Hemorrhagic Dengue with Spontaneous Splenic Rupture: Case Report and Review

Dengue fever is an endemic mosquito-borne viral disease of the tropical and subtropical regions of the world that is transmitted by the bite of *Aedes aegypti* mosquitoes. All four dengue serotypes cause a variety of clinical manifestations such as sudden onset of fever with chills, headache, retro-orbital pain, general malaise, myalgias, arthralgias, cutaneous erythema, early neutropenia with lymphocytosis, thrombocytopenia, and mild elevation of liver enzymes.

A more-severe clinical form of the disease is the dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS), which is characterized by hemoconcentration (hematocrit increased >20%), thrombocytopenia (platelet count, <100,000/mm³), vascular collapse, abdominal pain, and hemorrhagic manifestations. Other manifestations of the disease include circulatory failure, respiratory distress, pleural effusion, and encephalopathy. Laboratory test results reveal severe thrombocytopenia, hemoconcentration, and signs of consumption coagulopathy (e.g., hypofibrinogenemia and prolonged partial thromboplastin time). Treatment for both classic dengue and DHF/DSS is symptomatic and supportive. We describe what we believe is the first case of spontaneous splenic rupture in a patient with dengue hemorrhagic fever in Latin America [1, 2].

A 23-year-old female who had a 5-day history of fever (temperature, 39°C), severe malaise, nausea, vomiting, headache, and generalized myalgias was admitted to the emergency department with abdominal pain and severe thrombocytopenia (platelet count, 33,000/mm³). Two hours later, she developed hypovolemic shock that was characteristic by severe hypotension (blood pressure, 80/40 mm Hg), dehydration, loss of consciousness, and severe diffuse abdominal pain with signs of acute abdomen.

Ectopic pregnancy and dengue hemorrhagic fever were ruled out. An abdominal echosonogram showed intra-abdominal bleeding, and an exploratory laparotomy revealed massive intra-abdominal bleeding (4 L), splenic rupture, peripancreatic edema, and endometriosis. Splenectomy was performed and revealed areas of spleen rupture measuring up to 0.4 cm and multiple parenchymal hematomas with no evidence of malignancy or granulomas (figure 1).

The patient was transferred to the intensive care unit; supportive therapy was immediately administered and included mechanical ventilation, vasopressor drugs (e.g., dopamine), lactated Ringer’s injection, platelets, RBC’s, fresh frozen plasma transfusions, ampicillin/subactam (3 g iv every 6 hours), and aztreonam (2 g iv every 8 hours). On admission to the intensive care unit, the patient’s laboratory values were as follows: hemoglobin, 6.5 g/dL; hematocrit, 18.3%; WBC count, 14,100/mm³ with 40% polymorphonuclear neutrophils and 50% lymphocytes; and platelet count, 42,000/mm³. Liver function tests revealed the following values: aspartate aminotransferase, 157 U/L; alanine aminotransferase, 54 U/L; lactate dehydrogenase, 1,204 U/L; and creatinine, 0.9 mg/dL. The prothrombin time (PT) and partial thromboplastin time (PTT) were prolonged (PT, >1.2 seconds; PTT, >6 seconds), and hypofibrinogenemia was noted; in addition, IgM antibodies to dengue were detected.

The patient remained in the intensive care unit, but her condition worsened and she had a second episode of intra-abdominal bleeding. A second exploratory laparotomy revealed multiple hematomas. Following this procedure she developed poliserositis, severe hyperbilirubinemia (total bilirubin, 57 mg/dL), acute renal failure that progressed to anuria and required hemodialysis, and mild thrombocytopenia; in addition, there was a progressive increase in the level of liver enzymes (aspartate aminotransferase, 5,014 U/L; alanine aminotransferase, 2,209 U/L) and in the uncoagulable prothrombin time and partial thromboplastin times. Therapy with methylprednisolone (2 g iv every 8 hours) and plasmapheresis were initiated, and the patient’s hematologic profile normalized.

The patient remained hemodynamically stable, and right-sided pneumonia developed; therapy with imipenem/cilastatin (500 mg every 12 hours) was started after blood samples were drawn for culture. Blood cultures yielded *Candida tropicalis* that was susceptible to amphotericin B, and cultures of endotracheal secretions yielded multiresistant *Sienotrophomonas maltophilia* and *Klebsiella pneumoniae* as well as *Serratia marcescens* that was susceptible only to cefepime.

