Dengue haemorrhagic fever with unusual prolonged thrombocytopaenia

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ABSTRACT

We describe a case of dengue haemorrhagic fever with prolonged thrombocytopaenia. A 22-year-old Malay man with no prior illness presented with a history of fever and generalised macular rash of four days duration. Initial work-up suggested the diagnosis of dengue haemorrhagic fever based on thrombocytopaenia and positive dengue serology. Patient recovered from acute illness by day ten, and was discharged from the hospital with improving platelet count. He was then noted to have declining platelet count on follow-up and required another hospital admission on day 19 of his illness because of declining platelet count. The patient remained hospitalised till day 44 of his illness and managed with repeated platelet transfusion and supportive care till he recovered spontaneously.

Keywords: dengue haemorrhagic fever, macular rash, mosquito, platelet transfusion, prolonged thrombocytopaenia, thrombocytopaenia

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INTRODUCTION

Dengue fever is an acute viral illness. It has a spectrum ranging from mild illness to serious shock-like state with significant mortality. Dengue fever is usually a self-limited mild illness if detected early and managed properly. It is transmitted to humans by the mosquito *Aedes aegypti*. Annually, there are an estimated 50 to 100 million cases of dengue fever and 250,000 to 500,000 cases of dengue haemorrhagic fever (DHF) in the world, and over half of the world's population live in areas at risk of dengue fever[1,2]. The case fatality rate in patients with dengue shock syndrome can be as high as 44%. The epidemic of dengue fever originated in Southeast Asia (Manila) in 1953 but now the disease has spread to India, Pakistan, Sri Lanka and China[1]. Dengue fever needs to be recognised early and managed properly to decrease its mortality.

CASE REPORT

A 22-year-old Malay man with no previous past medical history, presented with fever and generalised macular rash of four days duration. He was residing in an army camp and had no history of recent travel abroad. He was admitted to hospital with a provisional diagnosis of dengue fever, based on his low platelet count at presentation. The diagnosis of dengue fever was confirmed later by positive dengue serology. The patient's platelet count was 7,000/μL (normal range:150,000-400,000/μL) at presentation but no active bleeding was noted. He was discharged from hospital on day 12 of his illness. He required 12 units of platelets to maintain his platelet count in the range of 30,000 to 40,000/μL. At the time of discharge from hospital, his platelet count was 61,000/μL and he was asymptomatic. He was advised regular follow-up at a local clinic with regular checks on platelet count and the platelet count improved to 130,000/μL.

On day 19 of his illness, his platelet count again dropped to 89,000/μL with a high haematocrit. He was again admitted to hospital and worked-up for concurrent infection but work-up for sepsis was negative. His platelet count dropped again and remained low till day 40 of his illness, and the lowest platelet count of 7,000/μL was noted on day 38. During this hospital admission, 35 units of platelets were transfused. At this point of time, possibilities of underlying platelet disorder or development of anti-platelet antibodies were considered but the patients' platelet count started improving spontaneously by day 39 and reached 163,000/μL on day 44 of his illness. The pattern of prolonged thrombocytopaenia with initial recovery was unusual in our case.

DISCUSSION

Dengue is the most important human viral disease transmitted by arthropod vectors. Dengue is a homonym for the African Ki denga pepo, which first appeared in English literature during an 1827-28 Caribbean outbreak. Benjamin Rush described the first case of dengue in 1789. DHF and dengue shock syndrome are now leading causes of hospital admissions and deaths among children in Asia[3-4].

Dengue fever is caused by four dengue viruses labelled as types 1, 2, 3 and 4. Clinical features of dengue virus infection range from mild illness to shock leading to death. Dengue fever is an acute febrile illness lasting five to six days. Headache, retroocular pain, muscle and joint pain, vomiting and rash are common manifestations[5,6]. The virus disappears from the blood after an average of five days[7,8]. DHF is characterised by a bleeding tendency, secondary to thrombocytopaenia and evidence of plasma leakage as determined by a rising haematocrit.

Dengue shock syndrome is defined as dengue fever with signs of circulatory failure. The prognosis depends on prevention or early recognition and treatment. Case fatality rate is as high as 12% to 14% once shock has set in. Other severe manifestations described with dengue syndrome include hepatic damage, cardiomyopathy and encephalopathy[9,10]. In a typical case of dengue fever, thrombocytopaenia is seen on days five to six, and the mean duration of thrombocytopaenia is few days[11]. In our case, thrombocytopaenia lasted more than a month after initial recovery. This pattern of thrombocytopaenia is unusual for dengue.

Laboratory diagnosis requires serum for virological or serological studies. The virus can be isolated during the febrile period, which is usually around five days. The virus may be isolated utilising cell culture and detected rapidly by using PCR but this is not available freely and only is experimental[12]. Serological diagnosis requires either a presence of IgM antibody or a rise in IgG antibody in paired acute and convalescent phase serum. IgM antibody may be detected in 90% of patients by day six, and will remain positive for 60 days.

Currently, the most common IgM assay is a capture ELISA (enzyme linked immunosorbent assay)[13]. IgG can be measured by haemagglutination inhibition test or ELISA. Confirmed diagnosis of dengue requires isolation of the virus but a probable diagnosis can be made on positive serology. Paired acute and convalescent samples are more suggestive of current infection rather than single IgM titre which may reflect a recent infection as long as 30 days ago.

Management of dengue fever requires rest, oral fluids to compensate for losses via diarrhoea or vomiting, antipyretics and analgesics. Intravenous fluid may be required for few days since the period of vasculopathy causing plasma leakage may be short, lasting only a few days. Plasma leakage is evidenced by a rising haematocrit. Patients who present with shock may require central venous pressure monitoring. An arterial line may be required in unstable patients for the assessment of blood gases, electrolytes and coagulation profile to help identify patients needing ventilatory support. Insertions of vascular lines should be done under blood products support in view of the thrombocytopaenia and possible coagulopathies.

Patients should remain in hospital till at least day three of recovery from shock. A decision for discharge from hospital may be made once the patient is stable and platelet counts are greater than 50,000/μL. In our case, the patient suffered prolonged thrombocytopaenia following DHF, which is unusual for this infection. The possibility of the patient acquiring bacterial infection during recovery phase leading to sepsis was considered, but work-up for sepsis was negative. The possibility of underlying platelet disorder was also considered, however, the patient recovered spontaneously. We postulate that this could be an unusual or mutated strain of the dengue virus. A further consideration was that the patient acquired another infection of dengue virus with a different strain during the recovery phase. However, the patient was not febrile at the time of second presentation to the hospital and the isolation of the virus is only possible during the short febrile period, which corresponds to the period of viraemia.

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