

Case Report

Acalculous Cholecystitis as a Complication of Epstein-Barr Virus: A Case Report

Ahmed Al-Muhsin^{1*}, Hesham Eltomy¹, and Antonio Privitera²

¹Department of General Surgery, King Fahd Military Medical Complex, Kingdom of Saudi Arabia

²Department of General Surgery, Kin Fahad Specialist Hospital Dammam, Kingdom of Saudi Arabia

***Corresponding author:** Dr. Ahmed Mohammed Al.Muhsin, Department of General Surgery, King Fahd Military Medical Complex, Dammam, Kingdom of Saudi Arabia, Tel: +966501589990; E-mail: amuhsin90@gmail.com

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Abstract

Acute acalculous cholecystitis (AAC) is an uncommon disease mostly occurring in critically ill and immunosuppressed patients. Very few cases have been reported during the course of infectious diseases in particular Epstein-Barr virus (EBV). A wide range of complications have been reported in EBV infection including liver involvement that is usually self-limiting and characterized by mild elevation of liver enzymes. AAC during EBV infection can be the result of direct invasion of the virus or induced by cholestasis associated with infective hepatitis. Serological tests and ultrasound scan are the most common tools for diagnosis. Most cases resolve with antibiotic treatment. Very rarely a cholecystectomy is indicated. The authors present another case of the unusual association in a young female patient and review the literature.

Keywords: acute acalculous cholecystitis, epstein-barr virus, primary infection

Introduction

Acute Acalculous Cholecystitis (AAC) is a well-recognized disease characterized by inflammation of the gallbladder in the absence of stones. Most cases of AAC occur in immunosuppressed patients, following trauma, severe burns, long stay in the intensive care unit, and long-term total parenteral nutrition. Resuscitation from hemorrhagic shock, cardiac arrest, congestive heart failure, abdominal vasculitis has also been associated with the disease [1]. AAC has rarely been described in the course of systemic infections with secondary gallbladder involvement. Very few cases have been associated with the causative agents of Infectious Mononucleosis (IM), in particular Epstein Barr Virus (EBV) [2,3]. The authors report another case of this uncommon complication during EBV infection and review the literature.

Case Report

Exposure

A 27-year-old female presented to the emergency department with a 7-day history of fever, epigastric pain, nausea and vomiting. Past medical history was unremarkable apart from self-administration of herbal medications for weight loss. There was no history of smoking or alcohol intake. On examination she had mild fever of 37.9°C.

Abdominal examination showed tenderness in the right upper quadrant with positive Murphy's sign. There was no lymphadenopathy or any signs of upper respiratory tract infections.

Laboratory tests showed an elevated WBC $16.4 \text{ (NR } 4 \times 10^9/\text{L)}$ with lymphocytosis 64.6% (NR 20-45%). Liver function tests were deranged: ALK 136 u/L (NR 50-136 u/L), ALT 289 u/L (NR 12-78 u/L), AST 237 u/L (NR 15-37 u/L), total bilirubin 20 $\mu\text{mol/L}$ (NR 3-17 $\mu\text{mol/L}$), direct bilirubin 16.2 $\mu\text{mol/L}$ (0-3 $\mu\text{mol/L}$), albumin 30 g/L (NR 34-50 g/L). Amylase and lipase were normal. ESR was 67 mm/hr. EBV IgM was Positive, CMV IgM Positive. Hepatitis and HIV screen were negative.

During her admission the WBC raised and reached up to 26 with differential showing 74 % of lymphocytes.

An abdominal ultrasound scan revealed mild thickening of the gallbladder measuring 4.4 mm with no evidence of gallstones or dilatation of the biliary tree (Figure 1).



Figure 1: Abdominal ultrasound showing gallbladder wall thickening with absence of stones

A CT scan of the abdomen showed hyperenhancing gallbladder wall with mucosal edema and adjacent fat stranding. No stones were demonstrated. Subcentimetric paraortic, mesenteric and inguinal lymphnodes were noted.

An MRCP was carried out and this showed thickening and edema of the gallbladder with minimal pericholecystic fluid. The CBD was not dilated and had no filling defects.

A HIDA scan was performed revealing a homogeneous liver uptake while the gallbladder was not visualized suggesting acute acalculous cholecystitis.

The patient was treated conservatively with IV fluid and antibiotics (Ciprofloxacin). She made an uneventful recovery and was discharged on the 9th day post admission.

Discussion

AAC accounts for 5 to 10 % of all cases of cholecystitis. Many factors have been implicated in the pathogenesis including gallbladder ischemia, bile stasis, infections, and release of proinflammatory mediators [1].

