Infections and Thrombocytopenia

Falguni Parikh

F ebrile patient with thrombocytopenia is commonly encountered by physicians especially during monsoon and perimonsoon period. Infections with protozoa, bacteria and viruses can cause thrombocytopenia with or without disseminated intravascular coagulation.

Commonly dengue, malaria, scrub typhus and other rickettsial infections, meningococci, leptospira and certain viral infections present as fever with thrombocytopenia.

Occasionally these patients can go on to develop a stormy course with multiorgan dysfunction requiring intensive care unit admission associated with high morbidity and mortality.1,2

Infections cause decrease in platelet count both due to effects on platelet production and platelet survival.3 Thrombocytopenia in bacterial infections can occur as a part of sepsis with disseminated intravascular coagulation. Patients with sepsis may also develop hemophagocytic histiocytosis with phagocytosis of platelets and leukocytes in the bone marrow histiocytes. Both Gram-positive and Gram-negative bacterial infections can lead to sepsis. Elevated platelet-associated IgG has been implicated. Platelets tend to adhere to damaged vascular surfaces in meningococccemia.

V i r u s e s p r o d u c e thrombocytopenia by various mechanisms like impaired platelet production as a result of direct viral invasion, toxic effect of viral proteins on thrombopoiesis, virus-induced hemophagocytosis and increased platelet destruction caused by binding of virus-induced autoantibodies or viral antigen-antibody complexes.

Thrombocytopenia in dengue infection raises concern about bleeding risk. Bone marrow suppression by virus and peripheral destruction of platelets have been implicated.4 Platelet transfusions are not routinely recommended in the management of Dengue fever.5,6 According to recent guidelines by the World health organization and National Vector-borne Diseases Control Programme prophylactic transfusion of platelets is not indicated unless the patient has bleeding or a count of less than 10000/cumm.7,8

Thrombocytopenia during malarial infection may appear even before fever, anemia and splenomegaly become manifest.9 Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in marrow with diminished platelet production have all been postulated. During early stages of malaria, platelet agglutination as a result of endothelial cell activation and release of activated von Willebrand factor occurs which may cause thrombocytopenia.10 Occasionally platelets can be invaded by malarial parasites. Thrombocytopenia in malaria is rarely severe and treatment is focussed on eradication of malarial parasite.11

Platelet Transfusion

Platelet transfusion may be life-saving when haemorrhage is caused by thrombocytopenia. The usual dose of platelets is one unit for each 10 kg of body weight or approximately 6 units for a typical adult dose.12 To prevent bleeding in thrombocytopenic patients it is a common practice to transfuse platelets when platelet counts reach a trigger threshold (prophylactic transfusion).

Prophylactic platelet transfusion is indicated in preparation for invasive procedures in thrombocytopenic patients.13,14 Bleeding patients with thrombocytopenia should receive platelet transfusion with the goal of achieving a platelet count greater than 50,000/ul.14

Complications of platelet transfusions:12
1. Transfusion can cause viral infections like hepatitis B, C, and HIV though low incidence is low since introduction of NAAT based tests.
2. Volume overload
3. Febrile non-haemolytic transfusion reactions (FNHTR)
4. Transfusion-related acute lung injury
5. Allo immunization

Allergic reactions causing itching and urticaria are caused by soluble substances in donor plasma and mediated by immunoglobulin E response and histamine release in recipient.15

FNHTR manifests as fever, chills, nausea, vomiting and dyspnoea from contaminated neutrophils in stored platelet products.16 It mandates stopping the transfusion.

Platelet transfusions are
considered risky in patients with thrombotic thrombocytopenic purpura because it can exacerbate microvascular thrombosis.17

Drugs, malignancy, autoimmune conditions, associated liver dysfunction also need to be ruled out as they can cause thrombocytopenia.

Supply of platelets is always limited hence guidelines are necessary to guide the clinician about their judicious use.

Recent guidelines for management of tropical fever2 suggest that in patients of fever with thrombocytopenia one should avoid aspirin and anticoagulants, watch for bleeding and consider it if platelet count is less than 20,000 or there is clinical bleeding with specific therapy of infection once diagnosis is established.

Immature platelet fraction (IPF%) is an automated modern parameter that measures young reticulated platelets in the peripheral blood. IPF levels rise as the marrow production of platelets increases.18 It has been evaluated in Dengue patients and found to be useful to predict recovery of platelets.19 An IPF value of more than 10.0% indicates recovery of platelet count within 48 hours. It appears to be a promising and reliable parameter to guide decisions regarding platelet transfusions.

In the present issue of the Journal, Kshirsagar, et al18 have attempted to develop a risk score for febrile thrombocytopenia so that an early warning score can help decide regarding therapeutic intervention like platelet transfusion.

The authors have devised a risk score based on platelet count, vital signs and organ system involvement. Based on these parameters, the patients have been divided into low, moderate and severe risk category and the data has been retrospectively analysed to find if the total risk score could predict severity of illness, need for transfusion and outcome.

It is indeed a very good attempt to develop a scoring system as it can not only guide the clinician but also help avoid unnecessary transfusions with all the associated risks and burdening the blood banks. However as the authors also point out, there are several limitations of this study.

1. The study is retrospective.
2. The cause of febrile thrombocytopenia is not taken into account. Many diseases like dengue and malaria do not require platelet transfusions if there is no overt bleeding even when the counts are very low.
3. The patient number is small and the study is done over a short duration.

Hence it is not possible to draw definite conclusions about the utility of the score from this study. However the score can be definitely validated by further larger studies.

For validation of risk score a prospective study also looking into the causes of febrile thrombocytopenia and associated comorbidities with appropriate sample size will be helpful for drawing practical conclusions.

References

5. Azeredo EL, Monteiro RQ, Pinto LM. Thrombocytopenia in dengue: interrelationship between virus and the imbalance between coagulation and fibrinolysis and inflammatory mediators. vol 2015 article ID 313842, 16 pages http://dx.doi. org/10.1155/2015/313842.
