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CASE REPORT

SEVERE DENGUE COMPLICATED BY ACUTE PANCREATITIS

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ABSTRACT

Dengue is a mosquito borne viral hemorrhagic fever which is endemic in the tropical countries and adjacent subtropics. Severe dengue is of two types, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), both of which are life-threatening. In the medical literature, a large number of atypical presentations of dengue fever have been documented till now. However, we are reporting a rare and deadly complication of dengue fever in the form of acute pancreatitis. A 16 year old female had presented with severe dengue with shock and acute pain in abdomen because of pancreatitis. The physiopathogenesis of acute pancreatitis in dengue has not been worked out yet, but there are various possible mechanisms which have been postulated. The need of the hour is to know in depth the pathogenesis of acute pancreatitis in severe dengue, so that specific management strategies can be devised for this critical complication.

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INTRODUCTION

Dengue is a viral hemorrhagic fever which is endemic in the tropics and adjacent subtropics (Tantawichien, 2012). This mosquito-borne viral infection has humans and monkeys as the host reservoirs (Weaver, 2005). We can trace back the history of dengue compatible symptoms to the people of Chin Dynasty, which existed during 265 – 420 AD (Gubler, 1998). Today the global incidence of this deadly disease has been estimated to be greater than 200 million per year. Around 500 thousand episodes of severe form of dengue and over 20 thousand deaths related to dengue are known to occur annually (Murray *et al*., 2013). The severe forms of dengue are the dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) (Maria G. Guzman *et al*., 2013). It manifests in a deadly manner as fluid accumulation, plasma leakage, respiratory distress, severe hemorrhage and/or multi-organ involvement (Jain *et al*., 2014). The common complications of these severe forms of dengue are encephalitis, acute liver and renal failure, myocarditis, Guillain-Barre syndrome, hematophagocytic syndrome and systemic lupus erythematosus (Gupta *et al*., 2012).

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Acute pancreatitis is an extremely rare complication of Dengue fever. We report a case of acute pancreatitis complicating severe dengue.

Case Report

A 16 year old female presented in emergency department department of Capital Development Authority (CDA) Hospital with high grade fever, severe retro-orbital pain, myalgia and skin rash for last 3 days. Next day of hospital admission, she developed epigastric pain which was severe in intensity, localized to the mid upper abdomen, radiating to the back of her chest and was associated with recurrent nonbillous vomiting. She was irritable and unable to sleep. Her past medical, surgical, family, socioeconomic, menstrual and allergic histories were unremarkable.

On examination, she was found to have cold extremities, tachycardia (pulse = 110/minute) and hypotension (blood pressure = 100/60 mm Hg). Her temperature was recorded as 104˚F, respiratory rate was 20/minute and her oxygen saturation was 97%. Epigastric tenderness and guarding was present along with petechiae on arms and legs. Also, there was no neurological deficit in this patient. A series of laboratory studies revealed leucopenia, thrombocytopenia and proteinuria.

Blood picture showed hemoglobin 12 gm/dl, total leukocyte count 1200/cmm, lymphocytes 40%, polymorphs 60%, hematocrit 39%, platelet count 90000/cmm, Erythrocyte sedimentation rate (ESR) 15. The biochemical parameters demonstrated elevation of liver enzymes alanine transaminase (ALT) 80 U/L, aspartate transaminase (AST) 47 U/L. Urine examination showed proteinuria. Blood chemistry revealed serum lipase 600 U/L (Ref. range 114-286U/L), serum amylase 800U/L (Ref. range 25-115U/L), serum calcium 7.5 mg/dl (Ref. range 8-10.5mg/dl), Activated partial thromboplastin (APTT) 34 seconds (Ref. range 33 Seconds) and Prothombin time (PT) 14 seconds (Ref. range 13 Seconds).

Ultrasonography of the abdomen was done which revealed swelling and enlargement of pancreas. Contrast CT scan of abdomen showed pancreatic swelling and irregular pancreatic outline, obliterated peripancreatic fat, retroperitoneal edema and fluid in the lesser sac (Figure 1).