Ultrasound scan of the gallbladder is the most accurate tool for the diagnosis of AAC. A gallbladder wall thickening $>3 \text{ mm}$, distention of the gallbladder, localized tenderness, and pericholecystic fluid are the main diagnostic findings. The presence of two or more of these findings is considered diagnostic [4,5]. CT and radionuclide scans are also useful diagnostic modalities [1]. Supportive therapy and antibiotic treatment together with percutaneous cholecystostomy in severe cases are the mainstay of treatment. Cholecystectomy is rarely required [1].

The occurrence of AAC during IM is a rare event [1]. IM is a clinical entity characterized by the presence of fever, pharyngitis, and lymphadenopathy [2]. The most common causative agents are Epstein Barr Virus (EBV) and less commonly Cytomegalovirus (CMV). Toxoplasma gondii, viral hepatitis, and human herpes virus 6 can also rarely

be involved [3]. The majority of cases of IM experience an uneventful recovery, although a wide range of complications have been reported including liver impairment that is usually mild and self-limiting [6,7].

The exact mechanism of gallbladder involvement during IM is still unclear. Taking into consideration that viral hepatitis induces cholestasis, this may be considered a predisposing factor to inflammation [8,9]. Also, direct invasion of the gallbladder wall mucosa by the virus is possible since viral antigens have been isolated from the gallbladder epithelial cells [10].

Only 17 cases of AAC during EBV infection have been reported in the literature (Table 1) [11-25]. All cases are females, apart from one case diagnosed in a 21-year-old male patient. This contrasts with the general higher incidence of AAC in males [25]. AAC can occur at any age group but most commonly observed in adults especially in the fourth and eight decades of life. Most of the cases reported were young, presumably due to the greater occurrence of EBV infections in young adults [24]. Diagnosis was made with thorough clinical history and examination, pathognomonic features in peripheral blood films, and serological tests. In the reported case CMV IgM was thought to be a false-positive due to crossreactivity [26]. As in our case, patients presented with gastrointestinal symptoms including RUQ tenderness. The classical presentation of EBV infection with pharyngitis and lymphadenopathy was not predominant, and most cases showed elevation of liver enzymes [24]. Patients were treated conservatively with antibiotics and monitoring of liver function, although there was no difference in the outcome of patients receiving antibiotics compared to those who did not receive any antibiotic therapy. Surgical intervention for AAC during the course of EBV is usually unnecessary [24]. Only one of the reviewed cases underwent laparoscopic cholecystectomy for severe septic cholecystitis [15].

Table 1: Reported cases in the literature of AAC during EBV infection

Age / Gender	Lymphadenopathy	Pharyngitis	ALP (IU/L)	AST (IU/L)	ALT (IU/L)	Wall thickness (US /mm)	Management	Reference
53/F	-	-	1081 (40-120)	-	339	10	Medical	[11]
18/F	Yes	Yes	312 (38-148)	220 (5-45)	328 (5-45)	9	Medical	[8]
19/F	Yes	Yes	710 (<280)	426 (<40)	584 (<40)	8	Medical	[12]
20/F	Yes	Yes	727	171	299	-	Medical	[13]
22/F	Yes	Yes	2.2 μ kat/L (0.5-2)	6.87 μ kat/L (0-0.65)	12.79 μ kat/L (0-0.8)	6	Medical	[14]
22/F	-	-	-	-	-	7	Surgical	[15]
29/F	Yes	Yes	161 (53-151)	121 (10-35)	166 (10-35)	15	Medical	[16]
18/F	No	No	146	118	-	>10	Medical	[17]
22/F	No	No	-	-	89	5	Medical	[18]
22/F	No	-	239	329	464	14	Medical	[19]
18/F	Yes	No	165	321	214	12	Medical	[20]
20/F	Yes	No	131	453	494	16	Medical	[20]
48/F	Yes	-	516 (90-260)	221 (5-35)	165 (5-40)	Marked	Medical	[21]
34/F	No	Yes	429 (35-105)	-	61 (10-45)	11.3	Medical	[22]
21/M	No	No	179 (<140)	172 (<40)	232 (<40)	4.5	Medical	[23]
30/F	Yes	No	376 (50-136)	233 (8-37)	220 (15-65)	7.4	Medical	[24]
27/F	No	No	136	237	289	4.4	Medical	Reported case (2017)
ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ALP: Alkaline Phosphatase (): normal value range, mentioned in the study								

Conclusions

AAC may result as a complication of IM and a high index of suspicion is needed in patients developing GI symptoms during the course of the disease. Ultrasound scan represents the main diagnostic investigation. Most cases can be treated conservatively with antibiotic therapy, and surgical intervention is rarely needed.

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