

Bleeding Manifestations in Patients with Dengue

Hemorrhage

Hemorrhagic manifestations most commonly occur around the time of defervescence. Mild hemorrhagic manifestations such as petechiae, purpura, epistaxis, and gingival bleeding are relatively common even in nonsevere dengue cases; they occur in as many as one third of these cases. While the etiology of hemorrhage in patients with dengue is poorly understood, mild hemorrhagic manifestations might be due to increased capillary fragility as a result of thrombocytopenia or platelet dysfunction. Normally, platelets release factors that help maintain the integrity of the endothelial adherens junctions. Major mucosal bleeding (gastrointestinal or vaginal) in dengue patients can be occult and is often associated with prolonged shock and metabolic acidosis.

Coagulopathy

Coagulopathy is common in dengue patients. There are conflicting opinions as to whether disseminated intravascular coagulation occurs. A recent prospective study of 375 children with confirmed dengue found most cases had elevated partial thromboplastin time (APTT), decreased fibrinogen, and normal fibrin degradation products. The coagulopathy was worse in the critical phase and among those with more severe vascular leakage. The etiology of the coagulopathy is not known, but researchers have hypothesized that it might be due to loss of essential coagulation proteins due to plasma leakage. Interactions between dengue virus nonstructural protein 1 (NS1) and the endothelial glycocalyx layer may cause a change in filtration characteristics, resulting in leakage of plasma proteins and release of heparan sulfate into the circulation. Heparan sulfate, which can function as an anticoagulant, might contribute to the coagulopathy.

Thrombocytopenia

Thrombocytopenia is defined by the World Health Organization (WHO) as a platelet count of less than or equal to $100,000/\mu\text{L}$. Thrombocytopenia is common even among those with nonsevere dengue (i.e., in two-thirds or more of nonsevere cases). Thrombocytopenia is thought to result from early pancytopenic suppression of the bone marrow either by direct infection of progenitor cells or by macrophages that activate T-cells that release cytokines that suppress hematopoiesis. In addition, there is peripheral immune mediated platelet destruction via dengue virus binding to platelet in presence of NS1 antibody, so that the half-life of platelets are decreased in dengue patients.

