Case Report

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Post Dengue Reactive Thrombocytosis- A Case Report

Paediatrics Section

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ABSTRACT

Dengue fever is common in tropical countries like India. Typically, dengue fever and dengue haemorrhagic fever is characterised by high grade fever with arthralgia, myalgia and headache. Leukopaenia, thrombocytopaenia, and fluid leak is the hallmark of dengue which normalises with recovery. However, it is very uncommon in these patients to progress to severe thrombocytosis. Authors hereby report an unusual case of dengue followed by severe reactive thrombocytosis. A 13-year-old male child was admitted with complaints of fever and headache for the past two days and vomiting for one day. There was right hypochondrium tenderness. Investigations revealed leucopaenia (total leucocyte count was 3500/µL), platelets count was 150×10^3/µL, haematocrit was 34.5%, and dengue virus antigen detection (NS1) was positive. Coronavirus Disease-2019 (COVID-19) Reverse Transcription-Polymerase Chain Reaction (RT-PCR) was negative. The patient was managed conservatively with intravenous fluid ringer lactate, acetaminophen, antiemetics and antacids. After 72 hours of discharge, patient came back with thrombocytosis. He was medicated on aspirin and the platelet count was monitored on a daily basis. The platelet count kept on increasing, and on 4th day it reached 1350×10^3/µL, but declined to normal (450×10^3/µL) over the next 10 days. Hence, aspirin was stopped. The patient was later discharged, and on follow-up the blood counts were normal.

Keywords: Aspirin, Thrombocytosis, Thrombopoietin

CASE REPORT

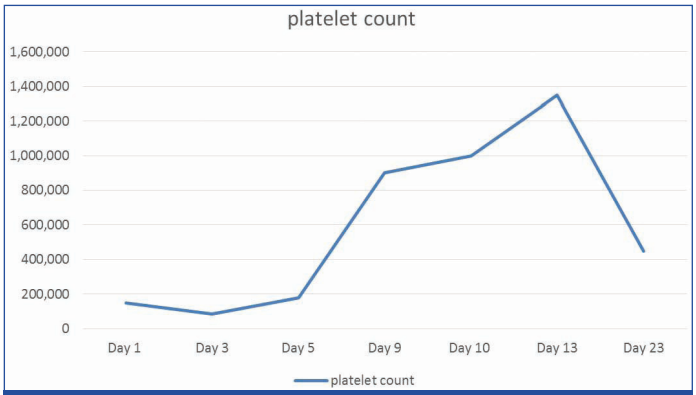
A 13-year-old male child was admitted with complaints of fever and headache for the past two days and vomiting and pain in abdomen for one day. The vital parameters and clinical examination were within normal limits, except right hypochondrium tenderness.

The blood samples were collected for complete blood count, malaria, dengue, enteric fever, liver function tests and blood culture. Initial investigations revealed leukopaenia (total leucocyte count was 3500/µL), platelets count was 150×10^3/µL, haematocrit was 34.5%, and dengue virus antigen detection (NS1) was positive. Coronavirus Disease-2019 (COVID-19) Reverse Transcription-Polymerase Chain Reaction (RT-PCR) was negative. Ultrasound abdomen was suggestive of gall bladder sludge with hepatomegaly. Hence, a provisional diagnosis of dengue with warning signs was made.

The patient was managed conservatively with intravenous fluid ringer lactate, acetaminophen, antiemetics and antacids. After 24 hours the child became afebrile. Platelet count fell to nadir 85×10^3/µL on the 5th day of illness and hematocrit increased to 39% on day 6th of illness. Over the next 48 hours, the platelet count returned to previously normal levels and the patient was discharged after 6 days of hospitalisation with the advice to follow-up in Outpatient Department (OPD).

After 72 hours of discharge, the patient returned to the OPD with a high grade fever for one day. The patient was admitted and relevant investigations were sent. All the investigations turned out to be negative except for increased platelet count (900×10^3/µL). The fever subsided within 24 hours of admission but the platelet counts progressively increased to 1000×10^3/µL after 10 days of illness. The platelets were mostly small and in clumps on peripheral smear examination with a normal mean platelet volume. The C-reactive protein (35 mg/L), erythrocyte sedimentation rate (41 mm in the first hour) were increased after 24 hours of admission. Serum ferritin was also slightly raised (169.60 ng/mL). The leucocytes, red blood cells count, and morphology were within normal limits. Low dose aspirin was started prophylactically and the patient was kept under close observation i.e, monitored for arterial, superficial, and deep vein thrombosis and haemorrhage. There was no evidence of mesenteric vein, portal vein, and renal vein thrombosis on colour doppler. Based on clinical findings and laboratory investigations, the final diagnosis was kept as post dengue reactive thrombocytosis.

