Resistant thrombocytopenia in an HIV and hepatitis C patient: treatment response with novel agent eltrombopag

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Abstract

HIV-associated thrombocytopenia is a disease which can be recurrent to standard therapy which includes highly active antiretroviral therapy (HAART) therapy, steroids and immunoglobulin. We report a patient with HIV and hepatitis C who presented with resistant thrombocytopenia. Treatment with Eltrombopag — a thrombopoietin receptor agonist showed initial good response with recurrent thrombocytopenia. This novel agent could be considered as a treatment option prior to splenectomy and may be useful as a temporizing measure.

Introduction

Thrombocytopenia occurs in 5-10% of HIV infected individuals and is more severe in intravenous drug abusers. The underlying pathophysiology includes a combination of peripheral platelet destruction and ineffective production of platelets from megakaryocytes. Clinically they are similar to other immune thrombocytopenias but cautious treatment is advised as immunosuppressive treatments can flare up infections and some malignancies.¹ Treatment response is also variable when the patient has other infections like hepatitis C as in our case.

Case Report

A 50 year old male with a history of intravenous drug abuse, HIV and chronic hepatitis C infection, presented with melena of 2 weeks duration and was found to have a platelet count of 4000/µL. He was diagnosed to have immune thrombocytopenia secondary to HIV (HIV-1 RNA titer of 54,910/mL) and chronic active HCV (HCV RNA positive with a HCV log10 of 7.064 (RNA quantitative 11,591,000 international units) and genotype 4 infection. He was treated initially with oral prednisone and intravenous immunoglobulin. Patient’s platelet count increased to a maximum level of 64,000/µL and was discharged on highly active antiretroviral therapy (HAART) including zidovudine and oral prednisone.

Two months following discharge, the patient was readmitted with complaints of generalized petechial rash and a platelet count of 2000/µL. During this admission, platelet transfusion, immunoglobulin, anti-helicobacter pylori treatment, corticosteroids and high dose zidovudine were tried without any success in increasing the platelet count. His HIV-1 RNA titre was 140/mL at that point suggesting effective HAART. Bone marrow biopsy revealed normocellular trilineage with a mild increase in mature neutrophils and no increase in blast cells (Figure 1). Flow cytometry showed no evidence of monoclonal cells or aberrant antigen expression and CD4:CD8 ratio was markedly reduced (0.6). Due to the resistant thrombocytopenia, Eltrombopag (thrombopoietin receptor agonist) was started under direct observation in the hospital setting. After two weeks of treatment with Eltrombopag, the platelet count increased to 62,000/µL.

One month after the discharge, the patient on follow-up was found to have thrombocytopenia with platelet count of 2000/µL. He was treated with intravenous immunoglobulin and his platelet count rose to 27,000/µL. For the last year he is on outpatient follow up and receives intravenous immunoglobulin every 4 to 5 weeks with close monitoring of his platelet counts. This treatment helps him to maintain a platelet count of around 50,000 to 100,000/µL.

Discussion

HIV-associated thrombocytopenia (HAT) is a disease with frequent remissions and exacerbations. Treatment options include HAART therapy, steroids, immunoglobulin, danazol, vincristine, interferon alpha, low dose splenic irradiation and splenectomy. Steroids produce an initial rapid response but induce immunosuppression. Immunoglobulins do not have the risk of immunosuppression but lack sustained effect as observed with our patient. Zidovudine is now considered the first line treatment for HAT and is successful in 65 percent of patients.² In our patient, even though we observed a good response of HAART with respect to viral titers, this treatment failed to induce any improvement in platelet count, indicating the absence of direct inhibition of megakaryopoiesis. Splenectomy is reserved for resistant HAT and is curative in 50 percent.¹

Eltrombopag is an orally bioavailable, small-molecule thrombopoietin receptor agonist, that induces differentiation and proliferation of megakaryocytes. Busell and co-workers treated 118 adult patients of refractory chronic idiopathic thrombocytopenic purpura with eltrombopag and noted that 80% of patients had an increased platelet count by day 14. In their study they excluded patients with hepatitis C and HIV.³ Numerous studies have docu-

Figure 1. Bone marrow biopsy showing normocellular trilineage with mild increase in mature neutrophils.
mented the efficacy of eltrombopag in treating thrombocytopenia due to Hepatitis C, which could partially explain the temporary improvement in our patient. Phase III clinical trials are currently ongoing to evaluate the efficacy of eltrombopag in thrombocytopenia due to HIV infection.

Conclusions

Our patient showed an initial good response to eltrombopag, but after one month he returned with thrombocytopenia. The response to eltrombopag in our patient is very interesting since our patient had both HIV and Hepatitis C infections, which makes the thrombocytopenia more resistant to conventional treatment options. In our case, the effect of Eltrombopag was ill-sustained, but the long term effects of eltrombopag cannot be established by this sole report. Hence it can be considered an effective temporizing treatment option for resistant immune thrombocytopenia before splenectomy is considered.

References

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