Case Report

Acute pancreatitis complicating dengue hemorrhagic fever

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Abstract

Dengue infection can have spectrum of manifestations, often with an unpredictable clinical progression and outcome. There have been increasing reports of atypical manifestations. Abdominal pain or tenderness and persistent vomiting (warning signs) are present in the majority of cases with severe dengue prior to clinical deterioration. We report a 10-year-old child who presented with fever, persistent vomiting, and abdominal pain. A diagnosis of acute pancreatitis was made. This is a very infrequently reported complication of dengue hemorrhagic fever.

Keywords: Dengue hemorrhagic fever. Acute pancreatitis. Persistent vomiting.

INTRODUCTION

Dengue infection is a disease entity that can have different clinical presentations and often demonstrates an unpredictable clinical progression and outcome. There have been increasing reports of dengue fever (DF) and dengue hemorrhagic fever (DHF) with atypical manifestations due to involvement of liver, kidneys, heart, or nervous system (expanded dengue syndrome)⁽¹⁾. These atypical manifestations may be potentially serious and may result in increased rates of morbidity and mortality. Therefore, clinicians should be aware of these atypical manifestations. Acute pancreatitis is a rare complication of DF⁽²⁾. We report a case of acute pancreatitis complicating DHF; this is a very infrequently reported complication.

CASE REPORT

A 10-year-old girl, known with autoimmune hemolytic anemia, presented with a one-day history of fever, vomiting, and body aches. On examination, her vital signs were stable. Abdominal examination revealed a 2cm hepatomegaly and a palpable spleen. Examination of other systems was unremarkable. The investigations and the course of her illness are depicted in **Table 1** and **Figure 1**. She developed persistent vomiting with abdominal pain. A diagnosis was made of acute pancreatitis complicating DHF. She was managed conservatively and was discharged in a stable condition after 19 days of hospitalization.

DISCUSSION

In DF, abdominal and gastrointestinal symptoms are common^{(3) (4)}. Presentation with an acute abdomen in DF may pose a diagnostic dilemma and is a challenge for the treating clinician. In DHF, up to 40% of patients may present with abdominal pain⁽³⁾. Abdominal pain or tenderness and persistent vomiting are classified as warning signs⁽¹⁾. These symptoms (abdominal pain and vomiting) have been noted in the majority of patients with severe dengue infection prior to clinical deterioration⁽⁵⁾. Hence, there is a need for close monitoring of children with DF who display such warning signs. In a retrospective review of 8,559 patients with DF, 67% had abdominal and gastrointestinal symptoms. The most common symptom was nausea (52%), followed by abdominal pain (36%), and vomiting (29%)⁽⁴⁾. In dengue infection, the causes of abdominal pain include hepatitis, pancreatitis, acalculous cholecystitis, and peptic ulcer disease⁽³⁾. Acute pancreatitis is a rare complication of DF⁽²⁾. In a study of DF by Khanna et al., the various causes of abdominal pain were reported to include acute hepatitis [n = 20 (36.4%)], acalculous cholecystitis [n = 9 (16.4%)], acute pancreatitis [n = 8 (14.5%)], appendicitis [n = 3 (5.5%)], spontaneous bacterial peritonitis [n = 2 (3.6%)], enteritis [n = 8 (14.5%)], peptic ulcer disease [n = 2 (3.6%)], and gastric erosions [n = 3 (5.5%)]⁽³⁾.

Acute pancreatitis in children is associated with significant morbidity and mortality⁽⁶⁾. It was reported that of 589 cases of acute pancreatitis in children, viral infections accounted for 10%⁽⁶⁾. In a study by Setiawan et al., 29% (43/148) of children with DHF who experienced epigastric pain had an enlarged pancreas. However, serum levels of amylase and lipase were measured in only 20 children. The authors noticed slight increase

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TABLE 1
Investigation chart.

	Hb (g/dL)	TLC ($\times 10^9/L$)	Platelets ($\times 10^9/L$)	Serum bilirubin (mg/dL)	AST [U/L]	ALT [U/L]	Amylase [U/L]	Lipase [U/L]	Chest x-ray findings	Abdominal sonography findings
Admission	6.1	11.11 N=91%	276	Total=8.8 Direct=0.8	63	45	-	-	Normal	-
Day 3	11.1	-	147.47 Lakhs	-	-	-	-	-	-	Hepatosplenomegaly, 5-mm-thick gall bladder wall edema
Day 7	9.7	-	66	-	43737	318	284	421	Right upper and middle lobe consolidation. Right pleural effusion	Pancreas bulky, enlarged 24mm in body region, probe tenderness present. Ascites, bilateral pleural effusion, hepatosplenomegaly, 5mm thick gall bladder wall edema
Day 8	10.3	3.29 N=41%, L=52%	38	Total=2.38 Direct=1.3	200	183	-	-	-	-
Day 9	10.9	3.5 N=43%, L=45%	146	-	-	-	-	-	Right upper and middle lobe consolidation. Right pleural effusion	Pancreas bulky, enlarged 24mm in body region, probe tenderness present. Ascites and bilateral pleural effusion, hepatosplenomegaly. Gall bladder wall edema.
Day 13	10.3	-	209	Total=3.4 Direct=0.4	55	118	195	292	Normal	Pancreas normal, mild ascites, mild pleural effusion

