Pancreatitis in hand-foot-and-mouth disease caused by enterovirus 71

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Abstract

Some viruses, including certain members of the enterovirus genus, have been reported to cause pancreatitis, especially Coxsackie virus. However, no case of human enterovirus 71 (EV71) associated with pancreatitis has been reported so far. We here report a case of EV71-induced hand-foot-and-mouth disease (HFMD) presenting with pancreatitis in a 2-year-old girl. This is the first report of a patient with acute pancreatitis in HFMD caused by EV71. We treated the patient conservatively with nasogastric suction, intravenous fluid and antivirals. The patient's symptoms improved after 8 d, and recovered without complications. We conclude that EV71 can cause acute pancreatitis in HFMD, which should be considered in differential diagnosis, especially in cases of idiopathic pancreatitis.

Key words: Pancreatitis; Enterovirus 71; Hand, foot and mouth disease

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Core tip: Acute pancreatitis associated with enterovirus 71 (EV71) infection is extremely rare. We here report a case of EV71-induced hand-foot-and-mouth disease (HFMD) presenting with pancreatitis in a 2-year-old girl. This is the first case report of acute pancreatitis associated with EV71 infection. EV71 can cause acute pancreatitis in HFMD, which should be considered in differential diagnosis, especially in cases of idiopathic pancreatitis.

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INTRODUCTION

Enterovirus 71 (EV71) is a human enterovirus in the Enterovirus genus of the Picornaviridae family. Many of the EV71-infected cases have occurred in Asia-Pacific region, and posed a serious threat to children's health[1]. EV71 primarily causes hand-foot-and-mouth disease (HFMD) in young children, and many neurological complications such as encephalitis, brain stem encephalitis and fatal pulmonary edema occur occasionally[2]. However, no EV71-associated pancreatitis has been reported so far. We here describe a case of EV71-induced HFMD presenting with pancreatitis in a 2-year-old girl.

CASE REPORT

A 2-year-old girl was admitted to our hospital in June 2014 because of acute abdominal pain and vomiting for 2 d. Vomiting occurred about ten times a day. Moreover, 4 d before admission, maculopapular rashes had appeared on her hip and then spread to the palms of her hands and feet over the following 2 d, and she also had fever during the 4 d before admission. Her past medical history showed no record of pancreatitis and her family history was negative for pancreatic disease.

A physical examination on admission revealed a normal blood pressure, temperature, pulse rate, and breathing rate. Maculopapular rashes on her hip, palms and feet and vesicles in mouth cavity membrane were observed. Breathing sounds were clear on auscultation. Abdominal examination revealed only mild abdominal tenderness. No other abnormalities were found. Of note, she had not taken any drugs before admission.

On admission, her chest X-ray and electrocardiogram were both normal. A complete blood count, calcitonin and blood biochemical tests including C-reactive protein, glucose, bilirubin, triglycerides and calcium, were all within reference limits. The total levels of IgG, IgA and IgM in blood were normal. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were slightly elevated (ALT: 64 IU/L; AST: 68 IU/L; reference range: 10-35 IU/L), and serum amylase (385 IU/L; reference range: 0-220 IU/L) and urine amylase (5300 IU/L; reference range: 0-1200 IU/L) were also increased. Serological tests of various infectious agents including Epstein-Barr virus, varicella zoster virus, cytomegalovirus, HIV I and II, hepatitis A, B and C viruses, echoroviruses, syncytial virus, flu virus A and B, parainfluenza 1, 2 and 3, and adenovirus were all negative. Tumor markers were also negative. Other relevant tests and examinations during hospitalization were performed and the results were as follows: real-time reverse transcription PCR (RT-PCR) in a stool sample was positive for EV71, but negative for Coxsackie virus A16, and antibody titer against EV71 was markedly elevated and it was quadrupled during the recovery period. Ultrasonography of the abdomen revealed neither gallstones nor biliary sludge. Abdominal computed tomography (CT) showed acute pancreatitis with swelling of the pancreas, and peri-pancreatic exudation. No cholelithiasis or tumor occluding the common bile duct or pancreatic duct was observed (Figure 1). Magnetic resonance cholangiopancreatography (MRCP) performed in another hospital revealed peri-pancreatic exudation and no anatomical abnormalities in the pancreas or pancreatic duct. The girl was treated conservatively with nasogastric suction, intravenous fluid and antivirals. She was administered Cimetidine (0.15 g b.i.d.), antibiotics (Cefminox, 0.4 g q8h, iv), and antiviral agent (Leigh Bhave Lin, 0.15 g qd, iv).

