

CASE REPORT

DENGUE HEMORRHAGIC FEVER PRESENTING WITH HEMORRHAGIC PANCREATITIS AND AN INTRAMURAL HEMATOMA OF THE DUODENAL WALL: A CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract. Dengue fever may present with atypical manifestations. Here we report a 47 year-old male presenting with fever and sore throat for 2 days, followed by epigastric pain and tarry stool for 4 days. The esophagogastroduodenoscopy revealed multiple ulcers with a nodular margin in the duodenal bulb and second portion of the duodenum. A MRI of the abdomen revealed hemorrhagic pancreatitis, with a large intramural hematoma in the second portion of duodenum. The final diagnosis was dengue hemorrhagic fever, grade II, complicated with hemorrhagic pancreatitis and an intramural hematoma of the duodenal wall. Physicians should be aware of the atypical abdominal presentations of dengue fever.

Keywords: acute abdomen, acute pancreatitis, dengue virus, hemorrhagic pancreatitis, intramural hematoma

INTRODUCTION

Dengue fever is an arboviral infection which is a major public health problem in subtropical and tropical countries. In 2011, the incidence of dengue fever was 7.3/100,000 in Taiwan; dengue hemorrhagic fever and dengue shock syndrome accounted for 1.2% of cases (<http://www.cdc.gov.tw>).

The majority of patients infected with dengue virus are asymptomatic, and those who are symptomatic may present with biphasic fever, myalgia, retro-orbital pain, cough, skin rash, leukopenia and thrombocytopenia. Dengue infection may also present with atypical manifestations which may be underreported and lead to misdiagnosis. Atypical abdominal presentations include acalculous cholecystitis, splenic rupture, febrile diarrhea and acute pancreatitis (Gulati and Maheshwari, 2007). Common endoscopic findings in patients with dengue fever include hemorrhagic gastritis, gastric ulcers, duodenal

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ulcers and esophageal ulcers (Chiu *et al*, 2005). To our knowledge, this is the first case report of dengue hemorrhagic fever complicated with hemorrhagic pancreatitis and an intramural hematoma of the duodenal wall.

CASE REPORT

A 47-year-old male with diabetes mellitus and chronic hepatitis B virus (HBV) infection, presented to our emergency room with fever, chills, sore throat, vomiting and myalgia for two days. He lived in San Min District, Kaohsiung City, a dengue endemic area of Taiwan. In the emergency room he was diagnosed with having a respiratory tract infection and was sent home with oral medications. Four days later he presented again, this time with epigastric pain and black tarry stools and was admitted.

His initial physical examination revealed a blood pressure of 120/77 mmHg, a body temperature of 36.3°C, a heart rate of 93 beats/minute and a respiratory rate of 20 breaths/minute. His conjunctiva was not pale. He had epigastric tenderness to palpation and hypoactive bowel sounds. He had neither spider angiomas nor palmar erythema.

Laboratory testing revealed a white blood cell count of $3.54 \times 10^9/l$ with 65% granulocytes, 24% lymphocytes, 11% monocytes, a hemoglobin of 14.1 g/dl, a hematocrit of 41% and a platelet count of $33,000/mm^3$. His serum creatinine was 1.5 mg/dl (normal 0.7~1.5). His serum glutamate oxaloacetate transaminase (SGOT) of 107 U/l (normal 5~35), serum glutamate pyruvate transaminase (SGPT) was 85 U/l (normal 0~40) and alkaline phosphatase (ALP) was 52 U/l (normal 42~128). His serum amylase was 2,245 U/l (30~110) and lipase was 2,499 U/l (20~300). His

prothrombin time (INR) was 0.92 and activated partial thromboplastin time (aPTT) was 31.1/29.7. His serum triglyceride level was 116 mg/dl (normal < 200).

Esophagogastroduodenoscopy (EGD) performed on admission revealed multiple ulcers with a nodular margin, large adherent clots and a visible vessel in the duodenal bulb and second portion of the duodenum. The ulcers were injected with 9 ml distilled water and a biopsy was obtained (Fig 1 A, B). Pathology of duodenal biopsy specimens revealed duodenal mucosal tissue with infiltration and chronic inflammatory cells. Computed tomography of the abdomen on admission revealed a lobulated mass over the second portion of the duodenum (Fig 2A, B). A MRI of the abdomen on Day 4 of hospitalization revealed a large intramural hematoma of the duodenum and hemorrhagic pancreatitis (Fig 3). The patient developed dyspnea during hospitalization, and a chest x-ray revealed a right-sided pleural effusion (Fig 4). A thoracentesis showed transudative fluid.

