ORIGINAL RESEARCH PAPER

General Medicine

ELTROMBOPAG AS A PROMISING TREATMENT FOR REFRACTORY IMMUNE THROMBOCYTOPENIC PURPURA: A CASE REPORT

KEY WORDS:

PC Sandhya

Maj PL Chaitanya Varma

V Padma

Ishai Vannan

Sarath NallaPerumal

Heshish Reddy

Sujana Reddy

Rahul

INTRODUCTION:

Thrombocytopenia is a common hematological condition. It is caused by increased platelet destruction and impaired platelet production, mediated by autoantibodies in the peripheral circulation, leading to reduced platelet counts.(1) Conventional treatments for thrombocytopenia include glucocorticoids, immunosuppressants, intravenous immunoglobulin, or splenectomy. However, when these therapies do not produce satisfactory results, monoclonal antibodies targeting the thrombopoietin (TPO) receptor have emerged as a promising alternative. Eltrombopag, a TPO receptor agonist, has been approved for the treatment of chronic idiopathic (immune) thrombocytopenic purpura (ITP) in patients who do not respond adequately to conventional therapy.(4) Considering its mechanism of action and potential effectiveness, eltrombopag may be considered for use in refractory thrombocytopenia, as demonstrated in this case report where a patient with refractory thrombocytopenia showed a positive response to eltrombopag therapy.

Case Report

A 79-year-old male patient with a previous diagnosis of immune thrombocytopenic purpura (ITP) was referred to the Department of General Medicine at Sree Balaji Medical College and Hospital. The patient presented with spontaneous gingival bleeding and a low platelet count. He had been diagnosed with ITP five years ago on irregular medication usage of steroids.

The patient had a medical history of well-controlled hypertension using ACE inhibitors. There was no prior history of bleeding problems, and his family history was noncontributory. On examination, the patient appeared moderately nourished, and vital signs were within normal limits. Other than the spontaneous gingival bleeding, no petechiae or other bleeding manifestations were observed. There were no apparent signs of lymphadenopathy.

A complete hemogram revealed severe thrombocytopenia, with a platelet count as low as 3000/ L. Bleeding time, prothrombin time, and partial thromboplastin time were normal. A peripheral blood smear showed no abnormalities in differential leukocyte count or erythrocytic morphology. Further examination revealed an increased number of megakaryocytes without morphological abnormalities.

To investigate the underlying cause of thrombocytopenia, a urea breath test was conducted to detect the presence of Helicobacter pylori (H. pylori), testing for HIV, Hepatitis B,C and ANA which yielded negative results.

The patient initially received pulsed doses of dexamethasone (20 mg/day) for four days in an attempt to address the persistent severe thrombocytopenia. However, despite subsequent treatments such as intravenous immunoglobulin (IVIG) and plasma exchange (PEx), the patient's platelet count did not improve. Even after giving single donor platelet transfusion has shown only a temporary increase in the platelet count. Based on these findings, a final diagnosis of ITP was made.

Considering the refractory nature of the patient's thrombocytopenia, it was decided to initiate treatment with eltrombopag. The patient started taking eltrombopag orally at a starting dose of 12.5 mg, which was gradually increased to 50 mg daily. The platelet count responded positively to eltrombopag, with an increase to more than 25,000/ul within the first week of treatment. After a month of eltrombopag therapy, the platelet count further increased to 180,000/ul. Eventually, eltrombopag was discontinued, but even at three months after discontinuation, the patient's platelet count remained stable at 200,000/ul. No bleeding complications were observed following discharge.

DISCUSSION:

The discussion of our case report highlights the potential efficacy of eltrombopag in effectively managing refractory thrombocytopenia. By presenting our findings in conjunction with previous case reports, we offer valuable insights into the use of eltrombopag as a promising therapeutic option for patients who have shown poor responses to conventional treatments.

