ejpmr, 2022,9(8), 506-508

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

A CASE REPORT ON ELTROMBOPAG INDUCED VENOUS THROMBOEMBOLISM IN IMMUNE THROMBOCYTOPENIA

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Article Received on 08/06/2022 **Article Revised on 29/06/2022** **Article Accepted on 19/07/2022**

ABSTRACT

Eltrombopag is a (TPO)-receptor agonist. It is used in the management of condition called thrombocytopenia(ITP). Many recent literatures are indicating a increased risk of multiple thrombotic event after administration of Eltrobopag. A 20 year old young lady who was a recently diagnosed case of ITP presented with complaints of complaints of left sided headache which upon further evaluation was diagnosed as thromboembolism. This case study aims at creating awareness on cautious usage of TPO-RA in ITP.

KEYWORDS: Eltrombopag, Immune Thrombocytopenia, Venous thromboembolism, Platelets, TPO-RA.

INTRODUCTION

Eltrombopag is a (TPO)-receptor agonist.It is used in the management of condition called thrombocytopenia(ITP). It act by interaction with human TPO trans-membrane receptor domain of human TPO-receptor and initiates signaling cascades that induce proliferation and differentiation of megakaryocytes from bone marrow progenitor cells.[1]

Immune thrombocytopenia" (ITP) is an autoimmune disorder that leads to peripheral destruction, as well as a decreased production of platelets. The pathogenesis of chronic idiopathic thrombocytopenic purpura (ITP) involves antibody-mediated platelet destruction and reduced platelet production. Stimulation of platelet production may be an effective treatment for this disorder. Eltrombopag increased platelet counts in a dose-dependent manner in patients with relapsed or refractory ITP.[2]

Many recent literatures are indicating a increased risk of multiple thrombotic event after administration of Eltrobopag. Although the mechanism by which eltrombopag causing thrombosis is unknown, the rapid platelet increase induced the drug(0.8×10^9/L to 10.5×10^9/L per month)[3] is the most possible mechanism behind the adverse effect.

Venous thromboembolism (VTE) is a frequent and potentially lethal condition. Venous thrombi are mainly constituted of fibrin and red blood cells, but platelets also play an important role in VTE formation. Several known VTE risk factors also seems to apply in patients with thrombocytopenia. Also, patients with thrombocytopenia may be VTE risk stratified based on platelet count and comorbidities.[4]

CASE REPORT

A 20 year old young lady who was a recently diagnosed case of ITP presented with complaints of complaints of left sided headache since 2 days and heaviness of head. She was clinically diagnosed to have ITP and was initiated on IV steriods(Dexamethasone) and TPO analogues (Eltrombopag) but her platelets counts were still low. Suspecting an autoimmune pathology, ANA was sent and found to be positive (2+). Patient and family were informed of an immediate need of initiating her on IVIG in view of severe thrombocytopenia. After an informed consent, she was initiated on IVIG(1 g/kg) after pre-medications. She tolerated the transfusion well and her platelet counts on day 7 was 56000.She underwent a detailed evaluation and her MR Venogram showed filling defects noted in the left proximal and distal transverse sinus - s/o thrombosis. She was started on LWMH. Neuroimaging revealed thrombosis. She was managed accordingly and now being discharged on Inj. Clexane with advise to follow up on an OPD basis. TPO RA was discontinued.She remains well on follow up with complete resolution on follow up imaging.