Dengue fever was confirmed with positive serum immunoglobulin M and immunoglobulin G for dengue virus by enzyme-linked immunosorbent assay on the eight day after disease onset. The diagnosis of dengue hemorrhagic fever, grade II, was established on the basis of fever, thrombocytopenia ($<100,000/mm^3$), spontaneous bleeding from the gastrointestinal tract, a right sided pleural effusion and a drop in hematocrit of $>20\%$.

The patient was treated for acute pancreatitis with bowel rest and intravenous fluid, and given esomeprazole 40mg intravenously and was transfused with packed red blood cells. EGD was repeated on day 26 and 46 (Fig 1C and D, respectively).

Repeat abdominal CT on days 19 and

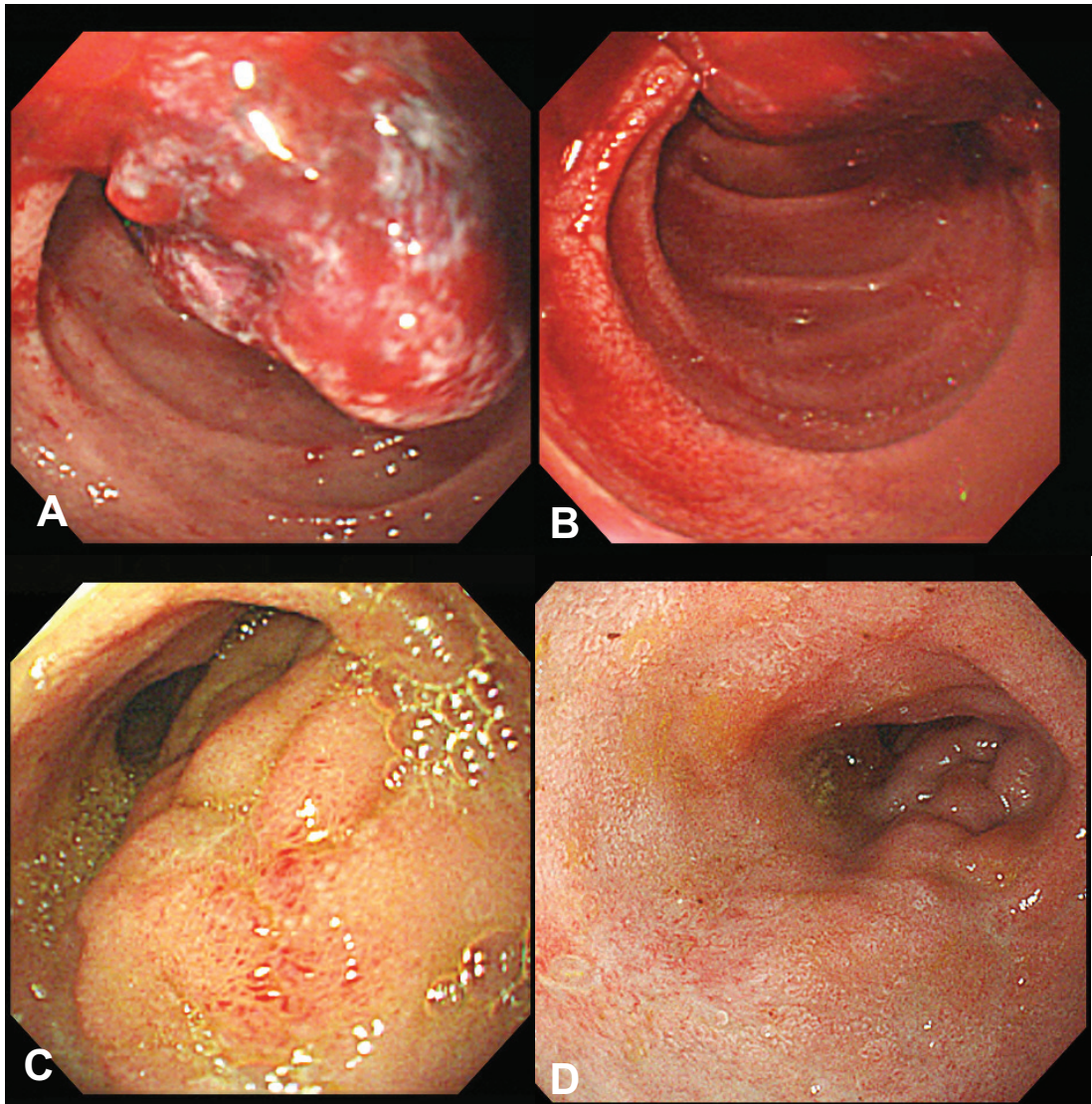


Fig 1—Esophagogastroduodenoscopy (EGD) findings. A, B, EGD on day of admission revealed multiple ulcers with adherent blood clots, a visible vessel in an ulcer base and a nodular margin of the ulcers, the ulcers were in the duodenal bulb and second portion of the duodenum. C, EGD on Day 26 revealing ulcer scarring in the duodenal bulb and edematous mucosa extending from the superior duodenal angle to the second portion of duodenum. D, EGD on Day 46 revealing giant folds with hyperemic mucosa in the second portion of the duodenum.

51 revealed resolution of the intramural hematoma and formation of a peripancreatic phlegmon (Fig 2 C-F). A CT-guided drainage of peripancreatic phlegmon

was done, and the culture revealed *Klebsiella pneumoniae*. After drainage and prolonged use of cefazolin the patient recovered well.

