

Case report

Epstein-Barr virus-associated acute pancreatitis

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SUMMARY

Epstein-Barr virus (EBV) infection is mostly subclinical and resolves spontaneously without complications. Gastroenterology involvement usually manifests as asymptomatic liver enzymes elevation. We report a new case of acute pancreatitis complicating EBV infection and review the literature. EBV-associated acute pancreatitis is rare, usually develops in the setting of clinically clear EBV infection, occurs mostly in children and young adults, has mild-to-moderate severity, and has excellent prognosis with conservative management. It should be suspected when patients with an EBV infection picture develop unexplained abdominal pain.

BACKGROUND

Epstein-Barr virus (EBV) is a commonly encountered viral infection and is typically asymptomatic especially in children.¹ Ninety percent of adults are EBV seropositive.² Symptomatic patients may present with a syndrome of malaise, headache and fever that may progress to lymphadenitis and pharyngitis.¹ Patients are typically managed with supportive care; the infection often resolves spontaneously over a course of a few weeks.¹

The gastroenterology system can be involved in EBV infection; with patients mostly presenting with asymptomatic elevations of liver enzymes.³ Pancreatitis is not commonly associated with EBV infection; only 16 cases have been reported.⁴⁻¹⁸ We report a new case and review the literature.

CASE PRESENTATION

An 18-year-old woman presented with a 12-day history of moderate unremitting upper abdominal pain, nausea and anorexia that were preceded by fever, sore throat, headache and malaise. Physical examination revealed a temperature of 36.8°C, blood pressure of 124/81 mm Hg, heart rate of 80 beats/min, respiratory rate of 14 breaths/min, bilateral non-tender cervical lymphadenopathy, mild pharyngeal injection and moderate epigastric tenderness. There was no hepatosplenomegaly or jaundice. She did not report taking any medications and denied any alcohol or illicit drug use.

Leucocyte count was $14.5 \times 10^9/L$ (15% neutrophils, 9% monocytes, 32% lymphocytes and 44% reactive lymphocytes), haemoglobin 127 g/L, haematocrit 36%, blood urea nitrogen (BUN) 7 mg/dL, creatinine 0.9 mg/dL, amylase 327 IU/L, lipase 2016 U/L, alkaline phosphatase 246 IU/L, aspartate aminotransferase 210 IU/L, alanine aminotransferase 283 IU/L and total/direct bilirubin 2/1.6 mg/dL. Calcium, random blood glucose and

triglycerides were within normal limits. Abdominal ultrasound revealed a mildly enlarged liver with coarse echotexture, contracted gallbladder, normal common bile duct, mildly enlarged right upper quadrant lymph nodes and no intrahepatic biliary ductal dilatation. Abdominal CT showed acute pancreatitis with mild splenomegaly.

Serology studies for hepatitis A (anti-HAV IgM), hepatitis B (HBsAg and anti-HBV core IgM), hepatitis C (anti-HCV), HIV (HIV 1 p24 antigen, anti-HIV1, and anti-HIV2 Ab), cytomegalovirus virus (quantitative PCR), antinuclear antibody, antismooth muscle antibody, antimitochondrial antibody, ceruloplasmin, ferritin/iron studies and acetaminophen level were negative. However, EBV heterophile antibodies was positive and further testing revealed elevated EBV IgG viral capsid antibodies (78.6 U/mL), EBV IgM viral capsid antibodies (>160 U/mL) and EBV IgG early disease antibodies (70 U/mL).

OUTCOME AND FOLLOW-UP

The patient was managed conservatively including pain management, hydration, fluids and slowly advanced diet. She improved clinically, lipase level gradually decreased, and she was discharged on the fourth day of hospitalisation.

DISCUSSION

According to the American College of Gastroenterology guidelines, acute pancreatitis can be diagnosed in the presence of two of the following three criteria: abdominal pain, serum lipase and/or amylase level higher than three times the upper normal limit, and radiological evidence of acute pancreatitis.¹⁹ Our patient fulfilled the three criteria. Common causes of pancreatitis, including alcohol, gallstones, drugs, hypercalcaemia and hypertriglyceridemia were ruled out. The presence of cervical lymphadenopathy and pharyngeal erythema led to suspicion of EBV infection, which was confirmed serologically. The pancreatitis in our patient was mild in severity (absence of systemic inflammatory response syndrome with normal haematocrit, BUN and creatinine) and recovered rather quickly within 4 days.

Clinical pancreatitis is rarely associated with EBV infection; review of the literature revealed only 16 cases in 15 reports.⁴⁻¹⁸ Including our patient, mean age was 17.8 (range 3–39) years with 53% being <18 years old; 53% were men; 94% complained of abdominal pain, 6% of left costovertebral pain and 76% of sore throat; 88% had fever, 47% cervical lymphadenopathy and 59% pharyngitis on physical examination. In 12 cases, serum lipase and/or



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amylase levels were diagnostic (>3 the normal upper limit); in 2 cases with non-diagnostic serum levels, there was evidence of acute pancreatitis on abdominal CT, and in 3 other cases there was elevated urine amylase level and no abdominal imaging was obtained. So the diagnosis of pancreatitis was confirmed, according to American College of Gastroenterology guidelines, in all but three cases (5, 6 and 8). Serological documentation for EBV infection was obtained in all 17 cases, EBV IgM viral capsid antibodies in 71% and EBV heterophile antibodies in 29%.