The patient then developed gram-negative sepsis and multiorgan failure (respiratory distress syndrome, severe renal failure, liver insufficiency, multifocal bleeding, and encephalopathy) and died. An autopsy was not performed.

There are two hypotheses for the pathogenesis of DHF/DSS. The first is that the severity of the disease is determined by the virulence of the different viral strains (i.e., antigenic variation). The second relates to an immunologically mediated pathogene-
components, fibrinogen, and platelet counts are decreased, brinogen, and platelet counts are decreased, leading to increased capillary permeability, hemococoncentration, and shock. Various complement components, fibrinogen, and platelet counts are decreased, which suggests that complement activation and consumptive coagulopathy occur [2–4].

Splenic rupture in patients with hemorrhagic dengue is uncommon. Only one case of splenic rupture was reported secondary to dengue fever (this occurred in an adult patient in French Polynesia), and the outcome of this case was favorable [5]. We presumed that the splenic rupture in our case was due to factors such as the level of severity of DHF/DSS (grade III) and the presence of consumption coagulopathy and severe thrombocytopenia (these factors were the cause of our patient’s death).

Large numbers of cases of dengue/DHF were reported in Venezuela from 1991 to June 1996. During this period, 54,224 cases of classic dengue were reported, 15,171 cases of DHF were reported, and 151 deaths were reported. In 1995, the largest ever outbreak of dengue/DHF in Venezuela was reported; there were 32,280 cases of dengue and 5,380 cases of DHF. Since 1968, 25 countries in the Americas have reported more than 35,000 confirmed or suspected cases of DHF and ~500 deaths [6, 7].

Splenic rupture has been described in patients who have sustained trauma or have Plasmodium vivax malaria, sickle cell disease, infectious mononucleosis, and lymphoproliferative disorders. Physicians should be aware of the possibility of splenic rupture in areas where dengue fever is endemic, and they should administer treatment early to avoid this potential complication [5–7].

High Serum Ferritin Concentration in an AIDS Patient with Miliary Tuberculosis

High serum ferritin concentrations may be a useful tool in the diagnosis and follow-up of disseminated histoplasmosis in patients infected with HIV [1–4]. In case-control studies, Kim et al. [1, 2] reported that a serum ferritin concentration of >10,000 ng/mL appeared to be a highly specific marker of disseminated histoplasmosis in AIDS patients and that it correlated with disease activity. Nevertheless, HIV-infected patients may have high serum ferritin concentrations as a result of other causes. We report the case of an AIDS patient with miliary tuberculosis and a serum ferritin concentration of >10,000 ng/mL.

A 23-year-old male presented to our hospital because of fever, asthenia, and general malaise that had lasted 15 days. He had been infected with HIV since 1987 but had refused treatment. He had a history of iv drug use until 1 year before presentation, when he was imprisoned. On presentation to the hospital his blood pressure was 100/60 mm Hg, his temperature was 38.8°C, he had oral candidiasis, and his liver and spleen were enlarged. The hemogram showed a WBC count of 5,800/mm³ (with no increase in immature forms), a hemoglobin level of 8.9 g/dL, a platelet count of 65,000/mm³, and a CD4 cell count of 209/mm³. Blood chemistry test results were normal except for a small elevation in the level of transaminases. A chest radiograph showed a bilateral miliary pattern. Zielh staining of a sputum sample was positive. The serum ferritin concentration was determined to be 13,547 ng/mL by EIA (IMX, Abbott Laboratories, Chicago).

The patient was treated with isoniazid (300 mg/d), rifampin (600 mg/d), ethambutol (1,200 mg/d), and pyrazinamide (1,500 mg/d), and his condition improved. His fever disappeared in 1 week, and the chest radiographic findings normalized at the end of 8 weeks. Culture of a sputum sample yielded Mycobacterium tuberculosis. Twelve months later, the patient was well; his CD4 cell count was 105 cells/mm³, and his serum ferritin level was 310 ng/mL.

Serum ferritin is produced by the monocytes and macrophages of the reticuloendothelial system. Serum ferritin concentrations may increase out of proportion to iron stores in patients with certain clinical syndromes (e.g., liver disease, renal disease, systemic infection and inflammation, malignancies, and sickle cell syndrome) and in patients who undergo repeated RBC trans-