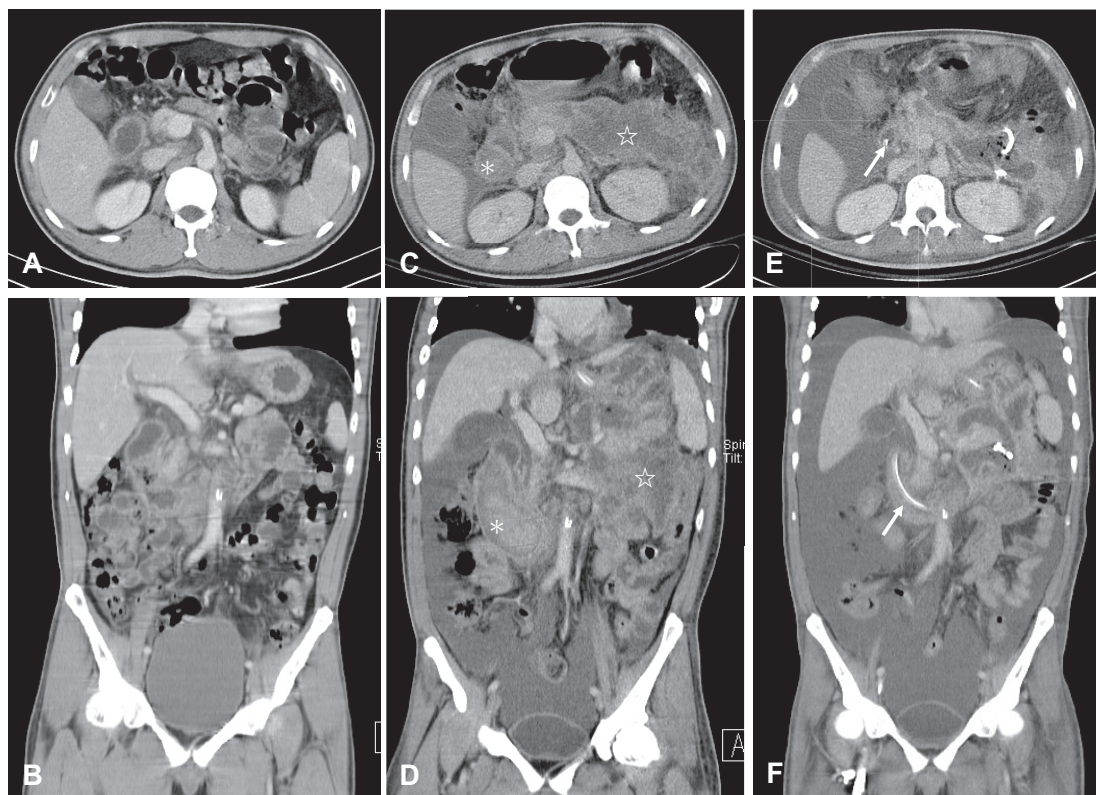


Fig 2—Computed tomography results. A, B. Computed tomography of the abdomen on day 1 revealing a lobulated mass, 2.8 x 2.7 x 4.1 cm in size, in the lateral wall of the secondary portion of the duodenum. C, D. Computed tomography of the abdomen on day 19 revealing a hematoma, 10 x 5 x 3 cm in size, in the lateral wall of the second portion of the duodenum (*) and the presence of a partially liquefied phlegmon in the left peripancreatic region, measuring 14 x 6 x 6 cm in size (☆). E, F. Computed tomography of the abdomen on day 51 revealing almost complete resolution of the intramural hematoma in the lateral wall of the second portion of the duodenum and the persistence of the left-sided, peripancreatic phlegmon, 11 cm in size, only partially resolved.

DISCUSSION

Hemorrhagic pancreatitis associated with dengue fever is rare and the clinicians should be aware of the atypical abdominal presentations of dengue fever.

Common etiologies of acute pancreatitis include gallstones, alcohol, hypertriglyceridemia, trauma and drugs (mainly antibiotics). Less common etiologies include periampullar diverticuli,

