasian woman, married and mother of a 13-month-old infant, working in a daycare center, was admitted to our hepato-gastroenterology department through the emergency room for diagnostic and therapeutic management of acute febrile

abdominal pain. Our patient had a personal history of tonsillectomy for recurrent tonsillitis at the age of twelve and an appendectomy at the age of fifteen for acute appendicitis, but she had no notable family history apart from a flu-like illness in her son a week ago. The history of her illness dates back to five days after her admission with the sudden onset of abdominal pain in the right hypochondrium in a hemi-girdle towards the right scapula, permanent, unbearable, rated at 9/10 on the pain scale, without aggravating or calming factors, so it was a pain of the hepatic colic type associated with bilious vomiting, arthralgia and myalgia, all evolving in a context of asthenia, anorexia and a fever of 40°C. The physical examination found a conscious patient well oriented in time and space, eupneic, tachycardia at 110 beats per minute, normotensive, the body mass index (BMI) was equal to 22 kg/m^2 and in whom the abdominal examination showed tenderness in the right hypochondrium with a positive clinical Murphy's sign without cervical lymphadenopathy or hepatosplenomegaly. Biologically, laboratory blood tests at admission revealed a hemoglobin level of 13.5 g/dL, a hematocrit of 40%, a platelet count of 179 × 109/L, and a white blood cell count of 12.1 × 109/L (neutrophils 30%, lymphocytes 51%). Atypical lymphocytes were noted on the peripheral blood smear. Non-specific liver workup showed cytolysis with aspartate aminotransferase, alanine aminotransferase were 360, 650 IU/L respectively and anicteric cholestasis with alkaline phosphatase, gamma-glutamyl transferase and total bilirubin were 224 and 271 IU/L and 0.7 mg/dL, respectively, in the absence of biological stigma of hepatocellular failure, a coagulation profile that was normal and albumin at 37 g/L. Other laboratory data showed a lipase level of 115 U/L and C-reactive protein 11.1 mg/L. Radiologically, the hepato-biliopancreatic ultrasound showed a small, thickened gallbladder wall, with no evidence of lithiasis and no peri-vesicular or extra-hepatic inflammatory reaction, absence of dilatation of the intra- and extrahepatic bile ducts and the abdominal-pelvic CT scan revealed a 4 mm submucosal edema of the gallbladder walls with an atrophic lumen with no identifiable lithiasis associated with periportal edema, without dilatation of the intra- or extrahepatic bile ducts. These radiological findings, combined with the clinical and biological data were consistent with the diagnosis of acute alithiasic cholecystitis. A viral origin was suspected and investigated by serological tests, the search for hepatitis A, B and C viruses, and cytomegalovirus were negative. On the other hand, EBV serology was in favor of an acute primary infection: IgM antibodies specific for viral capsid antigen (VCA) were positive, while IgG antibodies specific for Epstein-Barr nuclear antigen (EBNA) were negative. Our patient was fasted with a basic intravenous ration, rehydration and a probabilistic biantibiotherapy based on cephalosporin and metronidazole, these antibiotics were stopped as soon as the EBV infection was diagnosed. The evolution was marked from the third day of her hospitalization by the decrease of the abdominal pain and apyrexia, a control ultrasound showed a regression of the anomalies previously observed. The patient was discharged five days after admission and during a two-month follow-up, the patient was clinically asymptomatic. All liver function tests and abdominal ultrasound abnormalities returned normal. EBV seroconversion was documented six months after discharge with the appearance of positive VCA-IgG and EBNA-IgG antibodies confirming the diagnosis of primary EBV infection.

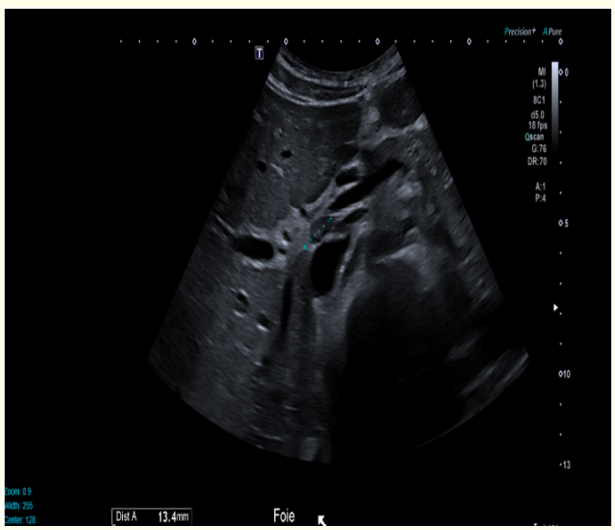

Figure 1: *Ultrasound image showing a small gallbladder with a thickened wall and no evidence of lithiasis.*

