

Persistent Thrombocytopenia in Dengue Hemorrhagic Fever

A five-year-old previously healthy, male child from Hubli presented with confirmed dengue hemorrhagic fever on seventh day of illness. At admission, his total leucocyte count was 8500/cmm, hematocrit 40% and platelet count 50,000/cmm. Liver function test was normal. There was no proteinuria or hematuria. On Day 3 of admission, he developed acute respiratory distress syndrome (ARDS) and was ventilated for next fifteen days (he later had ventilator-associated-pneumonia). Meanwhile, platelet count dropped to as low as 7,000/cmm requiring alternate day SDP (single donor platelets) transfusions. For next four weeks, he had persisting intermittent fever spikes without any focus of infection. He received a total of 10 units of SDP to maintain the platelet counts above 20,000/cmm, without bleeding manifestation. Bone marrow aspirate on fifth week of illness was normal. The patient received intravenous immunoglobulins (IVIg) and later, anti-D immune globulin (250IU/kg) intravenously; platelets transiently went up to 35,000/cmm. On day 44, the child suddenly developed features of raised intracranial tension and had massive pulmonary hemorrhage. He died of intractable hypovolemic shock. Just before death, platelet count was 12,000/cmm, confirmed by peripheral smear examination. DIC profile was normal. Autopsy findings suggested massive cerebral intraparenchymal hemorrhage along with pulmonary and gastric mucosal bleeding.

It is well known that thrombocytopenia is short-lived in dengue illness and platelet counts recover with clinical improvement. Primary post-dengue immune thrombocytopenic purpura (ITP) responds to steroid therapy [1]. Though we did not go for anti platelet-associated antibody (PAIg) assay, thrombocytopenia caused by such antibodies is transient [2]. Alloimmunization to multiple platelet transfusions is less likely as we used single donor platelets (SDP). In our case, Anti-D immunoglobulin failed to improve platelet counts. Lack of response to IVIg was similar to the observation by Dimaano *et al.* [3].

Dengue virus is known to induce aberrant immune activation and cytokine (IL-6) overproduction leading to enhanced production of anti-platelet and anti-NS1 (nonstructural protein-1 antigen) antibodies cross-reacting with human platelets [4]. However, none of the recent findings suggest any mechanism that can explain persistence of thrombocytopenia following dengue infection. Immune clearance of platelets by macrophages may not be the primary mechanism in this disease [3].

In view of possibility of intercurrent illness in ICU and sepsis delaying recovery from thrombocytopenia, we had blood and urine samples cultures twice which showed no growth of bacteria and fungal elements. We also considered the possibility of co-existing rickettsial infection and malaria and treated appropriately. Atypical evolution of dengue hemorrhagic fever can cause prolonged fever in dengue illness [5].

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