

Acute abdominal pain in dengue haemorrhagic fever: A study in Sri Lanka, 2009

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Abstract

We attempted to unravel the association of acute severe abdominal pain in 14 patients with dengue haemorrhagic fever during the epidemic in 2009. All had secondary dengue infection. The findings were severe thrombocytopenia (the mean platelet count $18 \times 10^9/l$, range 12–48), high liver enzymes (mean ALT 374U/l, range 82–2692), ascites in all cases, acute hepatitis in 11 cases (79%), acalculous cholecystitis in five cases (42%), and renal involvement in three cases (25%). All had normal serum amylase level and normal-looking pancreas in ultrasound scan. The abdominal pain in dengue infection warrants investigation to find a specific cause.

Keywords: Dengue haemorrhagic fever; secondary infection; abdominal pain; severe thrombocytopenia; Sri Lanka.

Introduction

Dengue, an endemic infection in the tropical and subtropical regions of the world, is widely distributed in many countries in Asia, including Sri Lanka.^[1,2] Over the past two decades, changing epidemiology with regular epidemics of dengue fever (DF) and dengue haemorrhagic fever (DHF) have been reported in Sri Lanka.^[2,3] All four serotypes, DENV-1 to DENV-4, are in circulation and are responsible for the changing face of epidemics.^[2,3]

The protean character of dengue fever ranges from mild febrile illness to profound shock; thus, it remains a challenge for saving lives. The common symptoms in dengue infection are fever, malaise, headache, musculoskeletal pain, nausea and vomiting. Nonetheless, a significant number of patients develop one or more complications that include bleeding, dengue shock syndrome (DSS), acute renal failure and seizures.^[4,5] Furthermore, other complications such as acute myocarditis,^[6,7] effusions, acute hepatic

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failure^[8] and dengue encephalitis have also been reported.^[9,10] The abdominal pain in dengue infection is a dilemma which could be either specific or non-specific. Of the specific cases, surgical emergencies like acute pancreatitis,^[11] acute acalculous cholecystitis^[12] and gastrointestinal bleeding^[13] are found in literature. In addition, there are reports of dengue enteritis mimicking appendicitis.^[14,15] However, in many cases, even in severe abdominal pain, the causes could not be found.

In mid-2009, Sri Lanka faced a severe epidemic of dengue infection with the highest case-load and deaths. In the midst of this epidemic, we observed frequent occurrence of abdominal pain in patients presenting to the Teaching Hospital, Peradeniya (THP), in the Central Province of the country. We investigated 14 such patients with dengue haemorrhagic fever, who presented with acute severe abdominal pain.

Materials and methods

We possess rich clinical records of all dengue infections admitted to the THP during May–August 2009. Of the total 337 patients with diagnosed dengue infections, those with severe abdominal pain were included in the analysis. In each patient, details such as symptoms, signs and medical management were recorded. All of them were managed according to the routine protocol of the Unit. Investigations such as regular measurement of full blood counts, blood urea, serum creatinine level, aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum amylase, blood culture, ascetic fluid culture, ECG, chest radiograph and ultrasound scan of the abdomen were done to detect complications. The ultrasound scan was

performed meticulously by the same radiologist to avoid personal bias.

Confirmation of the diagnosis was made by doing dengue-specific IgM and haemagglutination inhibiting (HI) antibodies test, and in selected cases, by viral identification with reverse transcriptase polymerase chain reaction agarose gel electrophoresis (RT-PCR-AGE) at Medical Research Institute, Colombo, Sri Lanka. The RT-PCR-AGE was done for patients who presented within four days of onset of fever. Paired sera were tested by the HIA and for IgM antibody using IgM antibody capture ELISA. If only dengue virus-specific IgM antibodies were detectable in the test sample, the patient was considered to have primary dengue infection, whereas the presence of both IgM and IgG or HIA titre above 1:2560, or both together, was considered as secondary dengue infection.

Results

The analysis included 14 patients with acute abdominal pain severe enough to keep them only on intravenous fluids until they were able to tolerate oral fluids. The series comprised males and females in equal numbers, with a median age of 28 years (range 12–47 years). All qualified the WHO criteria of DHF and, of them, four were included in the category of DSS.

Apart from fever, headache and bleeding tendency, many patients had vomiting (Table 1). The abdominal pain was more or less generalized in four patients and the others had pain located mainly in the epigastric region. The mean date of the onset of the abdominal pain was four days, with a range of two to five days. The mean duration of the abdominal pain was three days ranging from one to five days. Serologically, all had secondary dengue infection.