Blood culture and urine culture: sterile; **dengue serology:** NS1 antigen positive, IgM positive, IgG negative; **Peripheral smear for malarial parasite, Widal test, Weil-Felix test, Typhidot-M, and HIV test:** all negative; **serology for hepatotropic viruses (hepatitis A, B, C, E):** negative. **On day 7, echocardiogram:** normal. **Arterial blood gas:** pH 7.30, pCO₂ 32mmHg, pO₂ 52.8mmHg, HCO₃ 15.5mmol/L; **kidney function tests (urea, creatinine, Na⁺, K⁺):** normal on days 1, 3, 7 and 8. **Total proteins and albumin:** normal. **On day 8:** PT=16.9 (control=14.2) seconds; APTT=33 (control=29) seconds; INR=1.24. **Hb:** hemoglobin; **TLC:** total leucocyte count; **AST:** aspartate transaminase; **ALT:** alanine transaminase; **N:** neutrophils; **L:** lymphocytes; **NS1:** nonstructural protein 1; **IgM:** immunoglobulin M; **IgG:** immunoglobulin G; **HIV:** Human immunodeficiency virus; **PT:** prothrombin time; **APTT:** Activated partial thromboplastin time; **INR:** International normalised ratio.

Admission/Day	<p>Fever, vomiting, body ache for one day.</p> <p>Vitals: T 102 °F (38.9 °C), PR 140/min, RR 22/min, BP 100/68 mm Hg, CFT <3 sec, SpO₂ 98% in room air.</p> <p>Abdominal examination soft, non-tender, 2 cm liver palpable.</p> <p>Managed with iv RL according to WHO protocol for DSS.</p>
Days 1–6	<p>Child continued to have high fever, persistent vomiting, and developed abdominal pain on day 4. Vitals: stable.</p> <p>Managed with iv RL according to WHO protocol for DF.</p> <p>Parenteral pantoprazole started.</p> <p>Two packed red cell transfusions given in view of anemia (Hb 6.1 g/dL).</p>
Day 7	<p>Child developed severe abdominal pain and bilious persistent vomiting, and passed melena 3 times.</p> <p>Vitals: T 102 °F (38.9 °C), PR 112/min, low volume pulse, RR 22/min, BP 88/60 mm Hg, CFT <3 sec, SpO₂ 98%.</p> <p>Abdominal examination: soft, epigastric tenderness present, tender 6 cm liver palpable.</p> <p>Managed with iv RL according to WHO protocol for DHF/DSS.</p> <p>Two packs of platelets given.</p> <p>Echocardiogram: normal and inferior vena cava distention normal.</p> <p>Sonogram: enlarged, bulky pancreas of 24 mm in body region with probe tenderness. Ascites and bilateral pleural effusions present.</p> <p>Her systolic BP remained < 80mm Hg and she had cold peripheries therefore, we started a dopamine infusion at 5 microgram/kg/min.</p> <p>Lipase=421 U/L (normal=5–60 U/L), amylase=284 U/L (normal=20–100 U/L).</p> <p>She became tachypneic (RR 36/min). Bronchial breathing was heard over right lung fields.</p> <p>Vitals: maintained with supplemental oxygen and the dopamine infusion.</p> <p>Chest radiograph: right upper and middle lobe consolidation.</p> <p>Therefore, iv linezolid, meropenem, and metronidazole were started.</p> <p>Four platelet transfusions were administered.</p>
Days 9–13	<p>Abdominal pain decreasing in intensity. Vomiting persisted despite continuous Ryles tube aspiration.</p> <p>Day 10: BP >50th centile; hence, dopamine infusion tapered and stopped. Fever subsided.</p> <p>Day 12: vital signs stable without supplemental oxygen and inotropes.</p> <p>Antibiotics, parenteral pantoprazole, and iv fluids continued.</p> <p>Sonogram: normal pancreas, mild ascites, mild pleural effusion.</p> <p>Day 13: lipase = 292 U/L, amylase = 195 U/L.</p>
Days 14–16	<p>General condition improved. Normal vitals were maintained. Vomiting frequency decreased and abdominal pain disappeared.</p>
Days 17–18	<p>Started oral fluids. No vomiting or abdominal pain. General condition improved. Normal vitals were maintained. Abdomen soft, no tenderness.</p> <p>iv linezolid and meropenem were given for a total of 10 days</p>
Day 19	<p>General condition good. Oral intake good. No vomiting or abdominal pain. Vital signs normal. Abdomen soft, no tenderness.</p> <p>Child discharged in a stable condition.</p>

T: temperature; PR: pulse rate; RR: respiratory rate; BP: blood pressure; CFT: capillary filling time; SpO₂: oxygen saturation; iv: intravenous; RL: Ringer's lactate; WHO: World Health Organization; DSS: Dengue shock syndrome; DF: Dengue fever; Hb: hemoglobin; DHF: Dengue hemorrhagic fever.

