Research Article

Study of acute acalculous cholecystitis as an atypical manifestation in dengue fever

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Abstract

Background: Dengue is a rapidly emerging global health problem. It is an arboviral disease caused by four antigenically distinct dengue viruses. Dengue epidemic occurs annually with major outbreaks in various parts of the world. The disease has variable presentation. Atypical manifestations have increased as well, which are missed owing to lack of awareness. Among these, dengue fever (DF) with acute acalculous cholecystitis is also reported. A few case reports have also shown complications due to acute acalculous cholecystitis in dengue.

Objective: To study the incidence and outcome of acute acalculous cholecystitis in patients with DF.

Materials and Methods: This study was a prospective, hospital-based observational study conducted from September 2012 to October 2014. After satisfying the World Health Organization criteria, the diagnosis of DF was confirmed in patients on clinical presentation and by a positive immunoglobulin M antibody test result for a late-phase or convalescent-phase blood specimen. Abdominal ultrasound was performed to confirm the diagnosis of acute acalculous cholecystitis. A statistical analysis of the findings was carried out.

Results: Laboratory examination confirmed the diagnosis of dengue in 120 patients. All the patients were within the age group of 18–60 years. The most common atypical manifestation was hepatitis ($n = 52$; 43.33%), followed by acute acalculous cholecystitis ($n = 45$; 37.5%). Clinical manifestations of acalculous cholecystitis were abdominal pain, vomiting, and dyspepsia. Fever was present in 44 patients (97.77%). Liver function tests were deranged in all the cases. The study had a survival rate of 100%, without any complication.

Conclusion: Acute acalculous cholecystitis in dengue is not a very uncommon finding. Early diagnosis and appropriate treatment have very good prognosis.

KEY WORDS: Dengue fever, atypical manifestations, acute acalculous cholecystitis

Introduction

The first probable case of dengue fever (DF) was recorded during the Jin Dynasty (265–420 AD) in China. The global prevalence of dengue has grown rapidly in recent decades.

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A recent estimate indicates 390 million dengue infections per year.[1] It is estimated that 3900 million people, in 128 countries, are at risk of infection with dengue viruses.[2] In India, dengue is widespread and endemic in most major cities. The mortality rate has reduced although the number of dengue cases has shown a steady rise with every passing year. The overall mortality rate was 1.2% in 2007, which reduced to 0.25% in 2013.[3]

Dengue, an arboviral disease, is caused by a *Flavivirus* with four distinct serotypes (DV-1, DV-2, DV-3, and DV-4). There are several possible dengue vectors. The field seclusion of viruses and epidemiological proof clearly shows that *Aedes aegypti* and *Aedes albopictus* are responsible for the majority of dengue transmission.[4] The incubation period is

3–14 days (average 4–7 days). Clinical presentation of DF varies with a wide spectrum of signs and symptoms. Infection can be asymptomatic or cause a range of severity from mild DF to dengue hemorrhagic fever, which can then progress to dengue shock syndrome and death.[5] Typically, DF presents as a self-limiting disease characterized by fever associated with symptoms such as headache, nausea, vomiting, arthralgia, myalgia, and/or rash. However, during the course of the disease, some patients develop severe manifestations related to increased vascular permeability and plasma leakage, which can lead to death.[6] According to the World Health Organization (WHO), minimal criteria for the diagnosis of DHF are fever, hemorrhagic manifestations (e.g., hemoconcentration, thrombocytopenia, and positive tourniquet test), and signs of circulatory failure due to increased vascular permeability.[7] In addition, approximately one-third of patients develop conjunctival injection. Optic neuropathy has been reported and occasionally results in permanent and significant visual impairment.[8] Approximately 97% of patients with DHF develop pharyngeal injection. Findings of dengue shock syndrome include hypotension, bradycardia (paradoxical) or tachycardia associated with hypovolemic shock, hepatomegaly, hypothermia, narrow pulse pressure (<20 mm Hg), and signs of decreased peripheral perfusion. With rising disease burden, atypical manifestations have increased, which are missed most often owing to lack of awareness. The objective of the study was to look for the atypical manifestations of DF, with special emphasis to study the incidence and outcome of acute acalculous cholecystitis in patients with DF.