pancrease divisum, a periampullar mass and infectious agents, such as mumps, coxsackievirus and cytomegalovirus. We excluded these causes of acute pancreatitis in our case by history, laboratory exams and imaging studies.

We searched PubMed for the key words: acute abdomen, acute pancreatitis, dengue virus, hemorrhagic pancreatitis and found only fourteen cases of dengue infection complicated with acute pancre-

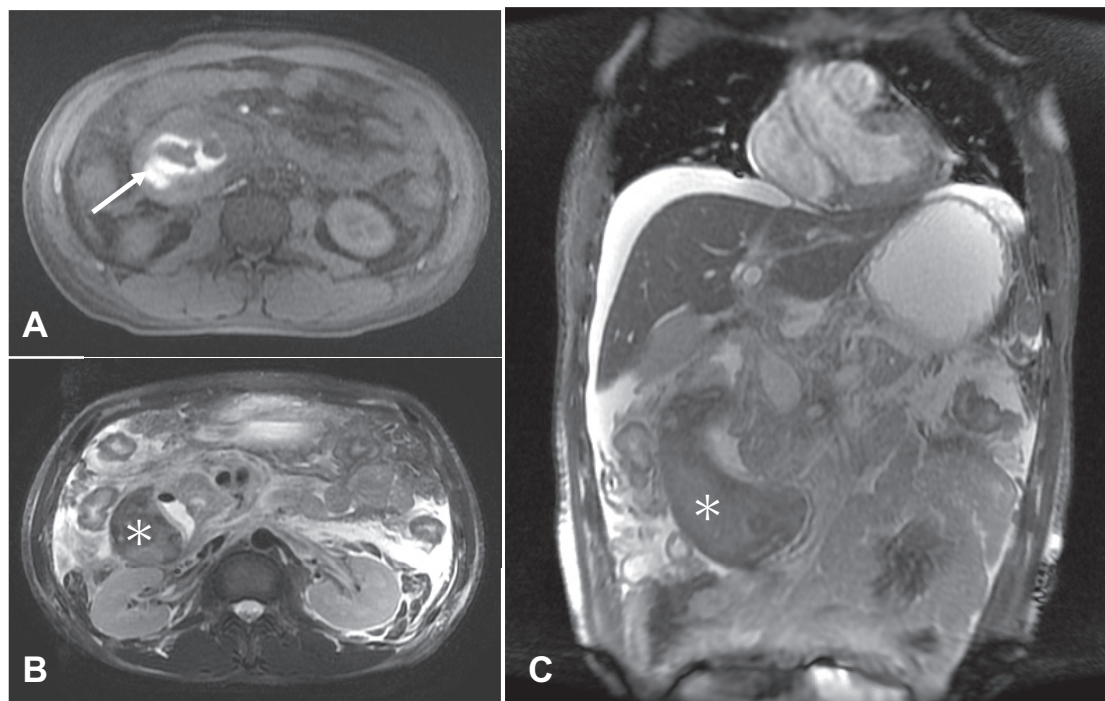


Fig 3—Abdominal MRI on Day 4. A. T1-weighted axial image revealing hyperdensity (white arrow) in the lateral wall of the duodenum. B, C. T2-weighted axial and coronal images revealing a 15 x 5 x 3.5 cm, intramural hematoma (star asterisk) in the lateral wall of the second portion of the duodenum.

atitis reported. The characteristics of these cases, including our case, are shown in Table 1. A unique feature in our case was the presence of an intramural hematoma in the duodenal wall. The hypothesized mechanisms for dengue virus-induced pancreatitis include direct viral infection and systemic hypotension due to dengue hemorrhagic fever. Difficulty in obtaining pancreatic tissue biopsy samples interfered with obtaining a definitive pathogenesis.

