Case Report

Zidovudine induced late bone marrow suppression : A rare occurrence

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Zidovudine is one of the important components of Anti retroviral Therapy in India. However, therapy with Zidovudine is associated with many side effects. Anemia or Bone marrow suppression leading to pancytopenia is common with Zidovudine in early days of initiation of therapy. We report a case where patient developed pancytopenia, four years after continuous Zidovudine therapy. Regular blood count monitoring is essential in patients on Zidovudine.

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Key words **: Zidovudine (AZT), Anemia, Bone marrow suppression, (ART) Anti retroviral therapy**

Since 2000, ART is widely available in India. Because of cost constraints, AZT is still the main drug used in many parts of our country. Anemia or Bone marrow suppression is seen usually within few months of starting AZT therapy. The incidence of this side effect is more if before initiation of therapy there is presence of anemia. It is general consensus to avoid AZT in presence of anemia[1]. In addition to AZT, simultaneous use of other drugs like cotrimoxazole[2], Amphotericin B, Dapsone, Sulfadiazine increases the chance anemia. Some opportunistic infections like Mycobacteria, parvovirus can also cause bone marrow suppression in patients on ART. We report a case of HIV infected patient on ART who developed bone marrow suppression after 4 years of continuous AZT therapy. This side effect is rare to develop years after initiation of AZT. Anticipating this rare event and continuous blood count monitoring is recommended even if patient tolerates initial AZT therapy.

Case Report

A 30 years old female, housewife, was screened for HIV infection in view of history of herpes zoster. Her husband had died 6 years before and was HIV-1 infected. She was asymptomatic and her general and systemic examination was normal. She was positive for HIV-1 with ELISA and the same confirmed by western blot in August 2005.

Investigations — Her baseline investigations were Hb -11.9 gm/dl, TLC- 7500/dl (N64, L24, E9, and M3), Platlets-131000/dl, Liver and Kidney functions were normal. She was HBsAg and TPHA non reactive. Ultrasonography of abdomen showed absent right kidney with compensatory hypertrophy of left kidney. Baseline CD4 was 184/micro liter. Plasma viral load was not done. She was started on AZT+3TC+NVP from August 2005. She also received cotrimoxazole prophylaxis till august 2007.

Follow-up — On follow up after 2 months her investigations were Hb-9.2 gm/dl, TLC-3100/dl (N48, L45, E2, and M5) MCV-94.7, Platelets-131000/dl, and SGPT-14. She was shifted to D4T (Stavudine) +3TC+NVP from Oct 2005 because of anemia. One month later, hemogram improved (Hb-10.4gm%, TLC-4000/dl and platelets – 240000/dl). Her serial viral loads and CD4 counts are shown in Table 1.

Table 1 — *Serial PVL and CD4 counts*

Month	CD4 count per microlitre	Plasma Viral Load (copies/ml)
August 2005	184	Not done
August 2007	312	< 20
Feb 2008	360	Not done
Nov 2008	576	<50
March 2010	392	<50
Dec 2011	501	<20
Sept.2012	426	<20

All PVL were done by RT PCR except in Dec 2011 (COBAS TAQMAN)

After 3 years of D4T therapy, she was re-shifted on AZT+3TC+ NVP in February 2008, because of lipoatrophy. The option of other ART was not considered due to non affordability.

She developed fever, anorexia and nonproductive cough in Jan 2012. She was investigated in other hospital at her place and was found to have pleural effusion. The pleural effusion was exudative with lymphocytic predominance. She was advised to take 4 drug ATT (Isoniazide (H), Rifampicin (R), Pyrazinamide (Z) and ethambutol (E)). Her ART was not changed by her treating Doctor, at her town, probably was unaware of drug interactions between NVP & Rifampicin. Rifampicin is known to reduce blood levels of NVP low enough as if being given in sub therapeutic doses to produce resistance to NVP. Hence NVP is changed to Efavirenz when Rifampicin is to be given.

She visited our hospital in March 2012 with extreme fatigability, weight loss, and anorexia. On examination she had right sided pleural effusion. Her lab results were Hb-2.3 gm%, MCV-127fl, TLC-3300/dl (N51,L44,M5), Platelet count- 88000/dl, Sr. Ferritin-623ng/ml (F-4.63- 204ng/ml), Sr. Lactate 15.1 mg/dl(4.5-19.8mg/dl), Sr. Creatinine 1.04mg/dl, Pleural fluid Protein 3.58 Gm%, leukocyte count- 580 (N 2%,L 98%), ADA-24.2 (N <25). USG abdomen was normal except absent right kidney. Her bone marrow trephine biopsy showed hypo plastic marrow with megaloblastoid changes. Serum erythropoietin-17347 mIU/Ml (5.4-31). Her regimen was switched to 3TC+D4T+EFV and RHE was continued. She also received red cell support for anemia. After 2 months of follow up her Hemogram showed Hb- 11.2gm%, TLC-3600/dl (N41,L47,E3,M8), platelet 196000/dl. She received 6 months of ATT and is on 3TC+D4t+NVP. She is doing well at present. (Hb 14, TLC-5840, Plt-214000)

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Discussion

Zidovudine is important component of ART in India. Common side effects of AZT are anemia[3,4] granulocytopenia, lactic acidosis, hepatic steatosis, headache and nausea.

Anemia is most common hematologic abnormality in HIV infected patients. The specific reversible causes are drug toxicity, opportunistic infections like mycobacteria, parvovirus etc, and nutritional deficiencies. AZT causes maturation arrest in the marrow causing pancytopenia. The effect is more pronounced in erythroid precursors leading to anemia[5]. High serum erythropoietin levels can differentiate between anemia secondary to AZT and anemia due to other causes[6].

The phenomenon of anemia / bone marrow suppression secondary to AZT is seen mostly within few days to one year of initiating the therapy[7].

In our patient, the bone marrow suppression was seen after four years of uneventful AZT therapy from February 2008 to January 2012. She initially had mild anemia which subsided on shifting to D4T.Re- introduction of AZT has lead to severe bone marrow suppression. She had pleural tuberculosis for which she was on ATT (HRZE). There are no known drug interactions between HRZE and AZT which can increase the drug levels of AZT in blood[8]. INH itself can lead to sideroblastic anemia which was not the blood picture in our case. Moreover, she had high serum erythropoietin levels and her blood picture improved after stopping AZT.

At present she is on Stavudine, lamivudine and Nevirapine and her viral load is well suppressed.

This case highlights the importance of regular monitoring of blood counts in patients on AZT even after one year of uneventful therapy. Timely drug withdrawal can prevent future complications due to bone marrow suppression. Learning from this case, it would not be wrong to suggest avoiding re-challenge of AZT in such cases.

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