An event of Evans even in HIV

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Abstract

Autoimmune cytopenias may be the initial presentation in patients with HIV infection or can develop while on treatment with antiretroviral therapy (ART). These cytopenias usually resolve after initiation of ART. We report a rare case of HIV who presented with Evans syndrome on ART, being refractory to steroids and rituximab but with response to splenectomy.

Key words: Autoimmune cytopenia, Evans syndrome, HIV

Introduction

Hematological complications are common in HIV patients which can be attributed to HIV *per se* or secondary to opportunistic infections and antiretroviral therapy (ART) or even to nutritional deficiency. The prevalence of cytopenias has declined over the course of the HIV epidemic, likely due to earlier diagnosis and use of less toxic combination ART. Autoimmune cytopenias including autoimmune hemolytic anemia (AIHA) or immune thrombocytopenia (ITP) are mostly seen during the initial presentation of HIV and usually resolve after initiation of ART. Evans syndrome (ES), i.e., AIHA with thrombocytopenia, is however very uncommon. We report one such rare case of HIV on ART with ES and a stormy disease course.

Case Report

A 32-year-old female presented to emergency with breathlessness for 5 days. On examination, she was having severe pallor, mild icterus, and moderate splenomegaly (6 cm below costal margin) and no lymphadenopathy. She was also positive for HIV for the last 5 years and on tenofovir + lamivudine + efavirenz as ART. Chest radiograph did not reveal any abnormality. Complete blood picture showed hemoglobin (Hb) – 3.3 g/dl, total leukocyte count (TLC) – 6000/cumm, platelet – 26,000/cumm, reticulocyte count – 11%, total bilirubin – 4.8 mg/dl, direct bilirubin – 1.98 mg/dl, lactate dehydrogenase – 974 u/l, and direct and indirect antiglobulin test – 4+. A request for an urgent packed red cell transfusion was deferred by blood bank in view of difficulty in crossmatching. Bone marrow aspiration and biopsy showed erythroid hyperplasia. She was managed as a case of ES and received IV methylprednisolone for 3 days followed by oral prednisolone at standard doses, along with transfusion of least incompatible packed red cell units. ANA titer was 4+ (homogenous pattern), but ANA profile was negative. A contrast-enhanced computed tomography (CECT) scan of the thorax was normal, and CECT abdomen revealed mild hepatomegaly and splenomegaly with splenic hemorrhages. She was then discharged after few days with oral steroids.

However, she got readmitted the next fortnight with Hb of 3 g/dl, reticulocyte count of 17%, and platelet count of 53,000/cumm. Drug interactions with the ongoing ART were checked. CD4 + count was 121/µl. In view of severity of symptoms and rapidity in fall of Hb, she received four doses of intravenous rituximab at 375 mg/m^2/dose/week followed by continuation of oral prednisolone.

She remained symptomatic even after completion of rituximab doses, and Hb was 4 g%. She got admitted for pain abdomen in the left upper quadrant and re-evaluated. A CECT abdomen this time showed splenomegaly with splenic infarcts. Surgery consultation was done, and we planned for splenectomy for both refractory Evans and painful splenic infarction. She was vaccinated and underwent splenectomy.

On follow-up after 2 weeks, she had Hb –12.9 g/dl, reticulocyte count – 1.6%, TLC – 14,000/cumm, and platelet – 248,000/cumm [Figure 1]. Now almost 4 months postsplenectomy, she is doing well and is still continuing to

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Table 1: Studies related to Evans syndrome

Study	Total patients	Number of ES	Etiology		HIV-associated	Requiring second line therapy	Requiring splenectomy
			Primary	Secondary			
Michel *et al.*[7]	68	68	34	34	0	50	19
Dhingra *et al.*[8]	6	6	6	0	0	0	0

ES=Evans syndrome

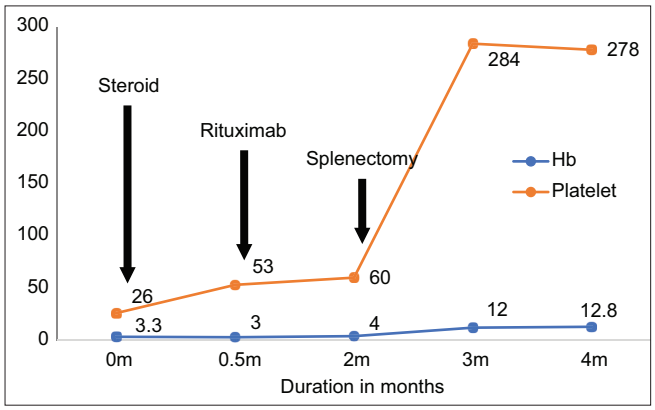

Figure 1: Hemoglobin and platelet trends in relation to therapy (Hb in g/dl and platelet count as *10^3/µl)

have a complete response. She is on follow-up to address any complications following the therapy.

Discussion

ES, which was first described in 1951, is an autoimmune disorder characterized by the simultaneous or sequential development of AIHA and ITP and/or immune neutropenia in the absence of any underlying cause. In the context of HIV, the prevalence of cytopenias has declined over years, likely due to earlier diagnosis and use of less toxic combination ART. However, cytopenias continue to occur, both on presentation or during the course of the disease or its treatment.

HIV can infect hematopoietic stem cells and impair production of any hematopoietic lineage (lymphocytes, granulocytes, red blood cells, or platelets).[1] HIV infection can also suppress the bone marrow through production of proinflammatory cytokines that block hematopoiesis.[2,3] Opportunistic infections due to HIV-induced immunosuppression can also affect developing blood cells, either directly or through cytokine upregulation. Autoimmune phenomena are common in HIV-infected individuals and they reflect chronic immune activation and dysregulation of B- and T-cells.[1] The autoimmune manifestations in HIV are usually more likely during the initial phase of HIV infection when the CD4+ counts are higher or it may be after immune reconstitution following initiation of ART when CD4+ counts tend to restore.[4] However, in the current case, the CD4+ count was 121/µl and autoimmune manifestation in this count is quite unusual. Unlike cases of ITP, these patients have decreased CD4+ (T-helper), increased CD8+ (T-suppressor), and a reversal of CD4:CD8 ratio. Apart from usual mechanisms of autoimmune diseases, molecular mimicry either from opportunist pathogens or from HIV itself may be responsible for autoimmune cytopenias. The institution of ART is likely to resolve or at least improve the cytopenias.

Choi *et al.*[5] showed that in cases of HIV, over 90% of the cytopenias resolved with institution of combination ART.[5] Vannappagari *et al.*[6] showed that the time to improvement of platelet count varied from approximately 1 month in the HIV clinical trials group to approximately 5 months in the CHORUS cohort.[6] Studies related to ES are shown in Table 1. Drug-induced cytopenias can also occur in HIV-infected individuals, often in the setting of antibiotics and/or cancer chemotherapy, and may be due to immune reactions, bone marrow toxicity, or oxidant injury. In contrast to antibiotics and chemotherapy, drug-induced cytopenias due to combination ART are uncommon, though cytopenias were common during the use of zidovudine.

Opportunistic infections can also cause cytopenias in patients with low CD4+ counts (<200 cells/µL) though there is no absolute cutoff. In addition, coexisting malignancies and hemophagocytosis should be evaluated.

However, the occurrence of these autoimmune phenomena is an apparent paradox in the setting of profound immunodeficiency and immunosuppression which characterizes HIV infection and reflects complex nature of the immune system and its regulatory mechanisms.

Conclusion

Although autoimmune cytopenias may be the initial presentation in HIV infection, it is common in individuals on ART and might have been underreported. Workup for cytopenias needs to be done taking into account many differentials, which may be broadened further by the CD4+ count of the patient. Our case of ES highlights the further compromise of immune status following splenectomy in an already immunocompromised host.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Vishnu P, Aboulafia DM. Haematological manifestations of human immune deficiency virus infection. Br J Haematol 2015;171:695-709.
2. Redig AJ, Berliner N. Pathogenesis and clinical implications of HIV-related anemia in 2013. Hematology Am Soc Hematol Educ Program 2013;2013:377-81.
3. Andersen CL, Tesfa D, Siersma VD, Sandholdt H, Hasselbalch H, Bjerrum OW, *et al*. Prevalence and clinical significance of neutropenia discovered in routine complete blood cell counts: A longitudinal study. J Intern Med 2016;279:566-75.
4. Roszkiewicz J, Smolewska E. Kaleidoscope of autoimmune diseases in HIV infection. Rheumatol Int 2016;36:1481-91.
5. Choi SY, Kim I, Kim NJ, Lee SA, Choi YA, Bae JY, *et al.* Hematological

manifestations of human immunodeficiency virus infection and the effect of highly active anti-retroviral therapy on cytopenia. Korean J Hematol 2011;46:253-7.
6. Vannappagari V, Nkhoma ET, Atashili J, Laurent SS, Zhao H. Prevalence, severity, and duration of thrombocytopenia among HIV patients in the era of highly active antiretroviral therapy. Platelets 2011;22:611-8.
7. Michel M, Chanet V, Dechartres A, Morin AS, Piette JC, Cirasino L, *et al.* The spectrum of Evans syndrome in adults: New insight into the disease based on the analysis of 68 cases. Blood 2009;114:3167-72.
8. Dhingra KK, Jain D, Mandal S, Khurana N, Singh T, Gupta N. Evans syndrome: A study of six cases with review of literature. Hematology 2008;13:356-60.