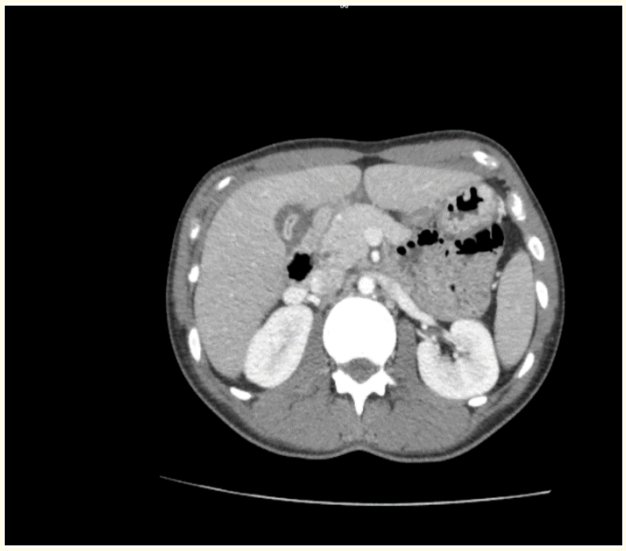

Figure 2: *CT image showing a 4 mm submucosal edema of the gallbladder walls with an atrophic lumen without identifiable lithiasis associated with a periportal edema.*

Discussion

AAC is an inflammation of the gallbladder in the absence of gallstones; most often AAC is a complication of severe medical or surgical conditions [5]. There are many cases of CAA complicating burns, sepsis, severe trauma and surgery. Secondary infection of the gallbladder may occur during leptospirosis, salmonellosis, cholera or campylobacter enteritis. CAA has also been observed in several infectious diseases, such as brucellosis, dengue fever, hepatitis A or B, palidusma and infectious mononucleosis [6,7].

AAC is rare in primary EBV infection. In the literature, we have found about twenty cases of CAA in adult patients with primary EBV infection [9-29]. We noted a predominance of females. Most of the cases were less than 25 years old, but our patient was 30 years old, another case of a 30-year-old woman was published in 2017 as well [22]. We noticed that most of the reported cases occurred in Europe which is the case of our patient.

In the series studied. The clinical symptomatology of CAA on infectious mononucleosis is not often accompanied by symptoms of primary EBV infection: the predominant sign remains abdominal pain localized in the upper quadrants most often in the right hypochondrium or sometimes in the epigastrium, which may be associated with vomiting and a positive Murphy's sign with fever on clinical examination. Our patient had presented primarily with intense febrile hepatic colic-like pain associated with bilious vomiting. Other symptoms of CAA secondary to EBV are: pharyngitis, lymphadenopathy which may appear during the course of the disease, hepatosplenomegaly, our patient had fever, myalgia and arthralgia without other accompanying symptoms [10-14].

Biologically, the picture is most often characterized by hyperleukocytosis with the presence of atypical lymphocytes on the peripheral blood smear and an increase in liver enzymes, especially cytolysis depending on alanine aminotransferase, as well as icteric cholestasis most often. Our patient had a hyperleukocytosis of 12.1 × 109/L (neutrophils 30%, lymphocytes 51%). Atypical lymphocytes were noted.

The non-specific hepatic workup showed cytolysis mainly dependent on alanine aminotransferase which was equal to 650 IU/L and anicteric cholestasis [15-19].

Diagnostic confirmation is obtained by positive EBV serological tests and abdominal ultrasound which may show increased thickening of the vesicular wall with sometimes a laminated appearance or may show the presence of pericholecystic fluid or distension of the gallbladder. The pathognomonic ultrasound sign remains the thickening of the vesicular wall without individualization of lithiasis. Our patient had an EBV serology in favour of an acute primary infection with positive IgM antibodies specific to the viral capsid antigen (VCA), and IgG antibodies specific to the Epstein-Barr nuclear antigen (EBNA) were negative. Radiologically, our patient had a thickening of the vesicular wall which was small without individualization of calculi or dilations of the intra and extra hepatic bile ducts [25,26].

The mechanism of AAC in primary EBV infection is still unknown. Although there are hypotheses that primary EBV infection causes hepatitis, which is a cause of cholestasis, resulting in gallbladder inflammation and CAA, the level of evidence for these hypotheses remains very low [27].

The treatment of CAA in primary EBV infection is usually symptomatic. Antibiotic therapy is not indicated in these patients, so in the cases studied antibiotics were discontinued after the diagnosis of EBV infection, which was the case in our patient. In only one case was surgery indicated due to the rapid worsening of the disease in a patient on Azathioprine immunosuppressants. The evolution was favourable in almost all the cases studied, our patient also had a favourable clinical, biological and radiological evolution [28,29].

Conclusion

CAA is a fairly rare complication of primary EBV infection and is seen in adolescents and young adults, most often females. Its clinical presentation is that of CAA with acute pain most often of the hepatic colic type associated with vomiting and fever. Sometimes it can be insidious and hidden in the clinical picture of infectious mononucleosis. Its positive diagnosis is essentially radiological by abdominal ultrasound which makes the diagnosis of alithiasic cholecystitis coupled with EBV serology in favor of an acute infection. The treatment is essentially based on rest and treatment of clinical symptoms. The evolution is in the majority of cases favorable.

Conflict of Interest

We do not have any conflict of interest.

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