CASE REPORT

Acute Appendicitis, Peritonitis, Shock and Encephalitis; A rare combination caused by Epstein-Barr virus.

Al Gibali O.Y., Khalafalla H.M., Haidar N A.,* Bozom I.
Pediatrics Department,* Histophatology Department, Hamad Medical Corporation
Doha, Qatar

Abstract:
A nine-year old girl presented in shock preceded by fever vomiting, lower abdominal pain and rebound tenderness with signs of peritonitis. Ultrasonography supported a diagnosis of acute appendicitis confirmed later by the presence of peritoneal fluid and by histopathology. She had also the clinical picture of meningoencephalitis with positive meningeal signs and an abnormal electroencephalogram (EEG). Cerebrospinal fluid (CSF) showed high protein, normal cell count and normal pressure. Brain CT scan and MRI were normal. The polymerase chain reaction (PCR) in the blood was highly positive for Epstein Barr virus (EBV). She improved dramatically after urgent appendectomy with supportive management. This case is unusual in presenting with a combination of acute appendicitis, peritonitis and shock associated with acute encephalitis.

Introduction:
Epstein-Barr virus (EBV) has a wide spectrum of presentation. An incubation period of two to seven weeks is followed by the prodromal symptoms of fatigue, malaise, and anorexia. Older children and adolescents are more likely to develop the typical signs and symptoms of infectious mononucleosis (IM); fever, sore throat, accompanied by tonsillopharyngitis and lymphadenopathy. The adenopathy typically is nontender and involves both the anterior and posterior cervical lymph nodes but diffuse adenopathy may be present. Transient palatal petechiae are seen in about 50%, periorbital edema may be seen(1). Splenomegaly and hepatomegaly develop in about 69% and 54% of cases respectively, headache presents in 50%(2).

EBV has been associated with a wide range of acute neurologic diseases in children(3-8). In general, encephalitis caused by EBV in pediatric patients is considered a self-limiting illness with few or no neurologic sequelae(6). Neurological manifestations of patients who have IM may appear prior to the classic signs, symptoms, and laboratory findings. They can be the only clinical manifestations(3,6). The clinical presentation in some patients resembles herpes simplex encephalitis. An "Alice-in-Wonderland" syndrome, characterized by metaplasia (distortion of sizes, shapes, and spatial relations of objects) has been reported(8,9). Unusual presentations such as acute respiratory distress syndrome(10), peritonitis, appendicitis and pseudoappendicitis(11,14,15,16), aseptic meningitis, encephalitis, cranial nerve palsies, mononeuropathies and acute disseminated encephalomyelitis (ADEM) have been reported (3-5,17,18).

Case Report:
A nine-year old girl, previously healthy, presented with high grade fever for four days with headache, visual hallucination and mild vomiting. For two days before admission she was sleeping longer than usual with occasional drowsiness during the day. There was no history of drug ingestion, diarrhea, skin rash, joint pain, contact with a sick person or travel abroad.

She appeared sick and drowsy, temperature 39.4 °C, heart rate 128/min, BP 71/37 mm Hg, RR = 27/min, capillary refill >2 sec with cold extremities. Her compromised circulation responded to multiple fluid boluses, dopamine then noradreline drips. Her CVP after boluses was 6 to 8 cm H 2 0. She was maintained on 100 ml/kg/day, 5% dextrose innormal saline for the first 24 hours.

After stabilization she showed neck rigidity and positive Kerning's sign. The power, tone, deep tendon reflexes, sensory system, and cerebellar functions were normal. Her abdomen was rigid with rebound tenderness at the right lower quadrant with palpable organomegaly or masses. There was no lymphadenopathy. Lungs and heart were normal. A clinical diagnosis of acute appendicitis was confirmed by ultrasonographic (US) imaging of a thickened appendicular wall; total width of the appendix was 6 mm and was not compressible, and fluid in the peritoneum (Figures 1a, b).