Table 1: Other clinical features of 14 patients with abdominal pain

Clinical feature	No (%)
Fever	14(100)
Headache	13 (93)
Arthralgia	8 (57)
Myalgia	13 (93)
Vomiting	11 (79)
Bleeding tendency	14 (100)
Skin rash	2 (14)

A significant thrombocytopenia was the hallmark in the series with spontaneous bleeding tendency (Table 2). Thirteen patients had elevated levels of AST and all 14 had elevated ALT. Interestingly, the serum amylase levels were normal in all patients (Table 2).

Table 2: Investigation results of 14 patients

Investigation	Mean	Range
Platelet count (x10 ⁹ /l)	18	12–48
SGPT (IU/l)	374	82–2692
SGOT (IU/l)	418	163–2382
Serum amylase (IU/l)	57	34–97

The ultrasound scan of the abdomen showed ascitis, hepatomegaly, splenomegaly, acute liver parenchymal disease, acute acalculous cholecystitis with pericholecystic fluid collection, gall bladder distension and wall oedema and renal paranchymal involvement (Table 3). The renal involvements were acute renal parenchymal changes, pyelonephritis and perinephric fluid collection. Extra attention was paid to the pancreas, but all had normal-looking pancreas.

Table 3: Ultrasound scans findings of 14 patients

Finding	No (%)
Ascitis	14 (100)
Hepatomegaly	12 (86)
Hepatitis	11 (79)
Splenomegaly	3 (25)
Acalculous cholecystitis	5 (42)
Renal paranchymal changes	3 (25)
Pancreatitis	Nil

Blood cultures and ascetic fluid cultures were negative and a few patients had ECG changes. The RT-PCR-AGE gave negative results of a limited number of cases where it was done. All these patients were managed with antibiotics and supportive care and they recovered completely.

Discussion

We found that abdominal pain was non-specific in these cases, except in five cases where it could be attributed to acalculous cholecystitis. The cardinal finding was the presence of ascites and none had any form of pancreatitis. The pathogenesis of abdominal pain in dengue fever is not clearly understood; however, lymphoid follicular hyperplasia seems to play an important role and plasma leakage through damaged capillary endothelium had also been proposed.^[14,15] It could be the possible explanation for subserosal fluid collection and thickened gall bladder associated with dengue fever. The specific organ involvement, like hepatitis, acalculous cholecystitis, pancreatitis, appendicitis and peptic ulcer disease, could also produce abdominal pain.^[15,16]



Acute liver involvement with hepatitis and hepatomegaly was detected in more than 78% of the current case series. They all had elevated liver enzymes and, in some cases, the rise was alarmingly high. However, none of these patients went into acute liver failure. The rise of liver enzyme in DHF due to acute liver parenchymal disease had been discussed.^[17] Acute cholecystitis is an increasingly reported manifestation in DHF. The pathogenesis of acute cholecystitis in DHF is not fully understood, but may result from localized microangiopathy in the gall bladder wall.^[18] The role of secondary bacterial infection causing acute cholecystitis is not clear, but administration of broad-spectrum antibiotics helped our patients.

Even though pancreatitis has been reported in dengue haemorrhagic fever,^[16] none of these 14 patients had any evidence of pancreatitis such as elevation of serum amylase or ultrasound scan findings. But a pregnant mother, who succumbed to dengue infection at the beginning of the epidemic at THP showed florid pancreatitis at necropsy (unpublished

data). The three patients in the series who had renal involvement showed acute renal parenchymal disease and perinephric fluid collection in the ultrasound examination. Of them, the diagnosis of pyelonephritis was made in one patient who had pus cells and white cell casts in the urine full report. This patient was treated with antibiotics considering secondary bacterial infection, and the patient recovered. Furthermore, acute renal failure associated with DHF has been reported and one explanation given is the myoglobinuria in DHF causing glomerular damage.^[19,20]

All cases in this series had a severe form of the disease (DHF and DSS) caused by secondary exposure to dengue virus. Identification of the causative serotype was not possible in these cases, but DENV-1 was detected in five other patients during the current epidemic. Broad-spectrum antibiotics were given to all these patients as a desperate measure to prevent fatalities.

In conclusion, the abdominal pain in dengue infection warrants investigation to find out the specific cause.

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