In the context of immune thrombocytopenic purpura (ITP), this disorder is characterized by platelet destruction mediated by immune mechanisms, coupled with inadequate platelet production. The clinical presentation of ITP can vary widely, ranging from mild bruising and mucosal bleeding to severe bleeding from any site. However, symptomatic bleeding is relatively uncommon unless the ITP reaches a severe stage with platelet counts falling below 30,000/ L. While immediate therapy may not be necessary for patients with platelet counts between 20,000 and 50,000/ L in the absence of bleeding or predisposing comorbid conditions, rapidly increasing the platelet count above 30,000/ L is critical in severe cases to prevent life-threatening bleeding

symptoms.(1,2,3)

First-line therapy for ITP typically involves the administration of corticosteroids, IV immunoglobulin (IVIg), and anti-D antibodies. Notably, thrombopoietin receptor agonists such as romiplostim and eltrombopag have demonstrated significant effectiveness in patients with ITP that has relapsed after or proven refractory to initial treatments.(4,5,6,7,8,9)

Although cases of ITP presenting with oral bleeding are relatively rare, it is crucial for clinicians to consider underlying systemic diseases like ITP or leukemia when confronted with sudden and uncontrollable oral bleeding.

The positive response observed in our patient, along with similar outcomes reported by Maroun et al. and Magnano et al., further accentuates the potential of eltrombopag in increasing platelet counts and improving thrombocytopenia. This is particularly noteworthy due to the limited treatment options available for managing refractory thrombocytopenia in this specific patient population.

The mechanism of action of eltrombopag, which involves binding to the thrombopoietin (TPO) receptor and stimulating megakaryocyte maturation and platelet production, provides a plausible rationale for its effectiveness in increasing platelet counts. Moreover, its ability to stimulate trilineage proliferation of hematopoietic stem cells further bolsters its potential in addressing refractory thrombocytopenia.(6)

While eltrombopag is a promising thrombopoietin receptor agonist for treating thrombocytopenia, it is essential to acknowledge that other options, such as romiplostim, have also demonstrated efficacy in increasing platelet count. In our case, however, eltrombopag was chosen as the treatment option based on its mechanism of action and the existing evidence supporting its use.(10)

In conclusion, eltrombopag exhibits promise as a potential treatment option for refractory thrombocytopenia associated with ITP. Further research, including larger studies, is imperative to establish its optimal use and determine long-term outcomes for patients with this condition. By expanding our understanding of eltrombopag's role in managing thrombocytopenia, we can refine treatment strategies and enhance patient outcomes.

REFERENCES

1. Lazarus AH, Semple JW, Cines DB. Innate and adaptive immunity in immune thrombocytopenia. Semin Hematol 2013;50 Suppl 1(1): S68-70.
2. Cines DB, Blanchette VS. Immune thrombocytopenic purpura. N Engl J Med. 2002;346(13):995-1008.
3. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, et al. Standardization of terminology, def- initions and outcome criteria in immune thrombocytope- nic purpura of adults and children: report from an international working group. Blood. 2009; 113: 2386-2393.
4. Nurden AT, Villard JF, Nurden P. New-generation drugs that stimulate platelet production in chronic immune thrombocytopenic purpura. Lancet 2009(2);373(9674):1562-9.
5. Stasi R, Evangelista ML, Amadori S. Novel thrombopoietic agents: a review of their use in idiopathic thrombocytopenic purpura. Drugs. 2008;68(7):901-912.
6. Garnock-Jones KP, Keam SJ. Eltrombopag. Drugs. 2009;69(5):567-576.
7. Bussel JB, Provan D, Shamsi T, et al. Effect of eltrombopag on platelet counts and bleeding during treatment of chronic idiopathic thrombocytopenic purpura: a randomised, double-blind, placebo-controlled trial. Lancet. 2009;373(9664):641-648.
8. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA; American Society of Hematology. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011; 117: 4190-4207.
9. Kado R, McCune WJ. Treatment of primary and secondary immune thrombocytopenia. Curr Opin Rheumatol 2019;31(3):213-22.
10. Bussel JB, Kuter DJ, Pullarkat V, Lyons RM, Guo M, Nichol JL. Safety and efficacy of long-term treatment with romiplostim in thrombocytopenic patients with chronic ITP. Blood. 2009;113(10):2161-2171.