FIGURE 1. Sequence of events after admission

in 6 (75%) of 8 patients with mild DHF and in 10 (83%) of 12 patients with severe DHF. All children with mild DHF had a normal-sized pancreas and in all 10 severe cases children with increased serum levels of amylase and lipase had an enlarged pancreas⁽⁷⁾.

In a previous study, 14 out of 328 cases of DHF/dengue shock syndrome (DSS) had an acute abdomen; causes included acute cholecystitis (n = 10), nonspecific peritonitis (n = 3), and acute appendicitis (n = 1); none had acute pancreatitis⁽⁸⁾. In a study conducted in Pakistan, however, 43 (12%) out of 357 patients with DF had an acute abdomen and three (0.8%) had acute pancreatitis. All three patients with acute pancreatitis developed acute respiratory distress syndrome, and two died⁽⁹⁾. In our patient, DHF was diagnosed according to the World Health Organization's (WHO) criteria. She presented with fever, a bleeding tendency, thrombocytopenia (platelets $<100 \times 10^9/L$), and ascites, and her serology results were positive for nonstructural protein 1 (NS1) antigen and dengue immunoglobulin M (IgM) antibodies. She had continuous persistent vomiting that started one day prior to admission and stopped three days before discharge. Her initial abdominal sonogram and liver enzymes levels were normal. Given that the child's epigastric pain and associated persistent vomiting were not relieved by parenteral pantoprazole, and that she was hypotensive, we suspected acute pancreatitis and ordered serum amylase and lipase testing, and a repeat abdominal ultrasound. We diagnosed acute pancreatitis in view of clinical symptoms (abdominal pain and vomiting), hypotension, enlargement of the pancreas on ultrasound examination without features of hepatobiliary disorders, and increased serum amylase and lipase levels. We started antibiotics empirically for pneumonia and acute pancreatitis. Serum amylase and lipase levels decreased after one week. In DHF, the involvement of the pancreas may be due to direct viral invasion, secondary to host immune reactivity, or due to hypotension⁽²⁾.

Like septic shock, acute pancreatitis can be fatal⁽¹⁰⁾. As such, DHF/DSS can also cause mortality if not treated. Therefore, acute pancreatitis as a complication of DHF is dangerous, and clinicians should know when to suspect in patients with DF. Acute pancreatitis as a complication of DHF may be underdiagnosed due to lack of awareness⁽¹⁰⁾. Hence, clinicians might not request serum amylase or lipase investigation, despite abdominal pain and vomiting. Lee *et al.* compared 14 patients with hyperlipasemia (one with additional hyperamylasemia) and 57 without hyperlipasemia/hyperamylasemia among 71 DHF patients who presented with abdominal pain. They found that three patients in the hyperlipasemia group had pancreatitis, all of whom had enzyme elevation > 3 times the of normal⁽¹¹⁾. In acute pancreatitis, serum amylase usually rises within a few hours of the onset of symptoms and return to normal values within 3-5 days. However, because of sensitivity, specificity, and positive and negative predictive value limitations, serum amylase alone cannot reliably be used to diagnose acute pancreatitis; the more specific serum lipase test is preferred. Serum lipase remains increased for a longer period than amylase after disease presentation⁽¹²⁾. Abdominal pain and vomiting are common in DF, especially in severe DF. Even though important

common causes include acute gastritis, hepatitis, and acalculous cholecystitis, acute pancreatitis should be kept in mind as one of the causes. Simple investigations like serum lipase, amylase (levels more than 3 times the upper limit of normal), and abdominal ultrasound will establish the diagnosis. In a patient with dengue illness who has abdominal pain, it is probably justified to estimate and monitor serum lipase and amylase levels and to perform serial abdominal sonography.

To conclude, clinicians should be alert when there are warning symptoms (abdominal pain and persistent vomiting) in patients with DF, and should order testing of serum lipase and amylase levels along with abdominal sonography. Even though acute pancreatitis is a rare complication, early diagnosis and prompt treatment is necessary to prevent morbidity and mortality.

Conflicts of Interest

The authors declare that there is no conflict of interest.

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