

Case Report

Dengue Fever End Up with Immune Thrombocytopenic Purpura

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ABSTRACT

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by low platelet count and skin-mucosal bleeding. It commonly affects adult female in an idiopathic and chronic manner. Thrombocytopenia associated with dengue viral infection seems to result in both from a reduction in the production of platelets from megakaryocytes and from a decrease in the half-life of the platelets. The mechanisms behind thrombocytopenia are many. Persistent low platelets are not a feature of dengue fever. Furthermore, low platelets of dengue fever do not respond to steroids. It has been reported that acquired immune TTP is closely associated with Epstein Barr virus, cytomegalovirus, human immunodeficiency virus infection and influenza infection or vaccination. We herein report the first case of acquired TTP associated with dengue haemorrhagic fever in the east part of the Sri Lanka.

Keywords: Dengue fever, Immune thrombocytopenic purpura, and low platelet count

INTRODUCTION

Dengue fever (DF) and dengue hemorrhagic fever (DHF) are caused by one of four closely related, but antigenically different, virus serotypes (DEN-1, DEN-2, DEN-3, and DEN4) of the genus Flavivirus. ^[1] Infection with one of these serotypes does not provide cross-protective immunity, so persons living in a dengue-endemic area can have four different dengue infections during their lifetime. ^[2] In dengue fever, the spectrum of abnormal hemostasis including increased capillary fragility, thrombocytopenia, impaired platelet function, and consumptive coagulopathy in the most severe form disseminated intravascular coagulation (DIC) contribute to varying degrees of haemorrhagic manifestations. Although dengue virus-induced bone marrow suppression decreases platelet synthesis, an immune mechanism of thrombocytopenia caused by increased platelet destruction appears to be operative in patients with DHF. ^[3]

Immune thrombocytopenic purpura (ITP) is a form of acquired thrombocytopenia triggered by antiplatelet antibodies that destroy platelets peripherally, damage megakaryocytes, and inhibits platelet production in the marrow. An increased level of platelet-associated IgG antibody is observed in patients with idiopathic thrombocytopenic purpura (ITP) but is also found in a variety of diseases.

Acute idiopathic thrombocytopenia purpura (ITP) can develop 7 to 10 days after infectious such the cytomegalovirus, hepatitis-C virus, mumps, rubella, Epstein-Barr virus, and parvovirus B19, among others, have been identified as the culprits behind this form of ITP. ^[4,5] It generally occurs at a time when the virus is cleared from the circulation. Platelets that are sensitized by autoantibodies are destroyed by cells of the reticuloendothelial system, particularly those of the spleen. These autoantibodies against glycoproteins of the platelet membrane can be identified in 80%

of the patients. [6] The diagnosis of ITP is achieved by ruling out other possibilities. [7] However, other causes of low platelets should be investigated, such as systemic lupus erythematosus (SLE), HIV/AIDS, pregnancy, use of medications (heparin, sulfa and quinidine) and recent blood transfusion, among others. We reported a case of a lady who presented in dengue season in 2017 with fever and bleeding gum and were diagnosed as a case of dengue haemorrhagic fever. Subsequently, she developed persistent low platelets which required treatment on the lines of immune thrombocytopenia and responded to steroids. Other causes of thrombocytopenia were ruled out.

CASE HISTORY

A 28-year-old woman presented with five days of high fever with chills. One day before admission, she developed spontaneous gum bleeding with a generalized erythematous rash, especially over the lower limbs. She complained of arthralgia, myalgia and weakness. She had experienced of headache, and retro-orbital pain. There was no significant drug history. She had not taken any traditional forms of treatment. On examination, she appeared flushed, mildly dehydrated with a generalized erythematous macular rash more prominent over the lower limbs. Petechiae were also present, especially over the lower limbs. Her conjunctiva was injected and palatal petechial haemorrhages were noted. He had mild spontaneous bleeding from the gum margins. Her blood pressure was 125/65 with a pulse rate of 88/min. Fundoscopy did not reveal any hemorrhages. The rest of the physical examination was essentially normal. Fifth day of the fever, her both dengue IgM and IgG antibodies were positive.