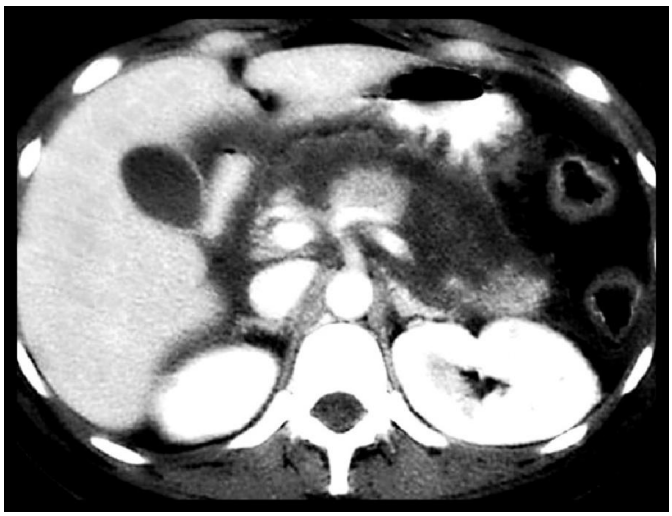

Figure 1. Contrast CT-scan showing pancreatic swelling and other features of acute pancreatitis

NS1Ag was positive which confirmed early diagnosis of dengue fever. Fasting lipid profile and ABGs were normal. Disseminated intravascular coagulation (DIC) profile was also normal. The diagnosis of acute pancreatitis secondary to dengue fever was made. Surgical consultation was taken. It was decided to manage her conservatively. Patient was transferred to intensive care unit (ICU) and managed with broad spectrum antibiotics (Meropenem), IV fluids, analgesics (Paracetamol), proton pump inhibitors and parenteral nutrition. Blood picture and blood chemistry were tested on a daily basis. On the 8th day of admission, her investigations revealed hemoglobin 12 gm%, TLC 3500/cmm, lymphocytes 30%, platelet count 135000/cmm, ESR 15, serum amylase 300U/L, serum lipase 300 U/L and serology revealed positive IgM antibodies against dengue virus. On the 10th day of admission, all her laboratory profile was normal and she was discharged in a stable condition. She was completely fine on follow up.

DISCUSSION

Dengue virus is a single-stranded RNA virus (Xu *et al*., 2005). It belongs to the family Flaviviridae along with the other deadly viruses like Yellow fever virus and Tick Borne Encephalitis viruses (Leyssen *et al*., 2000). It is transmitted by the vector Aedes aegypti (Scott and Morrison, 2010). Dengue virus has four serotypes: DENV-1, DENV-2, DENV-3 and DENV4 (Shu *et al*., 2004). The clinical spectrum of dengue virus infection varies from an asymptomatic seroconversion to a symptomatic disease which in turn ranges from a minor flu-like illness to a critical and fatal disease (Jain *et al*., 2014). Dengue Fever can be divided clinically into three phases: a febrile phase, a critical phase, and a recovery phase (Rajapakse *et al*., 2012). After 4-5 days of febrile phase, the critical phase of severe dengue is preceded by the warning signs (Yacoub and Wills, 2014). There occurs tachycardia, metabolic acidosis, peripheral vasoconstriction and narrowed pulse pressure (Handbook for clinical management of dengue, 2012). During the critical phase, the patient's capillary permeability increases severely and leakage of plasma takes place. As a result, there occurs severe hemorrhage (Rajapakse *et al*., 2012). The resulting profound shock along with thrombocytopenia, acidosis and hypoxia, can cause disseminated intravascular coagulation and multi-organ impairment (Lum *et al*., 2002). Our patient had severe dengue with cold extremities, tachycardia and decreased systolic pressure on presentation. Leucopenia, low platelet counts and a rising hematocrit due to the leakage of plasma usually highlights the critical phase of dengue (Handbook for clinical management of dengue, 2012). On presentation, our patient had leucopenia, thrombocytopenia and proteinuria. The proteinuria may be explained by the altered filtration of the glycocalyx since dengue virus and the NS1 attach to heparan sulphate, a part of the glycocalyx (Vasanwala *et al*., 2014). The atypical presentations of Dengue Fever which have been documented in the literature are mainly those related to the nervous system, cardiovascular system and the liver. The neurological manifestations include reduced consciousness, convulsions, encephalopathy, neuritis, Guillain Barre Syndrome, seizures, myelitis, acute viral myositis, mononeuropathies and hypokalemic paralysis (Solomon *et al*., 2000; Verma *et al*., 2014). In heart, the atypical presentations reported are myocarditis, bradycardia, ventricular arrhythmia or even transient atrioventricular block. The severe myocardial cell damage may lead to cardiogenic shock and/or acute pulmonary edema (Ing-Kit Lee *et al*., 2010). The liver is involved as acute liver failure, coagulopathies and hepatomegaly (Trung *et al*., 2010). The other atypical cases documented with respect to the dengue fever are uveitis, SLE (systemic lupus erythematosus), acute kidney injury, hematophagocytic syndrome, Kawasaki disease and acute inflammatory colitis (Jain *et al*., 2014). Till now, only a few case reports have been documented with dengue fever complicated with acute pancreatitis from across the globe.