Materials and Methods

This study was a prospective, hospital-based observational study conducted at Rama Medical College and Hospital for a period of 2 years from September 2012 to October 2014. All probable dengue cases were investigated initially. After satisfying the WHO criteria and ruling out other causes of fever, the diagnosis of DF was confirmed in 120 patients on clinical presentation and by a positive immunoglobulin M antibody test result for a late-phase or convalescent-phase blood specimen. A detailed clinical history, physical examination, and baseline investigations were carried out, and patients were followed up till discharge. Real-time abdominal ultrasound was performed only in patients with confirmed laboratory diagnosis of dengue. The diagnosis of acute acalculous cholecystitis was made according to the clinical features and sonographic findings of a thickened gall bladder wall (>3.5 mm) and a positive Murphy's sign.[9] Non-survival was taken as poor outcome, and survival was taken as good outcome. A statistical analysis of the findings was carried out.

Results

Out of the 450 patients admitted with clinical suspicion of dengue in Rama Medical College and Hospital during the months of September 2012 to October 2014, 120 patients had confirmed laboratory diagnosis of dengue. Among these 120 patients, 76 were male and 44 were female. In these patients, apart from the common clinical features such as fever (99.16%), headache (65%), myalgia (81.66%), and rashes (66.66%), several atypical manifestations were also found [Table 1]. Among these atypical manifestations, the most common was hepatitis (*n* = 52; 43.33%), followed by acalculous cholecystitis (*n* = 45; 37.5%), diarrhea (*n* = 14; 11.66%), and renal failure (*n* = 8; 6.66%). One patient developed pancreatitis, and another one disseminated intravascular coagulopathy.

Abdominal ultrasonography was performed in all the confirmed cases of dengue (*n* = 120). Acute acalculous cholecystitis was diagnosed in 45 patients (37.5%) [Table 2]. The most common finding on ultrasonography was hepatomegaly (*n* = 49; 40.83%). Clinical manifestations of patients with acalculous cholecystitis were recorded [Table 3]. All the patients (100%) had complaints of abdominal pain, vomiting, and dyspepsia. Fever was present in 44 patients (97.77%). Myalgia, headache, and arthralgia were present in 66.66%, 62.22%, and 64.44% of patients, respectively.

Table 1: Atypical manifestations of dengue fever

Clinical manifestation	Number (*n* = 120)	Percentage
Hepatitis	52	43.33
Acalculous cholecystitis	45	37.5
Diarrhea	14	11.66
Acute renal failure	08	6.66
Acute pancreatitis	01	0.83
Disseminated intravascular coagulopathy	01	0.83

Table 2: Abdominal ultrasonographic findings in confirmed dengue cases

Ultrasonographic finding	Number	Percentage
Acute acalculous cholecystitis	45	37.5
Hepatomegaly	49	40.83
Splenomegaly	08	6.66
Ascites	12	10
Pleural effusion	02	1.66

Table 3: Clinical manifestations of patients with acalculous cholecystitis

Clinical manifestation	Number (*n* = 45)	Percentage
Fever	44	97.77
Myalgia	30	66.66
Headache	28	62.22
Arthralgia	29	64.44
Rashes	25	55.55
Abdominal pain	45	100
Vomiting	45	100
Dyspepsia	45	100

Table 4: Mean value of blood investigation of patients with acalculous cholecystitis

Investigation	Result (mean + SD)
Mean Hb (g%)	10.6 + 1.32
Mean platelet count (cells/mm^3)	30,133 + 15,742
Mean PCV (%)	24.18 + 4.72
Mean ALT (IU/L)	158.10 + 50
Mean AST (IU/L)	142.2 + 38.76
Mean alkaline phosphatase (IU/L)	124.4 + 32.89

ALT, alanine aminotransferase; AST, aspartate aminotransferase; Hb, hemoglobin; PCV, packed cell volume; SD, standard deviation

Blood test of patients with acalculous cholecystitis showed anemia, with a mean hemoglobin level (g%) of 10.6 ± 1.32. Platelet count was reduced in all the cases of acalculous cholecystitis, with a mean count of 30,133 + 15,742 cells/mm^3. Altered liver function tests were detected in 100% of the acalculous cholecystitis cases [Table 4]. There was only one case of mortality in the present study, the patient with disseminated intravascular coagulopathy with renal failure. In all the cases, liver function tests became normal with the recovery of the patients.