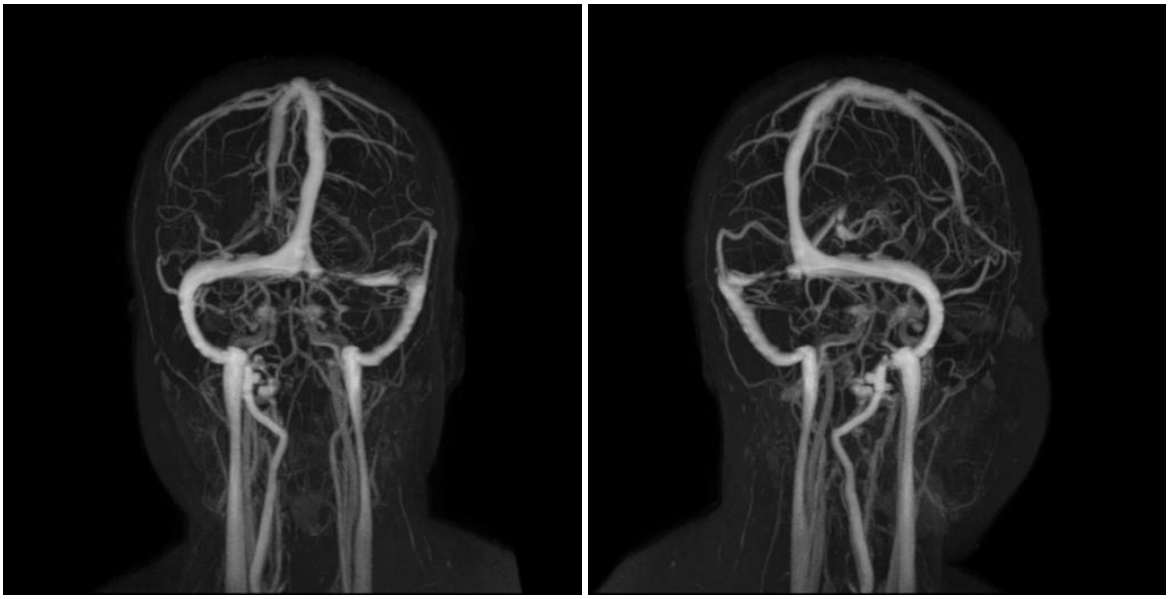

Figure 1 & 2: Mrv Brain.

DISCUSSION

Thrombopoietin receptor agonists (TPO-RA) such as romiplostim and eltrombopag have been approved to treat immune thrombocytopenia.

Eltrombopag,an oral thrombopoietin receptor agonist, induces the proliferation and differentiation of bone marrow stem cells to increase production of blood cells. Romiplostim, Fusion antibody-peptide is a thrombopoietic agent. These drugs are thrombopoietin receptor agonist which stimulates proliferation, differentiation and activity of monocytes, neutrophils, eosinophils, and macrophages[medscape]. Romiplostim (Nplate) was approved by the US Food and Drug Administration (FDA) on August 22, 2008. Currently, both the American Society of Hematology ITP management guidelines and the "International consensus report" guidelines recommend the use of TRAs for adults with ITP that persists following splenectomy or in patients who are not candidates for splenectomy and for who at least one other treatment has failed.[5]

The two TPO RA have comparable overall efficacy. Eltrombopag is given orally while romiplostim is dosed as a weekly subcutaneous injection. However, eltrombopag must be given on an empty stomach; in particular, it should be taken four hours after and two hours before food containing cations, e.g. iron, calcium, milk or other dairy products. In the US, different criteria for medical insurance are used for the two agents, which may impact on the decision to adopt one treatment or the other depending on which is likely to be approved first. If patients have absorption problems or transaminitis, it may be prudent to use romiplostim. If patients do not have stable platelet counts, or if they do not want to come to the clinic every week for injections, then eltrombopag may be better. Romiplostim and eltrombopag are well tolerated and effective therapies for ITP with acceptable toxicity. Both agents increase the platelet count in up to three-quarters of patients.

In early trials with TPO-RA, sporadic thromboembolic events (TEE) gave impetus to extensive epidemiological studies exploring the association between thrombosis and ITP and the role of TPO-RA. The incidence of TEE in patients with chronic ITP not exposed to TPO-RA was compared with age- and sex-matched non-ITP control. In summary, although they have not been substantiated in properly designed trials, the annualized thrombosis rates in adults appear to be 2-3 times higher (annualized incidence rate of TEE of 4-7%) with TPO-RA treatment than in an ITP population not treated with TPO-RA, and even higher if compared to non-ITP control populations.63 On the other hand, most available data on the risk of thrombosis are based on retrospective and registry studies, which probably underestimate the risk of thrombosis in the ITP population. The patient's individual risk profile should be considered when initiating treatment with a TPO-RA to evaluate if the expected reduction in bleeding risk outweighs the risk of thrombotisis. Comorbidities more prevalent in ITP should be considered and/or investigated; these include previous thromboembolism, splenectomy, presence of antiphospholipid antibodies, and concomitant medications like estroprogestinic preparations. Efforts should be made to correct modifiable risk factors, and thrombo-prophylaxis is recommended for surgery, provided the patient has a safe platelet count.67 Furthermore, antiplatelet agents or even anticoagulation could be considered in patients at high risk of thrombosis once platelet counts reach >50x109 /L after initiation of TPO-RA.[6]

In conclusion Eltrombopag increases the risk of venous thromboembolism in ITP patients. Further evaluation is essential to gain confidence in management to VTE in ITP. The exclusivity of VTE incidences is unknown.

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