Research Article

A Case Report on Zidovudine Induced Anemia and Its Management in HIV-1 Infected Patient

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ABSTRACT

Patient infected with human immunodeficiency virus-1 (HIV-1) are at increased risk of developing severe hematological complications when they are in Highly active anti retroviral therapy (HAART). Although there is a proven adverse drug reactions with those drugs, but it can be manageable with some supplement therapy which had seen in this case. We report a patient infected with HIV-1 positive that he was on regular treatment with Zidovudine (AZT), Lamivudine (3TC) and Nevirapine (NVP) for the past 2 months developed with the complaints of giddiness, loss of weight and appetite. The patient diagnosed with HIV in the year 2008 and the physician started with the regimen (Stavudine (d4T), Lamivudine, and Nevirapine). While the patient was in this regimen, it caused persistent liver abnormalities, Hepatomegaly and it was identified that Stavudine induced Hepatic Steatosis. Then the patient regimen switched to Zidovudine, Lamivudine and Nevirapine. During his next review after a month, the patient was subjected to laboratory investigations which showed abnormalities in hematological parameters. Hemoglobin-3.3 g/dl, RBC- 1.06×10 6/mm^3, HCT-8.1%, MCH-19pg, MCHC-22.7g/dl, RDW-37%. This was taken to physician desk by clinical pharmacist and it was determined that Zidovudine is the major cause for hematological abnormalities. In view of adverse effects with Stavudine and Zidovudine, the regimen was switched to Tenofovir, Lamivudine and Nevirapine. Then, 4 units of blood were transfused followed by Livogen –Z (Ferrous fumarate (250mg) and Folic acid (1.5mg) as a supplement which showed gradual improvement in hematological parameters with decreased viral load. Before initiating the Zidovudine containing ART regimen, it is essential to monitor the hematological parameters of the HIV-1 infected patient. Health care providers may consider this fact to bring good outcomes in HIV infected patients.

Keywords: Human Immunodeficiency virus, Adverse drug reaction, Zidovudine, Stavudine, Hepatic Steatosis, Anemia.

INTRODUCTION

AIDS is a severe immunological disorder caused by the retrovirus HIV, resulting in defect cell mediated immune response. It is estimated that approximately, 7 million people who live with AIDS can now access highly active antiretroviral therapy (HAART). The increasing number of patients receiving HAART therapy has lead to reduction in AIDS related morbidity and mortality. However, some patients need to change HAART medicines owing to their toxicity.[1] HAART is the combination of several antiretroviral medicines used to slow the rate at which HIV make copies of itself in the body. A combination ART is the current standard of care for treating patient with HIV/AIDS, which is more effective than just one medicine (monotherapy) to treat HIV. Combination therapy consisting of 2 nucleoside analogues [either Zidovudine or Stavudine along with Lamivudine] and one non-nucleoside reverse transcriptase inhibitor (NNRTI) [either Nevirapine (NVP) or Efavirenz (EFV)] are frequently used.[2] AZT, a nucleoside reverse transcriptase inhibitor (NRTI) is one of the earliest antiretroviral agents used as a combination in some of the HARRT regimens for the treatment of HIV/AIDS and it was the first drug approved by the US FDA, preferred mostly by the National AIDS Control Organization (NACO) sponsored ART centres in India.[3,4] Anemia is a very common finding in patient with HIV infection, particularly in individuals with more advanced HIV disease treating with Zidovudine. The epidemiological studies from various parts of the worlds shows that the prevalence of Zidovudine induced anaemia vary widely with 5.42-9.62%[3]. Over the years, there has been a decreased in the recommended dose of Zidovudine from 1500mg/day to 600mg/day, which has improved tolerability. In patient with CD4+ cell counts > 100 cells/ml, hematologic effect occurs in 2%-14% patients. However, the incidence is much greater among the patient with CD4+ cell counts <100 cells /ml.[2]

The most severe adverse effects of zidovudine includes bone marrow suppression, which causes Anemia and Neutropenia, but the most common ADR are nausea, malaise, myalgia, insomnia and headache. Bone marrow toxicity appears to be more common in those patients with advanced disease and is related to dose and duration of the treatment. Data from the AIDS clinical trials group showed that the incidence of anemia and Neutropenia associated with Zidovudine ranged from 1% to 31%, depending on the stage of disease and dose (1200 to 1500mg/day). Anemia can occur as soon as 1-2 months after Zidovudine is started but is more likely to develop after 2-4 months of therapy.[2]

CASE REPORT

47 years old male patient was diagnosed with HIV-1 infection in the year 2008, undergone regular treatment with stavudine, lamivudine and Nevirapine combination

was on routine medical examination. He was asymptomatic until 2011, and then he developed fever not associated with chills and rigor, abdominal pain in the right hypochondrium. His CD4 count was found to be 126(Normal 500-1000 cells/mm^3). His Liver Function Test's were deranged. Over this period, he had progressive abnormal enlargement of Liver. His CT abdomen showed Fatty liver (Multiple Heterogeneous mass seen on the right side of the liver) with Hepatomegaly (22cms). Due to persistent abnormal LFT's and Hepatomegaly with ascites, it was determined that Stavudine induced Hepatic Steatosis in 2012, and his regimen was changed to Zidovudine, Lamivudine and Nevirapine. After 1 month of using this regimen the patient complained of giddiness, heaviness in head, loss of weight and appetite for past 2 weeks. Then patient was made to stay in the hospital, on investigation, his vitals are stable, abdomen examination was suggestive of Hepatomegaly and spleenomegaly.

Hematological parameters showed RBC-$1.06\times10^6/mm^3$, Hb 3.3g/dl (Normal range 11-16 g/dl), HCT 8.1% (Normal range 35-50%), MCH 19 pg (Normal range 26-33 pg), and MCHC 22.7 g/dl (Normal range 31-35 g/dl), negative HBsAg(Hepatitis C virus antibodies), Serum Total cholesterol -160mg/dl (Normal range 130-220 mg/dl), Triglyceride level - 99 mg/dl (Normal range up to 170 mg/dl). His CD4 count was found to be 185cells/mm^3.

We, Pharm.D Students, by assessing the Patient medication chart we suggested that Zidovudine induced anemia and it was taken to the physician desk. After physician's consultation the patient was treated with 4 units of blood transfusion for anemia along with Livogen-Z (ferrous fumarate-250mg and folic acid-1.5mg). In view of adverse effects with Stavudine and Zidovudine he was shifted to a combination therapy of Tenofovir, Lamivudine, and Nevirapine. At the time of discharge RBC value was found to be 2.89 $\times10^3$, Hb- 9.1g/dl, CD4 count was 227 cells/mm^3, and the patient was clinically stable.

DISCUSSION

Anti retro viral therapy are associated with several adverse events such as peripheral neuropathy, myopathy, pancreatitis, nephrotoxicity, lactic acidosis, hepatic steatosis and bone marrow suppression. The most common adverse effects of Zidovudine include bone marrow suppression (Anemia and Neutropenia), nausea, malaise, myalgia, insomnia and headache.[6, 7]

Bone marrow toxicity appears to be more common in those patients with advanced disease and is related to dose and duration of the treatment. The AZT-induced anemia is rather unique and can be properly managed. The exact mechanism of anemia is still unknown. It was hypothesized that AZT may suppress erythropoisis or inhibit erythroid stem cells, thus ensuring pure red-cell aplasia (i.e; decreased reticulocyte counts and hemoglobin levels without hemolysis or blood loss), increasing MCV and elevating erythropoietin level. The AZT-induced anemia clearly presented after 4 weeks of AZT-based therapy and the high prevalence started from 4-24 weeks (or 1-6months). This could probably explain why iron supplements, folic acid (or Vit B12), or blood transfusions can be used to manage the anemia based on its severity.[1]

More recent studies of combination antiretroviral therapy have confirmed the relative low incidence of severe anemia at lower doses of zidovudine. Despite these findings, many patients receiving the drug in clinical practice will require occasional transfusion or change in drug therapy to ameliorate this toxicity.

CONCLUSION

This case mainly enlightens the potential toxicities of anti retroviral therapy in particularly the drug Zidovudine which led to severe Anemia, which can be prevented by occasional transfusions or alternative therapy or by using an iron supplement, regular follow up and monitoring the patient by assessing the level of CD4 count, hemoglobin and BMI may improve the quality of life in HIV-1 infected patients.

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