Our patient also was diagnosed with severe dengue complicated by acute pancreatitis which was demonstrated by raised serum amylase and lipase, ultrasonographic (USG) and Computerized Tomography (CT) scan findings. Although, increased serum lipase and enlargement of pancreas have been known to occur in Dengue Fever, but acute pancreatitis is a rare and atypical presentation (Jusuf *et al*., 1998; Chen *et al*., 2004; Fontal *et al*., 2011; Lee *et al*., 2007). Few isolated cases (and some case series) have been described in Thailand, Indonesia, Taiwan, Noumea (New Caledonia), Colombia and India

(Wijekoon and Wijekoon, 2010). The exact mechanism of the involvement of pancreas in dengue is still unknown. It can be as a result of direct viral invasion of pancreas leading to its inflammation and destruction of its acinar cells or as an autoimmune response to the islet cells of pancreas and the subsequent development of edema of hepatopancreatic ampulla causing obstruction to drainage of the pancreatic enzymes. It may be simply due to pancreatic damage as a result of shock in severe forms of dengue (Wijekoon and Wijekoon 2010; Karoli *et al*., 2012).

Our patient had thrombocytopenia (<90,000/cmm) which is the high risk condition for bleeding in patients with severe dengue (Makroo *et al*., 2007). However, bleeding was not significant and she had just petechiae in her arms and legs. Ultrasonography (USG) and CT scan are quite helpful in the diagnosis and management strategy formation for pancreatitis (Feng *et al*., 2014). While the ultrasonographic findings revealed swelling and enlargement of pancreas, contrast CT scan of abdomen also showed pancreatic swelling as well as irregular pancreatic outline, obliterated peripancreatic fat, retroperitoneal edema and fluid in the lesser sac which were consistent with the findings of acute pancreatitis as documented in literature (Finstad *et al*., 2005; Busireddy *et al*., 2014). Also, the NS1 Antigen was found positive in our patient which is a usual serum test for dengue fever (Hermann *et al*., 2014).

After taking surgical consultation, we decided to manage the patient conservatively. Compared to early surgical intervention, acute pancreatitis has a better outcome when conservative management is considered (Werner *et al*., 2005). Patient was transferred to ICU and managed with broad spectrum antibiotics (Meropenem), intravenous fluids, analgesics (Paracetamol), proton pump inhibitors and parenteral nutrition. Laboratory profile started to normalize within 10 days and she was discharged. The patient's follow up results were normal as well.

Conclusion

Severe dengue is an extremely critical illness. Although, a lot of atypical presentations of Dengue Fever have been documented in medical literature, but acute pancreatitis continues to remain a rare and a deadly complication of Dengue Fever. However, if immediate attention is taken in diagnosis of the complications by imaging and laboratory tests, there are chances that the patient can be saved from damage by its fatal complications. The need of the hour is to know in depth the pathogenesis of acute pancreatitis in severe dengue, so that specific management strategies can be devised for this critical complication.

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