

Epstein-Barr virus-associated acute pancreatitis: a clinical report and review of literature

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Abstract

Background: Acute pancreatitis is a disorder of reversible inflammation of the pancreas. Only few cases are related to infections and the most common pathogens are the viruses responsible for mumps, parotitis, and influenza. Epstein-Barr virus (EBV)-associated acute pancreatitis is a rare condition, both in children and adults.

Case presentation: A 3-year-old female was admitted to our hospital for vomiting and abdominal pain. Laboratory investigations revealed elevated amylase and lipase, with normal liver function tests. Abdomen ultrasound demonstrated an enlarged pancreas, with hypoechogenic areas; no biliary lithiasis was observed. Infectious disease serology was positive for the presence of EBV VCA IgM and IgG. A diagnosis of EBV-associated acute pancreatitis was made. The patient was treated conservatively and she recovered.

Conclusions: Acute pancreatitis is rarely associated with EBV infection; a review of the English literature revealed only 10 pediatric and 6 adult cases. Patients with pancreatitis should always be evaluated for EBV serology, even in the absence of the typical clinical and hematological features of infectious mononucleosis. For these patients, good prognosis is generally expected.

Background

Epstein-Barr virus (EBV) infection is a common viral infection, especially in children; it could have an asymptomatic course or may present as flu syndrome characterized by fever, malaise, headache, lymphadenitis, and pharyngitis [1]. EBV infection is usually a self-limiting disease and resolves spontaneously in a few weeks. The gastrointestinal system could be involved: enlarged spleen and liver, with elevated transaminase levels, are other common symptoms. Acute pancreatitis is a disorder of reversible inflammation of the pancreas. Only few cases are related to infections and the most common pathogens are the viruses responsible for mumps, parotitis, and influenza. EBV-associated acute pancreatitis is a rare condition, both in children and adults. Here we report on a 3-year-old girl with acute pancreatitis due to EBV infection; a review about this topic was also conducted thereafter.

Case Presentation

A 3-year-old female, previously in good health, was admitted to our hospital for vomiting and abdominal pain. She did not complain other symptoms. Vital signs were normal: she had a body temperature of 36.8°C, a blood pressure of 90/65 mmHg, and a heart rate of 99 beats/minute. On physical examination, she appeared sick, with moderate epigastric tenderness. Laboratory investigations showed hemoglobin 13.8 g/dl, platelet 340000/mm³, white blood cell count 16600/mm³ (neutrophils 20%, monocytes 11%, and lymphocytes 69%), aspartate aminotransferase 40 U/l, alanine aminotransferase 25 U/l, total bilirubin 0,11 mg/dl, amylase 913 U/l (normal range 30–100 U/l), and lipase 6450 U/l (normal range 3–32 U/l). Abdomen ultrasound revealed an enlarged pancreas, with hypoechogenic areas; no biliary lithiasis was observed. She had no past history of abdominal trauma, surgery or cholecystitis and any familial history of pancreatitis or gallstones was reported. She did not received any medications known to cause pancreatitis. Laboratory results for various infectious agents known to cause pancreatitis were all negative, except for the presence of EBV VCA IgM and IgG. Exudative pharyngotonsillitis, cervical lymphadenopathy, and hepatosplenomegaly were not present. A diagnosis of EBV-associated acute pancreatitis was made; the patient was treated conservatively, including fasting, peripheral parenteral nutrition, pain management with acetaminophen, and antibiotics. She improved clinically, lipase and amylase levels gradually decreased, and she was discharged home on the fifteen day of hospitalisation.

Discussion And Conclusions

Acute pancreatitis is an inflammatory disorder of the pancreas; the incidence rate is 3–13 cases per 100000 per year in pediatric population [2, 3], and 5–60 cases per 100000 persons per year in adulthood [4]. The most common etiology of acute pancreatitis is gallstones or microlithiasis; other causes include alcohol misuse, trauma, metabolic disorders (hypertriglyceridemia, hypercalcemia), infections (parotitis, mumps, influenza, herpes viruses, hepatitis viruses, coxsackieviruses, mycoplasma), systemic disease (hemolytic uremic syndrome, systemic lupus erythematosus, Henoch-Schönlein purpura, Kawasaki disease, inflammatory bowel disease), and autoimmune pancreatitis [4, 5]. EBV infection is a rare cause of acute pancreatitis; the pathophysiology remains unclear: both direct viral infection and inflammatory process induced by the virus are plausible pathogenic mechanisms [6, 7].

