CASE REPORT

Corticosteroid responsive prolonged thrombocytopenia in a case of dengue fever

Shailendra Prasad Verma,¹ Abdoul Hamide,² Jyoti Wadhwa,² Kalaimani Sivamani²

¹Division of Clinical Haematology, Department of Medicine, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Pondicherry, India

²Department of Medicine, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Pondicherry, India

Correspondence to

Dr Shailendra Prasad Verma, drspkgmu@rediffmail.com

SUMMARY

Thrombocytopenia and bleeding manifestations are consistent features of dengue fever. Usually thrombocytopenia resolves and platelet count normalises by day 10 of fever. Persistent thrombocytopenia is not a feature of dengue fever. Proposed mechanisms behind thrombocytopenia are many. Direct platelet destruction by dengue virus, immune-mediated platelet destruction and even megakaryocytic immune injury have been proposed as underlying mechanisms. We are reporting a case of an old man who presented in dengue season in 2012 with fever and bleeding and was diagnosed as a case of dengue fever. He developed persistent thrombocytopenia requiring treatment on the lines of immune thrombocytopenia and responded to steroids. Other causes of thrombocytopenia were ruled out.

BACKGROUND

Thrombocytopenia and bleeding manifestations are consistent features of dengue fever (DF). Usually thrombocytopenia resolves by day 10 of fever. Very few cases are reported worldwide having prolonged thrombocytopenia beyond day 10. All these reported cases behaved like immune thrombocytopenia (ITP) and improved completely with steroid therapy with prolonged maintenance of platelet counts. Usual thrombocytopenia of DF does not respond to steroids. Probably these reports, including ours, indicate that dengue virus infection can produce a clinical condition resembling ITP. Dengue should be suspected in any case with persistent thrombocytopenia that has a history of fever, as treatment with steroids is highly effective.

CASE PRESENTATION

This 65-year-old male farmer presented with the history of fever for 4 days, gum bleeding and malena for 2 days. The fever was high grade, intermittent, associated with chills and rigour, with generalised bodyache and headache. There was no history of vomiting, seizures, altered sensorium, cough, expectoration, or any features of urinary tract infection, bony pain or joint pain. The patient did not take any specific treatment except paracetamol for the fever. His history was insignificant for features of long-standing anaemia, recurrent fever, bleeding manifestations or blood transfusion. He did not have any comorbidity. He underwent abdominal surgery around 30 years back probably for gastric ulcer. Records of surgery were not available.

At admission he was conscious, oriented and afebrile. Blood pressure was 100/70 mm Hg and pulse rate was 90/min. General examination

revealed only mild pallor. There were no signs of capillary leak. Systemic examination was unremarkable except midline scar in upper abdomen. Based on the clinical manifestations the possibility of DF was the first thought.

INVESTIGATIONS

NS-1 antigen and IgM for dengue were positive and patient was finally diagnosed as a case of classical DF with bleeding manifestation according to the WHO criteria. Other investigations like HIV/ELISA, HCV antibody and antinuclear antibody were negative. Renal parameters, liver enzymes, prothrombin time and activated partial thromboplastin time were normal.

DIFFERENTIAL DIAGNOSIS

- Dengue with immune mediated thrombocytopenia
- Myelodysplastic syndrome

TREATMENT

The patient was admitted and treated with intravenous fluids, antipyretics and received 1 unit packed red cell and 4 unit platelets transfusion. He was started on oral iron as serum ferritin was low. Gum bleeding and malena stopped on day 2 of admission.

His platelet counts remained low even at day 14 of admission. On day 15 a bone marrow aspiration was performed to rule out marrow pathology which showed megakaryocytic thrombocytopenia consistent with peripheral destruction of platelets. Considering the possibility of immune mediated thrombocytopenia oral prednisolone was started at a dose of 1 mg/kg body weight on day 16 of admission.