Discussion

Classically, dengue infection presents with typical features such as fever, myalgia, headache, and rashes. However, atypical features have also been frequently reported. Among the atypical features, hepatitis (*n* = 52; 43.33%) was the most common, followed by acalculous cholecystitis (*n* = 45; 37.5%). Another study by Gulati and Maheshwari[10] also reported hepatitis, fulminant hepatic failure, and acalculous cholecystitis, among the gastrointestinal manifestations in dengue. Pathogenesis of acute acalculous cholecystitis is unclear. Some studies have shown cholestasis and increased bile viscosity, infection, as the probable causes.[11] However, the pathophysiology in the development of acute acalculous cholecystitis from infection with dengue virus is unknown. The main pathophysiologic change in DF is increased vascular permeability, causing plasma leakage and serous effusion with high protein content (mostly albumin), which then induces thickening of the gallbladder wall.[12] Manifestations such as abdominal pain, dyspepsia, and vomiting increase the difficulty in distinguishing dengue virus from bacterial infections. In the present study, all the patients (100%) with acalculous cholecystitis complained of abdominal pain, vomiting, and dyspepsia. Fever was present in 44 patients (97.77%). Myalgia, headache, and arthralgia were present in 66.66%, 62.22%, and 64.44% of patients, respectively. According to various studies, the cause of abdominal pain in DF is hepatitis, pancreatitis, or acalculous cholecystitis.[13] Patients who presented with fever, a thickened gallbladder wall, and a positive Murphy's sign on abdominal sonography were diagnosed as having acute acalculous cholecystitis. Abdominal sonography performed in dengue cases detected acute acalculous cholecystitis in 45 patients (37.5%). Hepatomegaly, splenomegaly, ascites, and pleural effusion were present in 40.83%, 6.66%, 10%, and 1.66% patients, respectively. A study by Wu et al. showed similar findings, which featured thickened gallbladder wall in 38 patients (59%), ascites in 24 patients (37%), splenomegaly in 22 patients (34%), and pleural effusion in 21 patients (32%).[14] Thrombocytopenia, anemia, and hepatic dysfunction are common features of dengue infections. Mild-to-moderate increases in transaminases are common, whereas jaundice and acute liver failure are generally rare.[15–17] Laboratory findings in patients with acute acalculous cholecystitis in DF showed anemia with mean hemoglobin level (g%) of 10.6 ± 1.32. Platelet count was reduced in all the cases, with a mean count of 30,133 ± 15,742 cells/mm^3. Altered liver function tests were detected in 100% of the patients with acute acalculous cholecystitis. A study by Kuo et al. also demonstrated similar findings, wherein abnormal levels of aspartate aminotransferase, alanine aminotransferase, bilirubin, alkaline phosphatase, and gamma-glutamyl transpeptidase were found in 93.3%, 82.2%, 7.2%, 16.3%, and 83.0% of the patients, respectively.[18] Liver functions returned to baseline with the recovery of the patients.

Conclusion

Over a study period of 2 years study, 120 patients were diagnosed with dengue. Acute acalculous cholecystitis was found in 37.5% cases, which is not an uncommon atypical feature. All these patients had complaints of abdominal pain, vomiting, and dyspepsia with deranged liver enzymes. However, no patient developed any complication due to acalculous cholecystitis. Some studies have shown complications such as perforation of the gall bladder and peritonitis due to acalculous cholecystitis. Hence, prompt diagnosis and surgical intervention, where necessary, may reduce the morbidity. However, larger case studies are needed to justify this recommendation. This study has shown that the prognosis of acute acalculous cholecystitis is essentially good in cases of DF.

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