A review of the English literature revealed only 10 pediatric [6, 8–16] and 6 adult cases [7, 17–21]. As regards pediatric reports (Table I), median age and mean age was 12 and 11.8 years respectively (range 3–18), 36% were male and 64% were female. As regards pancreatitis symptoms, abdominal pain was described in all cases, vomiting in 55%, and nausea in 27%; eight patients (73%) had also mononucleosis symptoms, like fever, lymphadenitis, and pharyngitis. Amylase and/or lipase levels were increased up to three times the normal limit in 100% of the cases. In 5 children, there was evidence of acute pancreatitis on abdominal computerized tomography (CT), while only in our case, ultrasound (US) revealed an enlarged pancreas with a heterogeneous echotexture. According to the American College of Gastroenterology guidelines [22], the diagnosis of pancreatitis was confirmed in all patients. Six children presented other complications related to EBV infection: the most common was cholestatic hepatitis (50%); cholecystitis, pneumonia, proctitis, portal vein thrombosis, and septic shock were also reported. Serological documentation for EBV infection was obtained in 10 cases, while in 1 child, the diagnosis was made clinically. All cases were treated with supportive care, that were fasting and parenteral nutrition; in 1 patient, antibiotics only was added, while in another case, antivirals and antibiotics were also used. All children recovered.

As regards adult patients (Table II), EBV-associated acute pancreatitis affects mainly young adult (range 21–45 years), with a slight female predominance (66%). All cases presented abdominal pain, associated sometimes with nausea, fever, and vomiting. In 3 patients (50%), signs and symptoms related to infectious mononucleosis were also observed. The diagnosis of EBV infection was made by positive serology in 5 patients; also in 2 cases, serum EBV-DNA was detected. Abdominal CT was executed in 5 patients, revealing signs of acute pancreatitis, such as enlarged and edematous pancreas; in 1 case, areas of

necrosis were also noticed. All patients except one had complications related to systemic EBV infection: hepatitis with or without cholestasis, gastritis, pneumonia with pleural effusion, ascites, pericardial effusion, autoimmune hemolytic anemia, and multi-organ failure. The patients were treated with symptomatic therapy; when a complicated disease course occurred, antibiotics, antivirals, and steroids were also administered. All patients except one fully recovered.

In conclusion, EBV infection is characterized by clinical heterogeneity; multiple organs could be involved, also the pancreas, both in children and young adults. Active surveillance is needed for prompt diagnosis and early treatment. In patients with signs and symptoms of acute pancreatitis, EBV infection should always be considered, even in the absence of the typical clinical and hematological features of infectious mononucleosis. Generally, EBV-associated acute pancreatitis is characterized by a favorable prognosis, with a spontaneous resolution.

Abbreviations

Epstein-Barr virus

EBV

computerized tomography

CT

ultrasound

US.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Parent's informed written consent was provided.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SS and MGua have participated in the diagnostic pathways and treatment. GAR, SS, MGua wrote the paper. SA, GC and MGiu revised the manuscript. All authors read and approved the final manuscript

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Tables

Table I. Clinical data of pediatric cases with EBV-associated acute pancreatitis reported in literature and our case.

