CASE REPORT

A FATAL CASE OF SPONTANEOUS RUPTURE OF THE SPLEEN DUE TO DENGUE VIRUS INFECTION: CASE REPORT AND REVIEW

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Abstract. Dengue hemorrhagic fever (DHF) is being seen more frequently in adults as a consequence of shifting patterns of infection and immunity and there has been an apparent increase in the complications of dengue infection. Spontaneous splenic ruptures are rare but life-threatening complications of infectious diseases. We describe a fatal case of spontaneous splenic rupture in an adult patient with DHF. A case of spleen rupture may be misdiagnosed as shock syndrome. Physicians should be aware of the possibility of splenic rupture in areas where dengue infection is endemic. Early diagnosis and treatment of splenic rupture should improve clinical outcomes.

INTRODUCTION

Dengue virus infection is a common mosquito-borne disease found in tropic and subtropic regions of the world. It is transmitted to humans by the bite of *Aedes aegypti*, and rarely by *Aedes albopictus*, mosquitoes. Dengue virus infection may be asymptomatic or lead to undifferentiated fever, dengue fever (DF) or dengue hemorrhagic fever (DHF). Dengue more commonly affected children early on but now young adults as well as older people are being infected. The incidence of epidemic and endemic dengue infection has increased substantially, notably in the Americas since 1997, and various epidemics have occurred (Guzman and Kouri, 2003). The increasingly widespread distribution and rising incidence of dengue virus infection is related to the increased distribution of *Aedes aegypti*, and its increase in urban areas of Southeast Asia and due to air travel (Pongsumpun *et al*, 2004). All four dengue serotypes cause DF, characterized by sudden onset fever, headache, retro-orbital pain, general malaise, myalgias, leukopenia with lymphocytosis, thrombocytopenia, and mild elevation of liver enzymes. It may also cause rash, mild hemorrhagic manifestations; and rarely severe hemorrhage leading to shock through blood loss (WHO, 1997). In a small percentage of dengue virus infections, a more severe form of disease, known as DHF, is characterized by acute fever associated with a hemorrhagic diathesis and a tendency to develop dengue shock syndrome (DSS).

DHF is more common in children less than 15 years of age and causes a significant number of deaths (George and Lum, 1997; WHO, 1997). The major pathophysiologic hallmarks that determine disease severity and distinguish DHF from DF are plasma leakage due to an increase in vascular permeability, and

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abnormal homeostasis, including increased capillary fragility, thrombocytopenia, impaired platelet function and disseminated intravascular coagulopathy, contributing to varying degrees of hemorrhagic manifestations (George and Lum, 1997; WHO, 1997). A clinical definition of DHF established by the World Health Organization (WHO) is based on the presence of continuous high fever, hemorrhagic manifestations (including at least a positive tourniquet test), hepatomegaly, thrombocytopenia (platelet count <100,000/mm^3), and hemoconcentration (hematocrit increased by > 20% above baseline value) (WHO,1997). The WHO definition further subdivides DHF into four grades on the basis of the presence of spontaneous bleeding and the presence and severity of shock. Treatment of both classic DF and DHF/DSS is symptomatic and supportive (George and Lum, 1997; WHO, 1997). There has been an apparent increase in the complications of dengue infection seen among adults in our practice, so physicians must be aware that dengue infection in adults with unusual complications may occur (Pancharoen *et al*, 2002). We describe a case of spontaneous splenic rupture in a patient with DHF in Thailand.

CASE REPORT

An otherwise healthy 24-year-old man was admitted to a provincial hospital in October 2007 with a one day history of high fever, severe malaise, nausea, vomiting and generalized myalgia. There was no history of abdominal trauma. The patient did not use acetyl salicylic acid or nonsteroidal anti-inflammatory drugs (NSAIDS). On admission, he was noted to have a temperature of 39ºC, a pulse of 84/minute, a blood pressure of 110/80 mmHg and a respiratory rate of 24/minute and injected conjunctivae. The findings on physical examination were otherwise normal. Laboratory investigation revealed a hematocrit of 41%, a white blood cell count of 4.6 x 10^9 /l, predominately neutrophils and a platelet count of 167 x 10^9 /l. He received standard supportive care. On the fifth day of illness, he had clinical and laboratory evidence of DHF with fever lasting 5 days, hepatomegaly, a hematocrit of 50% and a platelet count of 57 x 10^9 /l. A radioimmunochromatographic test for IgM antibodies against dengue was weakly positive and for IgG antibodies was positive. RT-PCR for detection of dengue virus RNA was performed on serum samples obtained on day 1 of hospitalization and was positive for dengue virus type 1 RNA. Following intravenous fluid resuscitation, his blood pressure was stable and creatinine was normal. Over the ensuing day, he developed hypovolemic shock that was characterized by severe hypotension (blood pressure 85/54 mmHg), deterioration in consciousness, and severe diffuse abdominal pain. The patient's laboratory values revealed a hematochit of 25%, a white blood cell count of 19.4 x 10^9 /l with 45% polymorphonuclear neutrophils, 31% lymphocytes, 10% monocytes and 14% atypical lymphocytes; and a platelet count of 21 x 10^9 /l. He also had abnormal liver function tests: aspartate aminotransferase of 787 U/l; alanine aminotrasferase of 281 U/l. These were accompanied by a prolonged prothrombin time and a partial thromboplastin time and acute renal failure with a creatinine, of 2.0 mg/dl.