The provisional diagnosis was dengue haemorrhagic fever (DHF). Investigations on admission: Haemoglobin 13.4 g/dl, PCV 0.43, platelet count 16×10^9 , total white blood cell 3.2×10^9 /l (neutrophils 19%, lymphocytes 68%,

eosinophils 1 %, monocytes 2%, atypical lymphocytes 10%). Prothrombin time ratio was 1.13, partial thromboplastin time 49.7 seconds as compared to normal of 36.3 seconds. Aspartate transaminase 60 iu/l, alanine transaminase 71 iu/l. Two days later fever was settled, and platelets started to raise to 25×10^9 /l.

Her rash was washed-out by the second day of the admission. She remained well without any signs or symptoms despite having severe thrombocytopenia in the 15 days after becoming afebrile. Ten days after admission, his platelet count was at its lowest at 8×10^9 /l. A bone marrow aspirate and trephine biopsy were performed. Adequate megakaryocytes were found in the marrow, indicating peripheral destruction as the most likely cause for the thrombocytopenia. We have started steroid which responded well.

DISCUSSION

Low platelets and bleeding manifestations are consistent features of dengue fever. [8] Typically, thrombocytopenia resolves by day 8 -10 of fever. [9] However, few cases were reported worldwide having lengthy thrombocytopenia beyond day 10. The exact mechanism of thrombocytopenia is still clearly not known. Direct platelet destruction by dengue virus, immune-mediated platelet destruction and even megakaryocytic immune injury have been proposed as underlying mechanisms. A study by La Russa has demonstrated dengue mediated bone marrow suppression causing low platelets. [10] However, Wang et al, cited that anti-body coated platelets were cleared by immune-mediated reaction which responsible for thrombocytopenia in dengue fever. [11] In addition to that peripheral destruction of platelet also contributes to thrombocytopenia mainly by anti-platelets IgM serotype. [12] A study by Petaja J demonstrated that both coagulation and fibrinolytic paths are triggered in dengue infection leading to consumption of platelets. [13] Furthermore, a study

demonstrated that cross-reactivity of antibodies against NS-1 antigen and the platelets proposes role of antiplatelet antibody as pathogenesis of thrombocytopenia during dengue virus infection. [14]

ITP is an auto-immune disorder characterized by low platelet count and skin-mucosal bleeding. [15] It commonly, affects adults in an idiopathic and chronic manner, and it is found twice as frequently among women as among men. There are two major mechanisms pay to the development of ITP; increased platelet destruction and inadequate platelet production. [16] Persistent thrombocytopenia after dengue fever is a rare entity with only few reported cases. In our patient's fever was settled seventh day after the onset of fever, but persistently platelets were in the low side. In the accepted history of illness all the patients show recovery and platelet count recovers to the pre-illness level. [17] A study conducted in India; where it revealed that thrombocytopenia following dengue fever do not response with high dose of dexamethasone. [18] A placebo controlled study was conducted in Sri Lanka demonstrated that low dose dexamethasone do not show any beneficial effect in severe thrombocytopenia caused by dengue fever. [19]

Our patient had a platelet count of 8 000/mm³ at day 15 of admission and responded to prednisolone promptly. There are few cases were reported that prolonged low platelets were well responded with steroids. [20] ITP in adults commonly requires treatment using oral prednisone at the time when it is presented (at a dose of 1 to 1.5 mg/kg/day). Intravenous immune globulin (1 g/kg/day for 2 to 3 consecutive days) is used for treating internal bleeding when the platelet count is less than 5000/ μ l despite corticoid therapy for many days, or when there is progressive or extensive purpura. [21] Patients who continue to show symptoms and who have severe thrombocytopenia (platelet counts of less

than 10 000/ μ l) after this time can then be assessed for the possibility of splenectomy.

Many viral infections such as infectious mononucleosis, cytomegalovirus, mumps, rubella, varicella virus and rubeola are reported to be associated with development of acute ITP. [22] It usually occurs 8–10 days after the onset of infection generally at the time when the virus is cleared from the circulation.

CONCLUSION

Thrombocytopenia associated with dengue viral infection seems to result both from a reduction in the production of platelets from megakaryocytes and from a decrease in the half-life of the platelets. Persistent low platelets are not a feature of dengue fever. The factors that determine whether post-viral thrombocytopenia will follow an acute or chronic course remain unknown.

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Availability of data and material: All data gathered during this study are included in this published article.