The frequency of acute pancreatitis in dengue fever may be underestimated. The diagnosis of acute pancreatitis depends on elevated serum amylase and lipase levels greater than three times the upper limit of normal after excluding gut

perforation and infarction. Serum amylase and lipase levels usually return to normal within seven days. The average time to diagnose acute pancreatitis dengue infection was about seven days (Table 1). Acute pancreatitis may be undiagnosed due to normalization of serum amylase and lipase levels unless complications of acute pancreatitis occur, such as pancreatic ductal disruption, ductal obstruction, or pseudocyst formation, conditions when the serum amylase and lipase can remain elevated for longer than 7 days.

The principal hemorrhagic phenomena of dengue fever include epistaxis, gum bleeding and mucosal bleeding from the gastrointestinal tract. The endoscopic findings of those with upper gastrointesti-

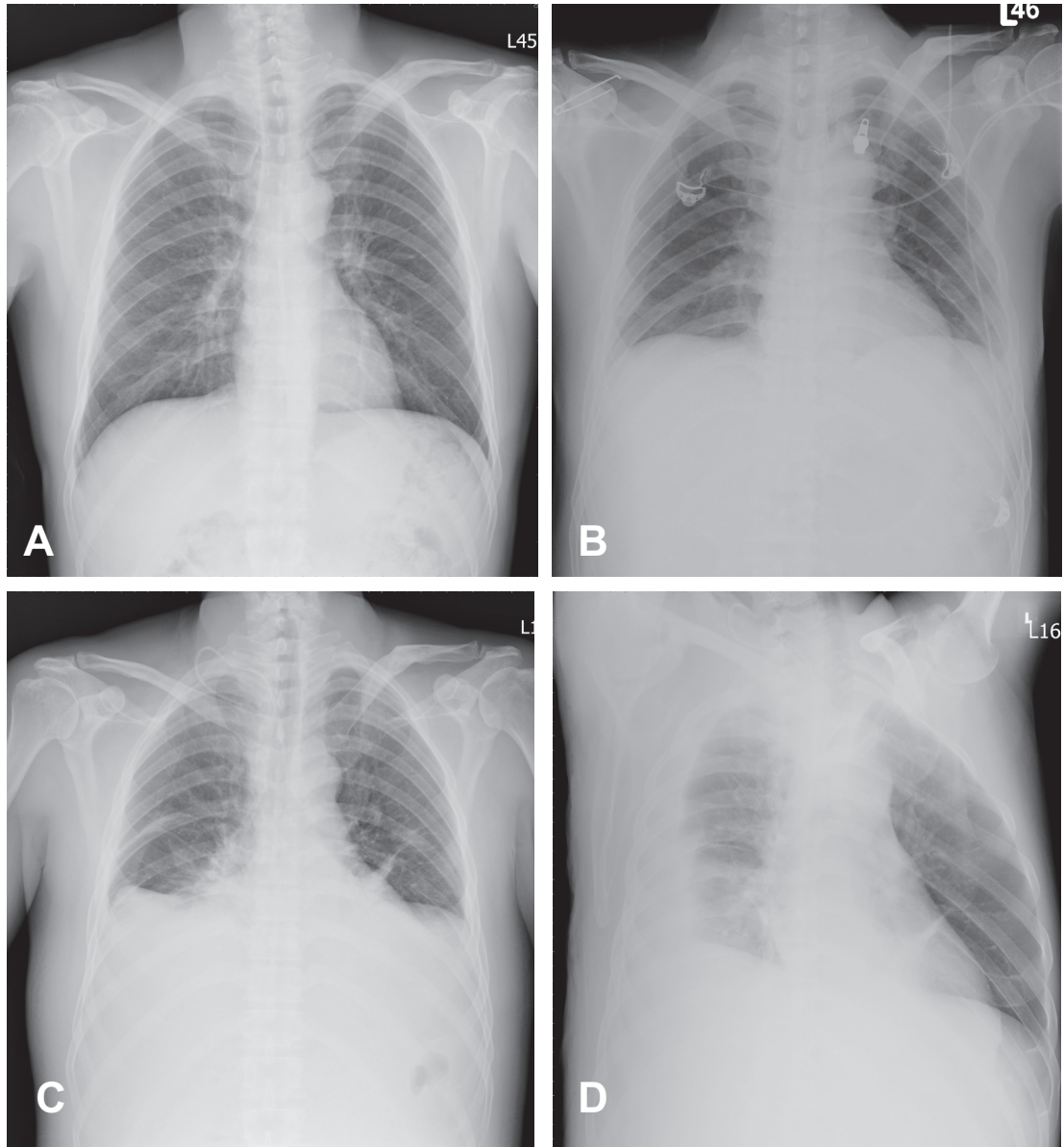


Fig 4—Chest x-ray during hospitalization. Serial (A, B, C) chest x-rays revealing a progressive increase in a right pleural effusion indicating plasma leakage. D. Decubital view revealing pleural effusion.

nal bleeding in dengue hemorrhagic fever include hemorrhagic gastritis, gastric ulcer, duodenal ulcer and esophageal ulcer, among which hemorrhagic gastritis is the most common finding (Perng *et al*, 1989;

Ammori *et al*, 1998; Chiu *et al*, 2005). For patients with dengue fever complicated with upper gastrointestinal bleeding, conservative therapy with blood transfusion is the mainstay of management rather

Table 1
 Characteristics of acute pancreatitis cases complicating dengue fever acute pancreatitis.

Case	Reference	Gender	Age (years)	Country	Comorbidity	Time to diagnosis (days)	DF/DHF/DSS	Complication
1	Jirapinyo <i>et al</i> , 1988	Female	10	Thailand	N/A	N/A	N/A	Liver failure
2,3	Méndez and González, 2006	One female; one male	<13	Colombia	N/A	N/A	DSS	N/A
4	Jusuf <i>et al</i> , 1998	Female	25	Indonesia	Nil	5	DHF, grade II	Hyperglycemia