The patient was transferred to the intensive care unit; supportive therapy was immediately administered which included mechanical ventilation, fluid resuscitation with normal saline solution and vasopresser drugs, platelets, packed red blood cells and fresh frozen plasma. The patient was treated empirically for nosocomial bacterial infection with meropenem 3 g/day intravenously. An abdominal paracenthesis revealed unclotted blood. Exploratory laparotomy revealed a massive hemoperitoneum, ruptured spleen, mild hepatomegaly, and normal hollow visceral organs. Splenectomy was performed at which

time spleen rupture was seen measuring 1.5 centimeters in length on the hilar surface; a tearing defect involving the splenic capsule and underlying splenic tissue on the hilar surface was also seen, with no evidence of malignancy or granulomas. Blood cultures were negative. After the operation, the patient later developed multiple organ dysfunction syndrome with severe multifocal bleeding anddied on hospital Day 7. An autopsy was not performed.

DISCUSSION

Often considered more common in children, DHF is now being seen more frequently in adults as a consequence of shifting patterns of infection and immunity (Pancharoen *et al*, 2002; Ooi *et al*, 2006). Although the pathogenesis and pathophysiology of severe dengue infection remains incompletely understood, possible contributory factors to increased disease severity have been described (Halstead, 1982; Green and Rothman, 2006). Age, sex, race, pre-existing co-morbidities, and viral-specific features have been noted to play a role in disease outcomes (Nimannitaya, 1987a; George and Lum, 1997).

The mainstay of treatment remains prompt fluid resuscitation to counteract massive plasma leakage. Timely and effective intravenous crystalloid replacement of plasma losses results in a favorable outcome in most cases (Nhan *et al*, 2001). In its severest form, dengue virus infection is associated with hemorrhagic complications, plasma leakage, shock, liver failure, and disseminated intravascular coagulopathy. Dengue virus infections are rarely fatal in adults, although fatal infections do occur (Nimmannitya, 1987b; Pancharoen *et al*, 2002). Bleeding, one of the major problems encountered in DHF, contributes to worsening morbidity. The pathogenesis of hemorrhage may be multifactorial and include vasculopathy, platelet deficiency and dysfunction, and blood coagulation defects (Halstead, 1982). The most common hemorrhagic manifestations are epistaxis, skin hemorrhages, and gastrointestinal hemorrhages (Pancharoen *et al*, 2002; Kittigul *et al*, 2007). Bleeding can occur in any organ.

Spontaneous splenic ruptures are rare but life-threatening complications of infectious diseases. The typical presentation is acute, but progressive forms are described (Peter and Gooden, 1986; Zingman and Viner, 1993). The spleen, which frequently has congestion, bears subcapsular hematomas in 15% of DHF cases (Bhamarapravati *et al*, 1967). Splenic rupture in patients with hemorrhagic dengue is uncommon but can happen spontaneously or as a result of trauma, which may be minor or unnoticed.

There are only three previously reported cases of spleen rupture in patients with dengue fever: a 35-year-old white man with dengue fever who underwent splenectomy in French Polynesia and had a favorable clinical outcome (Imbert *et al*, 1993); a 23-year-old woman who lived in Venezuela, had severe illness and died after splenectomy with gram-negative sepsis and multiorgan failure (Redondo *et al*, 1997); and a 52-year-old woman with dengue fever who underwent splenectomy in Brazil and had a favorable clinical outcome (Miranda *et al*, 2003).

We presume the splenic rupture in our patient was due to factors, such as the level of severity of DHF/DSS (grade IV) the presence of consumption coagulopathy and severe thrombocytopenia (these factors were the cause of our patient's death). In the first and third cases, the ruptured spleen developed in patients without the classical symptoms of DHF/DSS. Splenectomy is still the treatment of choice for splenic rapture but numerous recent reports have documented favorable outcomes with conservative treatment (Zingman *et al*,1993; Christien *et al*, 2002; Jacob *et al*, 2005; Brichkov *et al,* 2006; Jimnez *et al*, 2007).

A case of spleen rupture may be misdiagnosed as shock syndrome seen in DHF/DSS. Physicians should be aware of the possibility of splenic rupture in areas where dengue infection is endemic. Early diagnosis and treatment are needed to avoid a fatal outcome.

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