Gallstones were ruled out with abdominal ultrasound, CT, MRI, or oral cholecystography in 76% of cases. In one case, there was a 2-month history of heavy alcohol intake prior to presentation, which raises suspicion of alcohol-induced pancreatitis.⁵ Lifschitz *et al*²⁰ described a 10-year-old girl, initially hospitalised for infectious mononucleosis and hepatitis with positive EBV IgM viral capsid antibodies, who presented 6 weeks later with severe epigastric pain and was diagnosed with acute pancreatitis, cholelithiasis, and choledocholithiasis. This case was also included in the review by Khawcharoenporn *et al*.¹¹ It was not included in the current review as the authors believe the acute pancreatitis was most likely caused by gallstones.

Our patient had asymptomatic, moderately elevated liver enzymes as a co-complication. Other reported co-complications were parotitis,⁸ proctitis,⁹ pneumonia,¹⁰ septic shock and disseminated intravascular coagulation,¹¹ septic shock, myocarditis, and acute renal failure,¹² septic shock, acute respiratory distress syndrome, and pneumonia¹⁶ and sand paper like rash,¹⁷ each in one case.

EBV infection typically follows a benign course and resolves spontaneously.¹ As such most patients do not require any treatment outside of supportive care. On the other hand, acute uncomplicated pancreatitis is effectively treated with pain control, hydration and nutritional support.² This management was successfully used in almost all reported cases including ours. In two cases that were complicated with pneumonia, acyclovir and gancyclovir were used.^{10 16}

Learning points

- ▶ Epstein-Barr virus (EBV)-associated acute pancreatitis is rare and usually develops in the setting of clinically clear EBV infection.
- ▶ It occurs mostly in children and young adults, has mild-to-moderate severity, and has excellent prognosis with conservative management.
- ▶ It should be suspected when patients with EBV infection develop unexplained abdominal pain.

The pathophysiology of EBV-associated pancreatitis is not clear, given the reported course, direct viral infection is likely. It remains to be explored whether subclinical pancreatitis in the setting of EBV infection is more common and why only few patients develop clinical pancreatitis.

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REFERENCES

- 1 Vouloumanou EK, Rafailidis PI, Falagas ME. Current diagnosis and management of infectious mononucleosis. *Curr Opin Hematol* 2012;19:14–20.
- 2 Luzuriaga K, Sullivan JL. Infectious mononucleosis. *N Engl J Med Overseas Ed* 2010;362:1993–2000.
- 3 Carter RL, Penman HG. *Infectious mononucleosis*. Oxford and Edinburgh: Blackwell Scientific Publication, 1969: 47–62.
- 4 Wislocki LC. Acute pancreatitis in infectious mononucleosis. *N Engl J Med* 1966;275:322–3.
- 5 Everett DE, Volpe JA, Bergin JJ. Pancreatitis in infectious mononucleosis. *South Med J* 1969;62:359–60.
- 6 Hedström Sven Åke, Belfrage I. Acute pancreatitis in two cases of infectious mononucleosis. *Scand J Infect Dis* 1976;8:124–6.
- 7 Werbit W, Mohsenifar ZAB. Mononucleosis pancreatitis. *South Med J* 1980;73:1094.
- 8 Mor R, Pitlik S, Dux S, *et al*. Parotitis and pancreatitis complicating infectious mononucleosis. *Isr J Med Sci* 1982;18:709–10.
- 9 Koutras A. Epstein-Barr virus infection with pancreatitis, hepatitis and proctitis. *Pediatr Infect Dis J* 1983;2:312–3.
- 10 Zhu Z, Yin S-J, Kong Z-B, *et al*. Pancreatitis combined with Epstein-Barr virus-induced infectious mononucleosis. *Chin Med J* 2017;130:2001–2.
- 11 Khawcharoenporn T, Lau WKK, Chokrungrvaranon N. Epstein-Barr virus infection with acute pancreatitis. *Int J Infect Dis* 2008;12:227–9.
- 12 Teniente Urbina ME, Castañeda JC, José Ortiz Saavedra P. [Pancreatitis, myocarditis and interstitial nephritis associated with acute infection with Epstein Barr virus]. *Rev Gastroenterol Peru* 2009;29:367–73.
- 13 Marín-García D, Ruiz-Serrato A, Reina-González AM, *et al*. [Acute pancreatitis associated with Epstein-Barr virus infection]. *Semergen* 2012;38:476–7.
- 14 López-Ibáñez M.^a Cristina, Moreno-Conde M, Gallego-De-la-Sacristana-López-Serr Ángel, *et al*. Acute pancreatitis as atypical manifestation of Epstein-Barr virus infection. *Rev. esp. enferm. dig.* 2013;105:437–8.
- 15 Kang S-J, Yoon K-H, Hwang J-B. Epstein-Barr virus infection with acute pancreatitis associated with cholestatic hepatitis. *Pediatr Gastroenterol Hepatol Nutr* 2013;16:61–4.
- 16 Galzerano A, Nisi F, Angela S, *et al*. Acute Epstein-Barr virus pancreatitis with thoracic-abdominal abscess and portal compression. *Dig Liver Disease* 2014;46:574–5.
- 17 Narchi H, Bimal R, Epelman M, *et al*. Cholestatic hepatitis with pancreatitis as presenting features of Epstein-Barr virus infection. *JMED Research* 2014;2014:1–4.
- 18 Cook J, Kothari M, Nguyen A. Epstein-Barr virus infection with concurrent pancreatitis and hepatitis: a rare disease entity. *Am J Infect Dis* 2015;11:83–7.
- 19 Tenner S, Baillie J, DeWitt J, *et al*. American College of gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013;108:1400–15.
- 20 Lifschitz C, LaSala S. Pancreatitis, cholecystitis, and choledocholithiasis associated with infectious mononucleosis. *Clin Pediatr* 1981;20.

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