Address for correspondence:
Osama Yousif Al Gibali, MD
Pediatric Critical Care Unit, Pediatrics Department
Hamad Medical Corporation, P.O. Box 3050, Doha, Qatar
E-mail: osgibali2@yahoo.com
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Figure 1A:

After appendectomy her hemodynamic status improved, and the inotropic support was tailed off. Histopathology of the removed appendix confirmed the clinical and sonographic diagnosis of appendicitis, showed heavy infiltration of the appendix by inflammatory cells (Figures 2a, b).

Figure 1B:

Figure 2A:

Figure 2B:

She continued to be drowsy. CT and MRI of her head were normal. A lumbar puncture showed clear CSF with normal pressure, WBC 5/cmm, RBCs nil, protein 0.72 g/dl and a negative Gram stain for bacteria. Culture of the CSF and PCR for HSV, EBV, and CMV were all negative. An EEG showed a right occipital focus and a slow wave for her age. Hemogram showed leukocytosis (WBC= 25000\ mm3), 79% neutrophils, Hb 12.7 g/dl, platelets 220,000/mm3, ESR 37. Renal and liver functions and serum electrolyte concentrations were normal. Blood, urine and stool cultures were negative. Widal test, Brucella titer, mycoplasma titer, ANA, swab from ascitic fluid during surgery were all negative. Three samples of gastric aspiration for acid fast bacilli (AFB) and a purified protein derivative (PPD) tuberculin skin test were negative. The blood polymerase chain reaction (PCR) for EBV was positive with 283 copies/ml, and was negative for CMV and HSV.

On admission, the child had been started on ceftriaxone, vancomycin, acyclovair, and erythromycin for possible meningo-encephalitis. Acyclovir and erythromycin were discontinued after ruling out the HSV and mycoplasma encephalitis by negative PCR for HSV and mycoplasma titer in addition to the normal brain CT and MRI. Meropenem replaced the ceftriaxone and vancomycin which was discontinued after excluding bacterial infection by negative cultures and fast normalization of WBC count, ESR and CRP. She showed progressive improvement by the fifth day of admission. She was allowed to eat and move freely and was transferred to the pediatric floor where she was observed for a week then discharged home in good healthy condition.

Discussion:
Abdominal manifestations of EBV infection include hepatomegaly, hepatitis, splenomegaly, rupture of the spleen, ileocolitis, gastritis, mesenteric lymphadenopathy, pancreatitis, and transient malabsorption may occur. Although ileocolitis and abdominal syndromes mimicking appendicitis (pseudappendicitis) have been reported, only a few cases of true appendicitis have been
described previously (11). This case presented clinically with acute appendicitis with appendicular inflammation being limited to the mucosa and submucosal layers, indicating that her peritonitis was not secondary to the appendicitis but most likely part of the capillary leak syndrome due to the systemic inflammatory response syndrome (SIRS), a rare complication of EBV infection.

The state of shock was most likely due to significant EBV infection (viraemia), particularly as all investigations for bacterial causes were negative which to the best of our knowledge has not been reported in an immunocompetent patient. Connective tissue diseases were ruled out by negative anti-nuclear antibodies (ANA) and a normal level of C3 and C4 supported by the drop in ESR from 37 to 5 within a few days with a parallel clinical improvement.

The signs of meningeal irritation were among the presenting clinical features of our patient, similar to the description of EBV-associated meningoencephalitis (6); drowsiness, visual hallucination, and positive signs of meningeal irritation that persisted after correction of her shock, indicated that there was a primary brain involvement rather than one secondary to the shock. This was further supported by an abnormal EEG which showed a right occipital focus and slow wave in addition to the high CSF proteins, although there was no cellular changes in the CSF or anatomical changes in her brain CT scan or MRI imaging studies. In another study, totally normal CSF parameters were reported (17).

EEG changes similar to those in our patient have been described in a number of previous studies (6, 8). Slow background EEGs were seen in about 50% in another study of children with EBV-associated encephalitis (7). An acute disseminated encephalomyelitis with a predilection for posterior cerebral artery distributions has been reported with a normal EEG; the reverse of our patient where there was occipital EEG changes with no evidence of acute disseminated encephalomyelitis (5).

We conclude that it was due to the EBV viremia that our patient presented with an unusual combination of acute appendicitis, peritonitis, shock, and encephalopathy.

References: