Severe Immune Thrombocytopenia in a Patient with HIV-HCV Co-infection: Challenges in Management

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Abstract

Immune thrombocytopenia is a well-known complication of both HIV and Hepatitis C virus infections. Management becomes challenging when a patient with HCV-HIV co-infection presents with severe thrombocytopenia. Adverse drug reactions and drug interactions has to be considered while choosing treatment options for such patients. We report such a case which illustrates the difficulty in managing severe thrombocytopenia in HCV-HIV co-infected patients where evidence based clinical decision making helped in choosing the right therapy for the patient.

Introduction

Thrombocytopenia is a well described manifestation of human immunodeficiency virus (HIV) infection as well as chronic hepatitis C virus (HCV) infection. Treatment becomes challenging when HIV-HCV co-infected patients presents with severe thrombocytopenia. We report a case where a HIV-HCV co-infected patient presented with severe thrombocytopenia with bleeding manifestations and challenges faced while managing the same.

Case Report

A 28 year old male from Delhi was evaluated for recurrent sinusitis, fever and weight loss for one year duration. 10 days prior to the presentation he also noticed having bleeding from gums while brushing. He was found to be positive for HIV-1 by ELISA which was confirmed by Western Blot. His CD4+ lymphocyte count was 240/µL and HIV-1 viral load was 1322 copies/ml. Further evaluation showed that he was anti HCV antibody positive. His HCV RNA levels was 68600 copies/ml and the HCV genotype was 3. He was referred for initiation of anti-retroviral therapy (ART) to our clinic.

Upon evaluation at the ART clinic patient was conscious, oriented and was hemodynamically stable. He had purpuric lesions on bilateral lower limbs and wet purpura on the palate. He did not have any palpable lymph nodes. Examination of the abdomen revealed no hepatosplenomegaly. Rest of the physical examination was also normal.

Baseline laboratory evaluation showed a haemoglobin of 12.9 g/dL, a total leucocyte count of 5000/mm³ and a platelet count of 6000/mm³. Ultrasound scan of abdomen done was normal and a fibroscan done showed no evidence of fibrosis of liver. A peripheral smear done showed severe thrombocytopenia with normal red blood cells and leucocytes. A bone marrow aspiration and biopsy done showed normal cell lines in all lineages. CECT thorax and abdomen done showed normal cell lines in all lineages.

Discussion

Our patient had multiple issues to be addressed which can be discussed under the following headings

Thrombocytopenia

Thrombocytopenia in a patient with HCV – HIV co-infection can have a multitude of causes. Thrombocytopenia is seen in 5-30% of HIV patients.¹ The most common cause of thrombocytopenia in HIV patients is HIV-associated thrombocytopenia. The aetiology for HIV associated thrombocytopenia is complex and is due to both immune mediated peripheral destruction of platelets as well is reduced platelet production from the progenitor cells.² However secondary causes of thrombocytopenia needs to be ruled out in all patients with HIV infection. Common secondary causes for thrombocytopenia include infections (viral, bacterial, fungal and parasitic), malignancies, drugs,
hypersplenism and other causes of cirrhosis. In our patient no secondary cause could be found except for co-infection with Hepatitis C virus.

Various studies have shown that 10-36% of chronic ITP patients have underlying chronic Hepatitis C infection. Another study has shown that HCV infection is associated with an elevated risk of developing ITP. Various mechanisms has been postulated for HCV associated thrombocytopenia. Immune mediated peripheral destruction and hypersplenism secondary to portal hypertension are major causes.

Our patient thus had HIV-HCV co-infection. All opportunistic infections and malignancies were ruled out. Ultrasound abdomen showed no evidence of cirrhosis or splenomegaly. A diagnosis of immune mediated thrombocytopenia due to HIV/HCV co-infection was thus made. Considering the severe thrombocytopenia with bleeding manifestation the patient was given Intravenous Immunoglobulin 1g/kg single dose. Steroids were initially not given considering the flare up of underlying occult opportunistic infections and possible progressive liver damage due to Hepatitis C. He was also simultaneously started on ART and antiviral therapy for HCV.