The patient's symptoms improved after 8 d, and recovered without complications. On the day of discharge, all serum biochemical tests were normal. Two months later, findings on the abdominal CT scan were normal, all laboratory values were within the normal ranges, and the rashes had disappeared, and no further damage was observed. One year after follow-up, the patient was asymptomatic and showed no evidence of pancreatitis recurrence.

DISCUSSION

We have presented a case of EV71 infection associated with pancreatitis secondary to HFMD. EV71 was established as the causative pathogen of pancreatitis in this case based on the following evidence: EV71 positivity, negative history of alcoholic and drug use, no gallstones, no anatomical abnormalities in the pancreas or pancreatic duct, normal level of triglyceride and calcium, negative serological tests for other infectious agents, and presence of characteristic rash...
on hip, palms and feet. Based on these observations, it is tempting to speculate that the EV71 is the most likely pathogenic factor for pancreatitis in this case.

Acute pancreatitis can be triggered by a variety of etiologies. Gallstones and alcohol are the most common causes of acute pancreatitis in adults. However, the etiology in children is often drugs, infection, trauma, genetic mutation, and congenital structural abnormalities such as choledochal cysts and abnormal union of the pancreaticobiliary junction. The most common infections are mumps, viral hepatitis, Coxsackie virus and echovirus. At present, among anomalies of the pancreaticobiliary system, choledochal cyst is the most common cause of acute pancreatitis. Some acute pancreatitis cases without a detectable cause are considered as “idiopathic”. Viral etiology may be involved in idiopathic acute pancreatitis.

The Enterovirus genus is part of the large Picornaviridae family, and is known to be highly cytolytic. The species are small non-enveloped RNA viruses and the most common viruses causing human diseases. EV71 belongs to the Enterovirus genus in the Picornaviridae family, and has been recognized as one of the most important viral pathogens. EV71 infection causes countless diseases ranging from mild HFMD or herpangina to fatal brain stem encephalitis complicated with pulmonary edema, and has become a serious threat to children’s health. So far, no EV71-associated pancreatitis has been reported, but Coxsackievirus A and B have been reported to be causative pathogens of pancreatitis and type 1 diabetic mellitus. Studies have suggested the presence of enteroviruses in pancreatic tissue including the pancreatic islets of type 1 diabetic patients. Coxsackievirus has been shown to replicate and destroy human β-cells. But to the best of our knowledge, EV71-induced pancreatitis is quite rare, and our patient presented no other severe complications except for acute pancreatitis. A previous study analyzing the EV71 genome obtained from an immunocompromised host showed various EV71 lineages and indicated that a mutation in the VP1 BC loop region of EV71 (L97R) may play a critical role in cell tropism independent of the EV71 lineage. The mechanism of pancreatitis associated with EV71 is still unknown; EV71 might injure the pancreatic acinar cell membrane, leading to the leakage of intracellular enzymes, and at the same time, some other factors such as pancreatitis-related genetic susceptibility genes and virulence determinants in the genotype of the infecting strain should also be considered. Therefore, a multi-disciplinary approach is required to extend our understanding of this complex relationship.

In conclusion, EV71 can cause acute pancreatitis in HFMD, which should be considered in the differential diagnosis, especially in cases of idiopathic pancreatitis. It is important to screen the patients with acute pancreatitis for EV71 infections.

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