The platelet count was monitored on a daily basis, which kept increasing for 4 days to reach the maximum of 1350×10^3/µL, followed by a decline to normal limits (450×10^3/µL) over the next 10 days [Table/Fig-1]. Throughout the course, the patient was asymptomatic, without any evidence of thrombosis or haemorrhage. Aspirin was stopped as soon as the platelet counts returned to less than 450×10^3/µL after 10 days of readmission. The patient improved symptomatically as well as the laboratory values came back to normal. He was discharged within the next two days. He showed normal blood counts on further follow-up.



[Table/Fig-1]: Trend of platelet count (per mm^3) with time.

DISCUSSION

Dengue fever is a common arthropod-borne viral infection, caused by one of the four Dengue Viruses i.e, DENV1 to DENV4, characterised by biphasic fever, arthralgia, myalgia, rash, leukopaenia, thrombocytopaenia, and lymphadenopathy. Dengue haemorrhagic fever and dengue shock syndrome are severe forms of the disease characterised by increased capillary permeability, haemoconcentration, abnormalities of haemostasis, and in severe cases, a protein-losing shock syndrome. In neonates, platelet count in dengue patients show a mild to moderate decrease from

3rd to 7th day; a significant decrease on day 4, reaching, normal levels on the 8th or 9th day of the disease [1,2]. In the haemorrhagic and severe forms, thrombocytopaenia occurs from the onset of symptoms and remains stable throughout the progression of the disease. This is more evident in the older age group. In a classical dengue, thrombocytopaenia starts late [3].

Laboratory diagnosis of DENV infection is established directly by detection of viral components in serum or indirectly by serology. Detection of viral nucleic acid or viral antigen has high specificity [4]. However, due to easy accessibility and less cost, serology is preferred. During the first week of illness, viral antigen non structural protein 1 is typically positive. Immunoglobulin M (IgM) can be detected as early as four days after the onset of illness by lateral flow immunoassay or IgM antibody capture enzyme linked immunosorbent assay and is widely used to establish a presumptive diagnosis. The diagnosis may be confirmed via IgM seroconversion between paired acute and convalescent phase (obtained 10 to 14 days after the acute phase) specimens; a diagnosis of acute DENV infection may be established by a four fold or greater rise in antibody titre [4,5].

In dengue with warning signs, crystalloid are the preferred fluids. In the hospital, all children without hypotension should be given Ringer lactate or normal saline infusion at a rate of 7 mL/kg over one hour. After one hour, if haematocrit decreases and vital parameters improve, fluid infusion rate should be decreased to 5 mL/kg over next hour and to 3 mL/kg/hour for 24-48 hours [6].

Platelets being acute phase reactants can increase due to stimuli like systemic infections, inflammatory conditions, and tumours [7-9]. Although, infections are the most common cause of secondary (reactive) thrombocytosis, dengue is not a well-known one. The pathophysiology behind the occurrence of thrombocytopenia and bleeding is unknown, however, it has been observed that DENV directly or indirectly affects the progenitor cells in the bone marrow by inhibiting the proliferative capacity [3].

Megakaryocytopoiesis is regulated by thrombopoietin (TPO) by activation of TPO receptor C-MPL (myeloproliferative leukaemia virus oncogene). Secondary (reactive) thrombocytosis can occur because of various aetiologies, the most common being infections, inflammation, tissue damage, iron deficiency, severe exercise, haemolysis, hyposplenism, and malignancy. These conditions may be associated with elevated C-reactive protein or erythrocyte sedimentation rate [10].

A bone marrow aspirate is generally suggestive of megakaryocytic hyperplasia with a normal to a leftward shift in morphology [10]. An abnormal rise in circulating TPO is seen in reactive thrombocytosis which is similar to that seen in autoimmune diseases, infections, or malignancies. The TPO levels are inversely related to platelet count and are significantly increased in patients with dengue with severe thrombocytopenia [11]. Increased levels of TPO have been noted during the defervescence stage when platelet nadir occurs and falls to normal levels with remission of thrombocytopenia [12].

The degree of rebound thrombocytosis is directly proportional to the severity of preceding thrombocytopenia. It has been seen that on follow-up, the platelet counts are significantly higher in adults with dengue shock syndrome compared to adults with dengue fever [13]. For the management of reactive thrombocytosis, the British guidelines suggest giving 75 mg of aspirin to the patient [10]. However, no similar data supporting this practice could be found. The popular choice is to consider antiplatelets such as aspirin for patients with platelets more than 1,000,000/μL, and complications of thrombocytosis are present, or to be at risk of developing complications [14].

CONCLUSION(S)

Thrombocytosis is a rare complication in dengue infection which are mostly asymptomatic. It has been seen that aspirin plays a role in management of reactive thrombocytosis. Hence, a proper regular follow-up of dengue patients should be done in order to prevent such complications.

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