OUTCOME AND FOLLOW-UP

There was a rapid and progressive increase in platelet counts in next 4–5 days. The patient achieved a normal platelet count after 1 week of starting steroids. After 1 month prednisolone doses were slowly tapered over a 2-month period and were stopped. The patient maintained platelet counts in follow-up after 2 weeks, 1 month and on monthly follow-up for 3 months. Currently the patient is asymptomatic and is following up in the outpatient department (OPD) on a monthly basis. Platelet count monitoring in hospital stay and OPD follow-up is shown in the figure 1.

DISCUSSION

Thrombocytopenia is a common laboratory finding in DF and almost always found in dengue haemorrhagic fever/shock syndrome.¹ The pathogenesis of

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Figure 1 Platelet count trend in hospital stay and OPD follow-up. Thin arrow indicates the start of prednisolone and thick arrow indicates stopping after tapering.

thrombocytopenia is still clearly not known. Dengue virus mediated bone marrow suppression resulting in reduced platelet production is one of the proposed mechanisms.² Immune-mediated clearance of antibody-coated platelets has also been proposed as a cause of thrombocytopenia in dengue 2 virus infection. This occurs in the presence of virus specific antibodies.³ A study by Lin *et al*⁴ has demonstrated increased titres of IgM antibody against platelets in dengue virus infection which is responsible for complement mediated lysis of platelets. This study also demonstrated defective ADP-induced platelet aggregation in dengue patients. The crossreactivity of antibodies directed against NS-1 antigen, and the platelets suggests role of antiplatelet antibody as pathogenesis of thrombocytopenia during dengue virus infection.⁵ The molecular mimicry between dengue virus and our endogenous self-proteins should be considered in the presence of autoimmunity during a dengue viral infection. Other proposed hypotheses are a transient alteration in the humoral regulation of thrombopoiesis, probably a consequence of the lymphoid tissue damage, provoked by dengue viruses. Normally thrombopoietin (TPO) level rises during thrombocytopenia but in dengue haemorrhagic fever, it has been noted that the TPO levels do not increase in spite of low platelet counts in early phase. A rapid increase in TPO levels from the sixth to seventh day is followed by a rise in the platelet counts subsequently.⁶

Platelet count usually reaches its lowest level as the patient is about to recover, that is, about 1 week after the onset of fever and more than 70% of patients show recovery of their platelet count after that. It recovers promptly in the ensuing week, usually on day 9th to 11th of illness. In the natural history of illness all the patients show convalescence and platelet count recovers to the preillness level.⁷ Our patient had a platelet count of $<10\,000/\text{mm}^3$ at day 13 of admission and responded to prednisolone promptly.

Only a few case reports described persistent thrombocytopenia in patients with DF. Leong⁸ has reported corticosteroid responsive prolonged thrombocytopenia in a 15-year-old Chinese boy. The patient was successfully treated with steroids tapered over 3 months without any relapse for 6 months. Bhalla

*et al*⁹ reported a 34-year-old woman who had persistent thrombocytopenia for more than 10 days with bleeding manifestations and responded well to steroids. Luiz Jose de Souza *et al*¹⁰ has reported a 46-year-old woman with a dengue virus 3 infection with prolonged ITP which responded to steroids.

Various viral infections such as infectious mononucleosis, mumps, rubella and rubeola are reported to be associated with development of acute ITP.¹¹ It usually occurs 7–10 days after the onset of infection generally at the time when the virus is cleared from the circulation. Episode of upper respiratory tract infection is documented in some children who develop ITP.

Learning points

- ▶ To conclude, our case and other case reports describe that persistent thrombocytopenia beyond the usual recovery time may be a rare feature in Dengue fever patients.
- ▶ Good and stable response with steroids indicates that following infection with Dengue virus some immunological mechanism is responsible for prolonged thrombocytopenia. This categorizes Dengue virus as one of the viruses which can cause immune thrombocytopenia.
- ▶ Dengue infection should be ruled out in any patient with persistent thrombocytopenia who has history of fever in recent past.

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Competing interests None.

Patient consent Obtained.

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