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REFERENCES

1. World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention, and control. Spec Program Res Train Trop Dis [Internet]. 2009;x, 147. Available from: http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf
2. Ministry of Health Sri Lanka. Guidelines on Management of Dengue Fever & Dengue Haemorrhagic Fever In Adults [Internet]. 2012. 1-39 p. Available from: <http://www.epid.gov.lk/web/images/pdf/Publi>

- cation/guidelines_for_the_management_of_df_and_dhf_in_adults.pdf
3. Verma SP, Hamide A, Wadhwa J, Sivamani K. Corticosteroid responsive prolonged thrombocytopenia in a case of dengue fever. *BMJ Case Rep.* 2013;2–4.
 4. Kocak ED, Sherwin JC HA. Cytomegalovirus disease in immunocompetent adults. *Med J Aust.* 2015;202(8):419.
 5. Leong KW, Srinivas P. Corticosteroid-responsive prolonged thrombocytopenia following dengue haemorrhagic fever. *Med J Malaysia.* 1993;48(3):369–72.
 6. S K. Autoimmune (idiopathic) thrombocytopenic purpura. *Lancet.* 1997; 359(9064):1531–6.
 7. Harrington WJ MV and AG. The autoimmune thrombocytopenias. New York, Grune Strat. 1956;166L–176L.
 8. Penttinen K, Saikku P, Myllyla G, Brummer-Korvenkontio M, Oker-Blom N. The platelet aggregation test in group B arbovirus infections. *J Hyg (Lond).* 1970;68(1):71–6.
 9. Tuiskunen Bäck A, Lundkvist Å. Dengue viruses – an overview. *Infect Ecol Epidemiol* [Internet]. 2013;3(1):19839. Available from: <https://www.tandfonline.com/doi/full/10.3402/iee.v3i0.19839>
 10. La Russa VF IB. Mechanisms of dengue virus-induced bone marrow suppression. *Baillière's Clin Haematol.* 1995;8:249–70.
 11. Wang S, He R, Patarapotikul J et al. Antibody-enhanced binding of dengue 2 virus to human platelets. *Virology.* 1995;213:254–7.
 12. Lin CF, Lei HY, Liu CC, Liu HS, Yeh TM, Wang ST et al. Generation of IgM antiplatelet autoantibody in dengue patients. *J Med Virol.* 2001;63(2):143–49.
 13. Petaja J. Inflammation and coagulation. *Thromb Res.* 2011;127(2):S34–7.
 14. Faloconar AKI. The dengue virus nonstructural 1 protein (NS1) generates antibodies to common epitopes on human blood clotting, integrin/ adhesion proteins and binds to human endothelial cells: Potential implications in haemorrhagic fever pathogenesis. *Arch Virol.* 1997;142:897–916.
 15. Khan AM, Mydra H, Nevarez A. Clinical Practice Updates in the Management Of Immune Thrombocytopenia. P T [Internet]. 2017;42(12):756–63. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29234214%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5720488>
 16. Nugent D, McMillan R, Nichol JL et al. Pathogenesis of chronic immune thrombocytopenia: increased platelet destruction and/or decreased platelet production. *Br J Haematol.* 2009;146:585–596.
 17. Kumar P, Charaniya R, Ghosh A, Sahoo R. Intravenous immunoglobulin responsive persistent thrombocytopenia after dengue haemorrhagic fever. *J Clin Diagnostic Res.* 2016;10(4):OD010-OD011.
 18. Shashidhara KC, Sudharshan Murthy KA, Basavana Gowdappa H, Bhograj A. Effect of high dose of steroid on plateletcount in acute stage of dengue fever with thrombocytopenia. *J Clin Diagnostic Res.* 2013;7(7):1397–400.
 19. Kularatne SA et al. Efficacy of low dose dexamethasone in severe thrombocytopenia caused by dengue fever: a placebo controlled study. *Postgr Med J.* 2009;85(1008):525–9.
 20. Leong KW SP. Corticosteroid-responsive prolonged thrombocytopenia following dengue hemorrhagic fever. *Med J Malaysia.* 1993;48:369–72.
 21. George JN et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood.* 1996;88(1):3–40.
 22. Flores-Chang BS, Arias-Morales CE, Wadskier FG, Gupta S, Stoicea N. Immune Thrombocytopenic Purpura Secondary to Cytomegalovirus Infection: A Case Report. *Front Med* [Internet]. 2015; 2(November): 10–2. Available from: <http://journal.frontiersin.org/Article/10.3389/fmed.2015.00079/abstract>

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