5-7	Lee <i>et al</i> , 2002	N/A	N/A	Taiwan	N/A	N/A	N/A	One death
8	Chen <i>et al</i> , 2004	Female	66	Taiwan	Diabetes mellitus	16	DHF, grade II	Nil
9	Derycke <i>et al</i> , 2005	Male	29	New Caledonia	Nil	1	DF	Nil
10-12	Shamim, 2010	N/A	N/A	Pakistan	N/A	N/A	DSS	ARDS
13	Wijekoon and Wijekoon, 2010	Male	47	Sri Lanka	Nil	7	DSS	Nil
14	Fontal and Henao-Martinez, 2011	Male	27	Colombia	Diabetes mellitus, ESRD on hemodialysis	8	DHF, grade II	DIC
15	Present case	Male	47	Taiwan	HBV carrier, diabetes mellitus	6	DHF, grade II	Peripancreatic abscess Intramural hematoma of duodenal wall

DF, dengue fever; DHF, dengue hemorrhagic fever; DSS, dengue shock syndrome; N/A, not available; HBV, hepatitis B virus; DIC, disseminated intravascular coagulation; ARDS, adult respiratory distress syndrome.

than endoscopic injection. Those who are treated with endoscopic injection may require more transfusions with packed red blood cells (Chiu *et al*, 2005).

In non-dengue infected patients, the hemorrhagic complications of acute pancreatitis may be attributed to gastrointestinal bleeding or erosion of the vessel with or without a pseudoaneurysm caused by pancreatic necrosis or severe inflammation (Lin *et al*, 2002; Flati *et al*, 2003). Fifty-two to 68% of patients with acute pancreatitis may have an acute gastrointestinal mucosal lesion (AGML) (Chen *et al*, 2007). Common endoscopic findings in these patients include esophageal ulcers, gastric ulcers and duodenal ulcers. Most duodenal ulcers are in the duodenal bulb. Acute pancreatitis with submucosal hemorrhage in the descending portion of the duodenum has been reported (Alexander *et al*, 2008). The mechanism whereby an intramural hematoma of the duodenum develops in acute pancreatitis may be erosion of vessels caused by severe inflammation or necrosis. We postulate the rate of hemorrhagic complications due to acute pancreatitis in dengue infected patients is higher than those in non-dengue infected patients due to bleeding tendency in dengue infection.

