

Immune Thrombocytopenia

Tahir Sultan Shamsi*

Department of Clinical Hematology, National Institute of Blood Disease & Bone Marrow Transplantation, Karachi, Pakistan.

Immune thrombocytopenia (ITP) is characterized by immune mediated platelet destruction in the body. Autoantibodies are formed directed against platelet surface membrane glycoproteins; antibody coated platelets are removed from circulation by the macrophages of reticuloendothelial system in spleen, liver and other parts of the body [1]. When the rate of destruction of platelets exceeds the rate of platelet production in the bone marrow, platelet count starts to decline resulting in thrombocytopenia. The degree of thrombocytopenia may vary; this condition runs a relapsing and remitting course.

Symptoms of thrombocytopenia vary from person to person. Mucocutaneous bleeding is the most common presentation including petechial and purpuric rashes, bruises, haematoma formation, gingival bleeding, haemorrhagic blisters in oral cavity, haematuria, melena in both sexes and menorrhagia in women of childbearing age [1].

The ITP affects children more commonly than adults. It has an acute onset in children; 80% cases will resolve in few weeks to few months with or without treatment. Of the remaining 20%, majority will become chronic ITP and require treatment to maintain the platelet counts in safe limits i.e., above $30 \times 10^9/L$. Around 5% will have refractory symptomatic thrombocytopenia requiring long-term treatment. The ITP in adults mostly has a chronic course. Only less than 10-20% cases have acute onset thrombocytopenia that resolve with or without treatment. All other patients have a chronic relapsing and relapsing course.

The aetiology of ITP in children and adults seems to have a different origin. In children, the trigger to make antibodies is mostly a transient viral infection. Platelets are destroyed by a bystander mechanism. Only a small proportion of children with ITP form autoantibodies and have a prolonged illness. In adults, mostly, autoantibodies are formed due to immune dysregulation targeting the platelet glycoproteins. Regulatory T-cells (Treg cells) are found to be down regulated in majority of cases during symptomatic phase while their number either normalizes or are near to normal during asymptomatic phase [1].

Fever and organomegaly are not associated with ITP; Presence of enlarged spleen or lymphadenopathy is not the feature in this condition [2]. Their presence should prompt the clinician to review the diagnosis. In ITP, complete blood

count shows isolated thrombocytopenia while red cell and white blood cell parameters and morphology are normal. ITP is the diagnosis of exclusion. In a typical case of acute ITP in children and adults, usually bone marrow biopsy is not required. Bone marrow biopsy, if carried out, is almost always normal. Megakaryocytes number is increased or normal; no other pathology is found. In chronic ITP, autoimmune profile, Human immunodeficiency virus, Hepatitis C, and *Helicobacter pylori* are required to be tested. Other possible causes of cytopenia may also need to be ruled out.

First line treatment of acute ITP includes steroids and / or intravenous immunoglobulin. In children, prednisolone 2 mg/kg/day is the starting dose, while in adults 1 mg/kg/day usually suffice [1-5]. This needs to be continued for 2-4 weeks and then reducing it slowly to stop in next 4 weeks depending upon the response. Intravenous immunoglobulin is given at a dose of 2 gm/kg. It can be given over 2 days or 5 days. Over 80% patients respond to this approach. Approximately half of these cases have a durable response and this approach will never relapse, especially children. Others will need a repeat course or repeated courses of steroids with or without the addition of second line treatment of thrombopoietin receptor analogue i.e., Eltrombopag and Romiplostim. Adult ITP patients who are corticosteroid-dependent or refractory to corticosteroids should be considered for eltrombopag or Romiplostim. Usual starting dose of eltrombopag is 50mg/day.

Eventually, majority of acute ITP cases will resolve. Remaining patients will need to continue second line treatment with eltrombopag or romiplostim for months. Splenectomy is the only treatment which potentially cures chronic ITP. In adults with steroid refractory or steroid dependent ITP lasting beyond 3 months, spleen-sparing approach may be considered using Rituximab.

Children with newly diagnosed ITP and a platelet count of $<20 \times 10^9/L$ who have no or mild bleeding (skin manifestations) only, hospital admission may not be required [5]. They can be managed as an outpatient. They should be monitored every 3-4 days in the clinic and blood count monitored. But patients with uncertainty about the diagnosis, and those with social concerns, or live far from the hospital or live in other cities, and whose follow-up cannot be guaranteed, admission to the hospital is advisable. Asymptomatic or minimally symptomatic children with ITP who have a platelet count of $>20 \times 10^9/L$ can be managed as an outpatient.

*Address correspondence to this author at the Department of Clinical Hematology, National Institute of Blood Disease & Bone Marrow Transplantation, Karachi, Pakistan. E-mail: t.shamsi.62@gmail.com

Children with minimal symptoms and a platelet count above $20 \times 10^9/L$ may not be given steroids. Only symptomatic patients will require treatment. In children with ITP who have non-life-threatening mucosal bleeding and do not respond to first-line treatment, eltrombopag should be considered as second line treatment [5]. Splenectomy is usually not recommended as first line or second line treatment in children under the age of 8-10 years [4, 5]. In such situations, rituximab is a preferred treatment.

All other treatment approaches will require a prolonged treatment for years. Before considering splenectomy, patient and the family should be counseled for possible risks of infections and the need of vaccination against encapsulated organisms like Pneumococci, Meningococci and Haemophilus. Post splenectomy penicillin prophylaxis should also be offered.

A small minority of patients is refractory to first line and second line treatment. They may be refractory to splenectomy. They are extremely difficult to manage. Treating physicians have used immunosuppressive agents like azathioprine, cyclophosphamide, mycophenolate mofetil, cyclosporine, danazol etc. These agents may produce some response in stabilizing platelet count in 20-60% patients. Our preference is azathioprine at a dose of 2-3 mg/kg/day in 2-3 divided doses for as long as it is required. Some patients require it for 12-24 months.

CONFLICT OF INTEREST

Declared none.

ACKNOWLEDGEMENTS

Declared none.

Received: September 12, 2019

Accepted: September 26, 2019

© 2019 National Journal of Health Sciences.

This is an open-access article.

REFERENCES

- [1] Audia S, Mahevas M, Samson M, Godeau B, Bonnotte B. Pathogenesis of immune thrombocytopenia. *Autoimmun Rev* 2017; 16(6): 620-32. DOI: 10.1016/j.autrev.2017.04.012
- [2] Zimmer J, Andres E, Noel E, Koumariou A, Blickle JF, Maloisel F. Current management of adult idiopathic thrombocytopenic purpura in practice: A ' cohort study of 201 patients from a single center. *Clin Lab Haematol* 2004; 26(2): 137-42. DOI: 10.1111/j.1365-2257.2004.00591.x
- [3] Cheng G, Saleh MN, Marcher C, *et al.* Eltrombopag for management of chronic immune thrombocytopenia (RAISE): A 6-month, randomised, phase 3 study [published correction appears in *Lancet*. *Lancet* 2011; 377(9763): 393-402. DOI: 10.1016/S0140-6736(10)60959-2
- [4] Kojouri K, Vesely SK, Terrell DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: A systematic review to assess long-term platelet count responses, prediction of response, and surgical complications. *Blood* 2004; 104(9): 2623-34. DOI: 10.1182/blood-2004-03-1168
- [5] Neunert C, Terrell DR, Arnold DM, *et al.* American society of hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv* 2019; 3: 3829-66. DOI: 10.1182/bloodadvances.2019000966