Reference	Age/sex	Mononucleosis symptoms	Gastrointestinal symptoms	EBV diagnosis	Amylase-lipase	Imaging	Other complications	Therapy
Wislocki et al. 1966 [8]	18y/M	Yes	Abdominal pain, vomiting	Heterophil antibody	480 U/I-NA	NA	No	Fasting, parenteral nutrition
Hedstrom et al. 1976 [9]	12y/F	Yes	Abdominal pain, nausea	Clinical	8700 U/I-NA	NA	No	Symptomatic
Werbitt et al 1980 [10]	16y/M	Yes	Abdominal pain, nausea, vomiting	VCA positivity	378 U/I-NA	CT: no pancreatic abnormality	No	Symptomatic
Koutras et al. 1983 [11]	8y/F	Yes	Abdominal pain, vomiting	VCA IgM positivity	300-180 U/I	NA	Cholestatic hepatitis, proctitis	Symptomatic
Khawcharoenporn et al. 2008 [12]	18y/F	Yes	Abdominal pain	VCA IgM positivity	620-659 U/I	CT: edematous pancreas	Cholecystitis, septic shock, DIC	Symptomatic
Kang et al. 2013 [13]	11y/F	No	Abdominal pain, vomiting	VCA IgM positivity	4010-4941 U/I	CT: edematous pancreas, peripancreatic fluid accumulation	Cholestatic hepatitis	Fasting, parenteral nutrition
López-Ibáñez et al. 2013 [14]	15y/M	Yes	Abdominal pain	Heterophil antibody	1251 U/I-NA	CT: globular pancreas, hepatosplenomegaly, ascites	No	Not available
Galzerano et al. 2014 [15]	3y/F	No	Abdominal pain	VCA IgM positivity	3880 U/I-NA	CT: enlargement of the pancreatic head	Bilateral pneumonia, portal vein thrombosis, septic shock	Fasting, parenteral nutrition, antibiotics, gancyclovir
Narchi et al. 2014 [16]	8y/M	Yes	Abdominal pain, vomiting	VCA IgM positivity	80-1000 U/I	MRI: not visible pancreas	Cholestatic hepatitis, cholecystitis	Fasting, parenteral nutrition
Hammami et al. 2019 [6]	18y/F	Yes	Abdominal pain, nausea	VCA IgM positivity	327-2016 U/I	CT: signs of acute pancreatitis	Hepatitis	Symptomatic
Our case	3y/F	No	Abdominal pain, vomiting	VCA IgM positivity	913-6450 U/I	US: enlargement of the pancreas	No	Fasting, parenteral nutrition, antibiotics

Abbreviations: y years, M male, F female, NA not available, DIC disseminated intravascular coagulopathy.

Table II. Clinical data of adult cases with EBV-associated acute pancreatitis reported in literature.

Reference	Age/sex	Mononucleosis symptoms	Gastrointestinal symptoms	EBV diagnosis	Amylase-lipase	Imaging	Other complications	Therapy	Outcome
Jahann et al. 2012 [17]	22y/M	Yes	Abdominal pain	VCA IgM positivity	330-2300 U/l	NR	No	Symptomatic	Recovered
Cook et al. 2015 [18]	25y/M	No	Abdominal pain, nausea, fever	VCA IgM positivity	NA-429 U/l	CT: pancreatic edema	Cholestatic hepatitis, pleural effusions, ascites	Fasting, parenteral nutrition	Recovered
Singh et al. 2015 [19]	21y/F	Yes	Abdominal pain, vomiting, nausea	VCA IgM positivity	NA-4301 U/l	CT: pancreatic edema	Autoimmune hemolytic anemia	Symptomatic, prednisone	Recovered
Zhu et al. 2017 [7]	35y/F	Yes	Abdominal pain, vomiting	VCA IgM positivity	1300-1450 U/l	CT: pancreatic edema	Hepatitis, pneumonia	Fasting, parenteral nutrition, antibiotics, acyclovir	Recovered
Fiani et al. 2021 [20]	35y/F	No	Abdominal pain, fever	VCA IgM and IgG positivity, serum EBV DNA	129/408 U/l	CT: enlargement of the pancreas	Cholestatic hepatitis, pneumonia with pleural effusions	Symptomatic, antibiotics, antivirals, methylprednisolone	Recovered
Huang et al. 2021 [21]	45y/F	No	Abdominal pain	Serum EBV DNA	Increased up to three times the normal limit	CT: pancreatic necrosis	Pericardial and pleural effusions, gastritis, MOF	Symptomatic	Died

Abbreviations: y years, M male, F female, NA not available, NR not reported, MOF multi-organ failure.

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