Therapy for acute pancreatitis in dengue infection patient is not different from those without dengue infection. However, physicians should be alert to this complication in dengue fever because the diagnosis is probably under-recognized. It is especially important to monitor fluid status and replace fluid deficiency timely because of fluid sequestration in the third space caused by pancreatitis and plasma leakage caused by DHF.

In conclusion, acute pancreatitis is probably underestimated in dengue fever

due to delayed diagnosis with consequent normalization of serum amylase and lipase levels. However, those who present with acute pancreatitis may be at elevated risk for hypovolemia and upper gastrointestinal bleeding. Physicians should be aware of this unusual presentation of dengue fever.

REFERENCES

- Alexander S, Bourke MJ, Co J, Williams SJ, Bailey A. Submucosal hemorrhage in the descending duodenum: endoscopic findings of acute severe pancreatitis. *Endoscopy* 2008; 40 (suppl 2): E188.
- Ammori BJ, Madan M, Alexander DJ. Haemorrhagic complications of pancreatitis: presentation, diagnosis and management. *Ann R Coll Surg Engl* 1998; 80: 316-25.
- Chen TA, Lo GH, Lin CK, *et al*. Acute pancreatitis-associated acute gastrointestinal mucosal lesions: incidence, characteristics, and clinical significance. *J Clin Gastroenterol* 2007; 41: 630-4.
- Chen TC, Perng DS, Tsai JJ, Lu PL, Chen TP. Dengue hemorrhagic fever complicated with acute pancreatitis and seizure. *J Formos Med Assoc* 2004; 103: 865-8.
- Chiu YC, Wu KL, Kuo CH, *et al*. Endoscopic findings and management of dengue patients with upper gastrointestinal bleeding. *Am J Trop Med Hyg* 2005; 73: 441-4.
- Derycke T, Levy P, Genelle B, Ruzsniowski P, Merzeau C. Acute pancreatitis secondary to dengue. *Gastroenterol Clin Biol* 2005; 29: 85-6.
- Flati G, Andren-Sandberg A, La Pinta M, Porowska B, Carboni M. Potentially fatal bleeding in acute pancreatitis: pathophysiology, prevention, and treatment. *Pancreas* 2003; 26: 8-14.
- Fontal GR, Henao-Martinez AF. Dengue hemorrhagic fever complicated by pancreatitis. *Braz J Infect Dis* 2011; 15: 490-2.
- Gulati S, Maheshwari A. Atypical manifesta-

- tions of dengue. *Trop Med Int Health* 2007; 12: 1087-95.
- Jirapinyo P, Treetrakarn A, Vajaradul C, Suvatte V. Dengue hemorrhagic fever: a case report with acute hepatic failure, protracted hypocalcemia, hyperamylasemia and an enlargement of pancreas. *J Med Assoc Thai* 1988; 71: 528-32.
- Jusuf H, Sudjana P, Djumhana A, Abdurachman SA. DHF with complication of acute pancreatitis related hyperglycemia: a case report. *Southeast Asian J Trop Med Public Health* 1998; 29: 367-9.
- Lee IK, Khor BS, Kee KM, Yang KD, Liu JW. Hyperlipasemia/pancreatitis in adults with dengue hemorrhagic fever. *Pancreas* 2007; 35: 381-2.
- Lin CK, Wang ZS, Lai KH, Lo GH, Hsu PI. Gastrointestinal mucosal lesions in patients with acute pancreatitis. *Zhonghua Yi Xue Za Zhi (Taipei)* 2002; 65: 275-8.
- Mendez A, Gonzalez G. Abnormal clinical manifestations of dengue hemorrhagic fever in children. *Biomedica* 2006; 26: 61-70.
- Perng DS, Jan CM, Wang WM, et al. Gastroduodenoscopic findings and clinical analysis in patients with dengue fever. *Gaoxiong Yi Xue Ke Xue Za Zhi* 1989; 5: 35-41.
- Shamim M. Frequency, pattern and management of acute abdomen in dengue fever in Karachi, Pakistan. *Asian J Surg* 2010; 33: 107-13.
- Wijekoon CN, Wijekoon PW. Dengue hemorrhagic fever presenting with acute pancreatitis. *Southeast Asian J Trop Med Public Health* 2010; 41: 864-6.