Within 48 hours of initiation of IVIG, his platelet count improved reaching a maximum of 60,000/mm³ on the fifth day. Thereafter the platelet count started falling again and reached a level of 6000/mm³. It was decided to give a second dose of IVIG along with the addition of a second agent for long term management of ITP. Thrombopoietin receptor agonist, eltrombopag was considered in this patient. Eltrombopag was found to increases platelet counts in thrombocytopenic patients with HCV and advanced fibrosis and cirrhosis in randomised trials. The major side effect concern is the risk of thromboembolic event like portal vein thrombosis. Data regarding the use of the thrombopoietin receptor agonists, eltrombopag and romiplostim in HIV associated thrombocytopenia is limited. In five patients of refractory ITP associated with HIV, thrombopoietin receptor agonists improved platelet count in all of them. Two of them however succumbed to thromboembolic complications. We should therefore be careful when using these agents in patients with thromboembolic risk factors including hypertension, smoking, coronary artery disease, and obesity. Our patient did not have any thromboembolic risk factors and thus was a potential candidate for eltrombopag. However our patient could not afford the drug.

Second option considered in the patient was oral glucocorticoids. Prednisolone has been found to be effective in increasing platelet count in patients with HIV associated thrombocytopenia. However only a minority of patients will have sustained increase in platelets after cessation of steroids. Short term steroid use in these patients were not associated with any increased risk of infections. HCV related immune thrombocytopenia has also been shown to be responsive to steroids. However there is a risk of progression of liver disease in HCV patients who are treated with steroids.

Considering all these factors including his financial status, he was started on oral prednisolone (1 mg/kg) with frequent monitoring of liver function. With second dose of IVIG his platelet count increased 2,40,000/mm³. It was decided to taper the steroids once the platelet count are stable, expecting that the underlying primary pathology will be controlled by the antiviral drugs for HIV and HCV. On follow-up of the patient his platelet count was maintained between 80,000 to 90,000/mm³ and prednisolone were gradually tapered and stopped over a period of three months.

Antiviral therapy

This patient required treatment for both HIV and HCV infections. Among the anti-retroviral drugs zidovudine (AZT) is the drug that was found to have significant effect on platelet count as monotherapy. Zidovudine was found to increase platelet count by 60-70% when used at higher doses (1 g/day or more). Combination anti-retroviral therapy (HAART) is at least as effective as zidovudine for the treatment of HIV associated thrombocytopenia. Our patient was started on a fixed drug combination of tenofovir (TDF) (300 mg), lamivudine (300 mg) and efavirenz (600 mg) in accordance with the national AIDS control programme of India.

Options for hepatitis C treatment based on the international guidelines and local availability were either a fixed drug combination sofosbuvir/velpatasvir or a combination of sofosbuvir and daclatasvir. However coadministration of sofosbuvir/velpatasvir with efavirenz containing regimens is not recommended due to decreased concentrations of velpatasvir. Coadministration of daclatasvir with efavirenz decreased daclatasvir concentration as well. But this can be overcome by increasing the dose of daclatasvir to 90 mg instead of 60 mg. Our patient was therefore started on sofosbuvir (400 mg) and daclatasvir (90 mg) for the treatment of HCV.

Pneumocystis jiroveci prophylaxis

Our patient had a CD4+ T cell count < 250/µL and was also on steroids. PCP prophylaxis thus was to be started for him. We had to choose between Trimethoprim-Sulfamethoxazole (TMP-SMX) and Dapsone for this patient. We preferred Dapsone because of two reasons (1) TMP-SMX is known to cause bone marrow suppression and thus can potentially worsen his thrombocytopenia (2) Dapsone was found to be effective in raising the platelet count in some patients with HIV associated thrombocytopenia. Our patient was thus started on Dapsone 100 mg daily.

Follow up

His platelet count remained stable (40,000 to 60,000/mm³) without any bleeding manifestations, 2 months after stopping prednisolone. PCR for HCV RNA done 12 weeks after completion of anti-HCV therapy showed no detectable copies and liver function parameters remained normal. 6 months after ART his CD4+ lymphocyte increased to 264/µL and he did not contract any opportunistic infections in this time period.

Conclusion

Our patient was thus given tenofovir, lamivudine and efavirenz (fixed drug combination), sofosbuvir, daclatasvir, dapsone and prednisolone. His platelets remained stable without any bleeding manifestations and prednisolone was gradually tapered and stopped. The case illustrates the difficulty in managing thrombocytopenia in HCV-HIV co-infected patients where evidence based clinical decision making helped in choosing the right therapy for the patient.

References