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Corresponding Editor: William Cameron, Ottawa, Canada

16 April 2007

doi:10.1016/j.jjid.2007.06.011

## Epstein–Barr virus infection with acute pancreatitis

Epstein–Barr virus (EBV) infection occurs worldwide and most commonly in early childhood and adolescence. Common clinical presentations include infectious mononucleosis, upper respiratory tract infection, diarrhea, and abdominal complaints.<sup>1</sup> We report a case of EBV infection with a rare manifestation – acute pancreatitis – in an otherwise healthy patient.

An 18-year-old female was admitted to our hospital with a 4-day history of high-grade fever, sore throat, vomiting, abdominal pain, and decreased appetite. Her initial physical examination revealed a temperature of 40.0 °C, a blood pressure of 83/29 mmHg, mildly injected pharynx and tonsils, small bilateral shoddy non-tender cervical lymph nodes, and generalized abdominal tenderness, especially at the right upper quadrant area and epigastrium. Laboratory data revealed a total white blood cell count of  $1.9 \times 10^9/l$  (66% band neutrophils, 7% segmental neutrophils, 4% atypical lymphocytes), hemoglobin of 11.0 g/dl, platelet count of  $23 \times 10^9/l$ , prothrombin time of 15.2 s, activated partial thromboplastin time of 82 s, international normalized ratio (INR) of 1.2, fibrinogen of 80 mg/dl, fibrin degradation products (FDP) of  $>40 \mu\text{g/ml}$ , D-dimer of  $>20 \mu\text{g/ml}$ , aspartate aminotransferase of 181 U/l, alanine aminotransferase of 57 U/l, alkaline phosphatase of 97 U/l, total bilirubin of 7.4 mg/dl, amylase of 620 U/l (normal range: 60–180 U/l), and lipase of 659 U/l (normal range: 0–160 U/l). Ultrasound of the abdomen showed thickening of the anterior gallbladder wall without gallstones. Computed tomography (CT) of the abdomen and pelvis revealed moderate gallbladder wall thickening, pericholecystic fluid, edematous pancreas, and hepatosplenomegaly. A hydroxy iminodiacetic acid (HIDA) scan, however, did not suggest acute cholecystitis. The presumptive diagnosis was septic shock with acute pancreatitis and disseminated intravascular coagulation (DIC). The differential diagnoses include systemic viral infections or primary bone marrow disorders such as lymphoma or lymphoblastic leukemia. Blood cultures and a urine culture were taken, and empirical antibiotic therapy consisting of

aztreonam, clindamycin, and moxifloxacin was initiated given the patient's history of penicillin allergy. Concerning her pancytopenia, bone marrow aspiration was performed and revealed pancytopenia with dyshematopoiesis, increase in mononuclear cells (approximately 15%), normal blast cell population, and no evidence of granulomatous inflammation. Four days after treatment the fever subsided with improvement of abdominal signs. Blood cultures, urine culture, and bone marrow culture results were all negative. Viral hepatitis profiles (A, B, C), HIV RNA, monospot test, and cytomegalovirus immunoglobulin M and G were all negative. The diagnosis of EBV infection was made by the positive result of EBV immunoglobulin M and G (VCA, viral capsid antigen) and immunophenotyping of the bone marrow lymphocytes (CD4: 12%, CD8: 84%, CD4/CD8 ratio of 0.14 with increased numbers of CD57-negative CD8 T cells and gamma delta T cells) consistent with EBV infection. All antibiotics were discontinued after 4 days of treatment. The patient recovered uneventfully by day 7 after supportive treatment for pancreatitis.

The gastrointestinal (GI) system is one of the most common organ systems affected by EBV. Nausea, vomiting, anorexia, and abdominal pain are frequently reported symptoms, probably reflecting mild hepatitis, hepatomegaly, splenomegaly, and rarely pancreatitis.<sup>2</sup>

Nine cases of primary EBV infection with pancreatitis have been reported in the literature (Table 1). In these cases, the onset of GI symptoms occurred at an average 12 days (range 4–42 days) after the onset of initial constitutional symptoms. Serum amylase, urine amylase, and clinical presentations are the important diagnostic tools for acute pancreatitis. Imaging studies, such as CT or ultrasonography of the abdomen can be used to confirm diagnosis if they are performed late enough to see gross inflammatory changes of the pancreas. Symptomatic and supportive treatment was used successfully in all cases, and the overall outcomes of acute pancreatitis in the setting of EBV infection were good.<sup>3–9</sup>

Our patient also had other unusual clinical presentations for EBV infection. Firstly, she presented with shock most likely due to dehydration and third space fluid loss from acute pancreatitis. Secondly, she developed DIC, which can be caused by either pancreatitis or rarely, EBV itself. Thirdly, she had a

**Table 1** Clinical features of previously published cases of primary EBV infection with pancreatitis

Case No.	Age (years)/sex	Underlying conditions	Initial clinical presentation	EBV diagnosis	GI symptoms	Amylase <sup>a</sup>	Lipase <sup>b</sup>	Imaging	Treatment	Outcomes	Reference
1	10/F	None	NA	EBV antibody titer, heterophile antibody	Epigastric pain, vomiting	Serum: 5550 U/l	NA	USG: normal pancreas, distended gallbladder with cholelithiasis	Symptomatic and surgery for gallstone	NA	3
2	8/F	None	Fever, sore throat, myalgia, cervical lymphadenopathy	EBV antibody titer, heterophile antibody	Epigastric pain, nausea, vomiting	Serum: 555 U/l	180 U/l	NA	Symptomatic	Cured	4
3	16/M	None	Fever, sore throat, cervical lymphadenopathy	EBV antibody titer	Epigastric pain, nausea, vomiting	Serum: 699 U/l	NA	USG, CT AB and oral cholecystogram: normal	Symptomatic	Cured	5
4	18/M	None	Fever, sore throat, cervical lymphadenopathy	Heterophile antibody, ox-cell hemolysin titer	Abdominal pain, vomiting	Serum: 888 U/l	NA	NA	Symptomatic	Cured	6
5	15/F	Infectious hepatitis 5 months prior to this illness	Fever, painful swallowing	EBV antibody titer	Colicky abdominal pain	Urine: 3875 U/l	NA	NA	Symptomatic	Cured	7
6	24/M	None	Fever, throat pain	Monospot, heterophile antibody titer	Epigastric pain, nausea	Serum: 376 U/l Urine: 4700 U/l	NA	NA	Symptomatic	Cured	8
7	12/F	None	Fever, sore throat	Monospot, heterophile antibody titer	Abdominal pain, nausea	Serum: 703 U/l Urine: 8700 U/l	NA	NA	Symptomatic	Cured	8
8	23/M	Dyspepsia	Fever, sore throat, lymphadenopathy	Heterophile antibody titer	Nausea, vomiting	Serum: 271 U/l	417 U/l	Oral cholecystogram: normal	Symptomatic	Cured	9
9	18/F	None	Fever, sore throat, cervical lymphadenopathy	EBV antibody titer	Abdominal pain, nausea	Serum: 620 U/l	659 U/l	USG and CT AB: edematous pancreas, no gallstone	Symptomatic	Cured	Our case

M, male; F, female; EBV, Epstein–Barr virus; GI, gastrointestinal; NA, not available; USG, ultrasonography of the abdomen; CT AB, computed tomography of the abdomen.

<sup>a</sup> Serum normal range 60–180 U/l; urine normal range <1600 U/l. The units of all values, if not originally U/l, were converted to U/l for comparison.

<sup>b</sup> Serum value, normal range 0–160 U/l. The units of all values, if not originally U/l, were converted to U/l for comparison.

negative monospot test. The negative result of this test occurs in about 10% of patients with acute EBV infection due to 90% sensitivity of the test and delayed appearance of heterophile antibodies.<sup>1</sup> Lastly, she had a thick-walled, tender gallbladder without gallstones on ultrasonography, suggesting acute cholecystitis. However, this finding is non-specific and can be found in non-gallbladder diseases including acute viral hepatitis, alcoholic hepatitis, pancreatitis, severe malnutrition, heart failure, and septicemia.<sup>10</sup>

This reported case suggests that EBV infection can present with atypical features including acute pancreatitis, hypotension, DIC, and imaging findings mimicking acute cholecystitis. A high index of suspicion will facilitate early diagnosis and prompt treatment of the infection, and prevent unnecessary antibiotic use.

*Conflict of interest:* No conflict of interest to declare.

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Corresponding Editor: Craig Lee, Ottawa, Canada

4 May 2007

doi:10.1016/j.ijid.2007.07.001