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A Case Report of Pediatric Epstein Barr Virus (EBV) Related Cholestasis from Al-Adan Hospital, Kuwait

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Abstract

Infectious mononucleosis is an acute illness due to Epstein Barr virus infection, which occurs commonly in young adults. Liver involvement in acute EBV infection occurs in up to 95% of patients between the 6th and 15th day of illness and is usually mild [1]. Here we report on a 7-year-old girl treated by Gastroenterology, Hepatology, and Nutrition Unit of Al-Adan Hospital pediatric Department, presented with prolonged fever, lymphadenopathy, generalized edema, hyperbilurubinemia and elevated liver enzymes secondary to EBV infection. This case represents a rare presentation of common viral infection in pediatric population.

Keywords

Epstein Barr Virus (EBV)

1. Introduction

Epstein-Barr virus (EBV) infection typically causes the clinical syndrome of infectious mononucleosis. Liver involvement is usually mild, and resolves spontaneously [2]. Hepatitis with mild transient elevations in serum aminotransferases is often reported in Epstein-Barr virus (EBV) infectious mononucleosis. Mild jaundice develops in approximately 5% of cases and may result from cholestasis or virus-induced hemolysis [3]. However, the majority of patients recover without apparent sequelae and most patients will need only supportive treatment.

2. Case Report

A 7-year-old girl previously well was admitted to our hospital with a history of fever for 10 days, decreased ap-

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petite, malaise and abdominal pain. No history of vomiting or diarrhea, no skin rash, and no headache. In the first 5 days of her illness prior of admission, she was evaluated by a family physician and found to have pharyngitis and she was treated with oral Amoxicillin Clavulanate 45 mg/kg/day every 12 hours for 7 days.

On admission she was looking well but irritable, hydrated, febrile T: 40c, HR: 140/min RR: 30/min, BP: 101/65 mmgh, Capillary refilling time was 2 seconds. She had bilateral palpable cervical lymph nodes 5 mm size each. Abdominal examination revealed tenderness all over the abdomen with no signs of peritonitis, liver was enlarged 3 cm below costal margin and spleen was not palpable. The rest of the clinical examination was unremarkable.

Initial blood investigation showed, CBC white count of 9×10^9/L, Hb: 109 g/L, platelet 126. Liver function test (LFT) showed: LDH 587 U/L, ALT 126 U/L, ALP 315 U/L, AST 124 U/L, total bilirubin 18.10 micromol/L, direct bilirubin 12.5 micromol/L. Renal function and serum electrolyte were normal, CRP: 60, ESR: 11 mm/hr, paracetamol level was within normal range. Coagulation profile showed INR: 1.3 seconds.

Widal test normal and Brucella antibody was negative. Urine and blood culture were negative. Blood virology (EBV, CMV, Hepatitis A, B and C) were taken. Ultrasound of the abdomen done at Emergency Room with no evidence of gallstones or ascites or other abnormal findings.

Patient was treated as a case of pyrexia from unknown origin (PUO) and covered with Intravenous broad spectrum antibiotics, but with no improvement in her symptoms. Few days later, she had ever abdominal pain with fever, so U/S abdomen was repeated and revealed hepatosplenomegaly, contracted gallbladder with thick edematous wall, mild free fluid in the abdomen and the right iliac fossa. Computed Tomography (CT) abdomen with contrast was done which showed minimal fluid in the pelvis with no other abnormalities, so surgical causes needed to be rolled out at this point.

Furthermore, a diagnostic laparoscopy was normal, with unremarkable peritoneal fluid analysis and culture. She became clinically jaundiced and developed generalized edema. Her clinical examination at that time revealed irritable, febrile, pale and icteric young girl, but no signs of chronic liver disease were elicited. She had remarkable edema of face, abdomen and extremities. Her vital signs showed, RR: 30/min, P: 125/min, oxygen saturation was: 98% in room air and BP 100/60 mmhg. Abdomen was distended with generalized tenderness, moderate enlargement of the liver and spleen noted and evidence of shifting dullness were present. Other systemic examination was unremarkable.

Blood investigation was repeated, complete blood count revealed elevated white count with lymphocyte predominance and borderline platelet count at 154×10^9. Peripheral blood film showed reactive lymphocytosis. A repeat of her liver profile showed total: Bilirubin: 103 micromol/L with predominant direct fraction of 89.3 micomol/l. Her liver enzymes showed mainly a cholestatic pattern with significant elevation of GGT and ALP 427 U/L and 867 U/L respectively.

Albumin was low at 24 g/l. Her serum glucose, renal function test and electrolytes were normal. A repeat of coagulation profile: showed significant coagulopathy consistent with acute liver failure of INR 2.2.

Blood virology previously done confirmed acute EBV infection (PCR + IgM).

She was treated conservatively with Albumin infusions, Ursodeoxycholic acid, fresh frozen plasma and intravenous Vitamin K.

The patient continued to have high grade fevers along with the presence of generalized lymphadenopathy, bone marrow examination was done showed marginally increased relative proportion of lymphocytes with presence of 8 - 10 atypical (reactive) lymphocytes, no evidence of blast cells and no evidence of hematological malignancy was present.

Finally, after two weeks of admission, she had gradual clinical improvement. Liver enzymes and total bililrubin were dropping and she was discharged in stable condition. The patient underwent a repeat of liver function tests and ultrasound abdomen two weeks after discharge both of which were normal (**Table 1**).

3. Discussion

EBV is a ubiquitous human herpesvirus that is usually transmitted through close personal contact among young children and via intimate oral contact among adolescent and young adults [4]. Contact of Epstein-Barr virus (EBV) with oropharyngeal epithelial cells allows replication of the virus, release of EBV into the oropharyngeal secretions, and infection of B cells in the lymphoid-rich areas of the oropharynx [5].

The incubation period prior to the development of symptoms averages four to eight weeks [6]. The cardinal

Table 1. The patient's laboratory parameters overtime.

Parameters	At admission	At day 8	On discharge	References range
Hemoglobin	109	90	90	100 - 140 g/L
Total white count	10.67	22.6	18.6	5 - 19.5 × 10^9
Neutrophil	23	9.4	8.8	30% - 50%
Lymphocyte	61	86.2	87	38% - 58%
Total bilirubin	18	132.6	50.5	0 - 17 Micmol/L
Direct bilirubin	12.8	111.9	39.7	0 - 7 Micmol/L
ALT	126	40	46	7 - 55 U/L
AST	124	87	120	8 - 48 U/L
ALP	315	799	759	45 - 115 U/L
GGT	-	400	601	9 - 48 U/L
PT	14.8	24.5	13.3	9.5 - 13.8 seconds
INR	1.3	2.2	1.2	0.8 - 1.2
Albumin	31	24	38	35 - 55 g/dL

Abbreviations: ALT: alanine transaminase; AST: aspartate aminotransferase; ALP: alkalinephosphatase; GGT: γ glutamyltransferase; PT: prothrombin time; INR: international normalized ratio; U/L: units per liter.

symptoms of infectious mononucleosis are the well-known triad of fever, pharyngitis, and peripheral lymphadenopathy, especially involving the posterior cervical chains. A minority of patients have splenomegaly, gastrointestinal symptoms, rash, and headache [7].

Our patient had initially the clinical presentation of infectious mononucleosis but the prolonged fever and cholestatis made us think about other differential diagnosis like autoimmune hepatitis, alpha-1 antitrypsin deficiency and other. Recently EBV-induced hepatitis has been recognized as an important cause of cholestasis [8]. Sever cholestasis is rare and the mechanism is unknown. High concentrations of enzyme-inhibiting autoantibodies against the antioxidative enzyme, manganese-superoxide dismutase (MSD), have been postulated to play a role [9], but support for this concept is limited. In adults, Hepatitis caused by EBV is common, mild, and self limiting, although fulminant hepatic failure has been reported in 17 patients worldwide, with an overall mortality of 85% [10].

During the acute stage of her illness, our patient had serial abdominal sonography which was done because of the persistant abdominal pain throughout hospital admission. However, all of them had shown edematous gallbladder with thickened wall. Gallbladder wall thickening is rare in infectious mononucleosis syndromes and has been proposed as a sign of severity of the infectious mononucleosis and as an indicator for the need to carefully monitor the clinical course [11].

EBV has been associated with a variety of malignancies, particularly lymphoma. Many of these infections are subclinical, but Hodgkin lymphoma has been associated with a history of infectious mononucleosis [6], based on that, this girl had bone marrow examination to rule out possible hidden malignancies. Although of all of these complications and liver involvement, this girl responded well to the supportive treatment.

4. Conclusion

Atypical presentations of Epstein-Barr virus (EBV) infection are more common with increasing age but can also

be seen in young children. All pediatricians should be aware of various presentations of common viral childhood infection in order to provide a comprehensive cascade of investigation and supportive management for those children. The good news is that most of the viral infections are self limited and rarely can lead to significant morbidity and mortality in immunocompetent patients.

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