Zidovudine Induced Pure Red Cell Aplasia: A Case Report

***Hassan, A *Babadoko A A, *Mamman, A I ** Ahmed SA**

*Departments of *Haematology and **Pathology Ahmadu Bello University Teaching Hospital, Zaria Nigeria*

Abstract

Background: *Zidovudine, a Nucleoside Reverse Transcriptase Inhibitor (NRTI) is one of the earliest antiretroviral agents used as a combination in the Highly Active Antiretroviral Therapy (HAART) for the treatment of HIV infection. Its use is however not without adverse effect particularly bone marrow aplasia leading to varying degrees of cytopenias predominantly anaemia. This calls for adequate evaluation and monitoring of patients on this drug. Its major side effect of anaemia limits its use in some patients. We report a case of Zidovudine induced anaemia and bone marrow aplasia in a patient infected with HIV.*

Method: *The Hospital case note of a 27 year old widow with HIV infection and anaemia, who has been on HAART (Zidovudine, Lamivudine and Nevirapine) for one year, was reviewed.*

Result: *She presented with severe anaemia (PCV of 0.05), White cell and platelet counts were within normal limits and reticulocyte count of 0.001%. Bone marrow aspiration and biopsy were diagnostic of pure red cell aplasia on a background hypocellular marrow. She was transfused with four (4) units of packed cells and Zidovudine was replaced with Stavudine. She made remarkable improvement and remains transfusion independent afterwards.*

Conclusion: *Zidovudine is well a known cause of anaemia and thus should be used with caution in the initiation of antiretroviral therapy.*

Keywords: HIV, Zidovudine, Anaemia, Bone Marrow Aplasia.

Date Accepted for publication: 11th June 2009
Nig J Med 2009; 332 - 333

Introduction

The introduction of antiretroviral agents in the last two decades has remarkably improved the quality of life and prolonged the life of people living with HIV and AIDS all over the world[1].

There are various classes of antiretroviral agents and each class is associated with peculiar advantages, and adverse effects. The nucleoside reverse transcriptase inhibitor (NRTI) of which Zidovudine was the first antiretroviral agents to be licensed by the United states Food and Drug Administration in the late 1980s for treatment of HIV/AIDS[2]. Zidovudine was later found to be associated with life threatening bone marrow suppression mostly presenting as anaemia[2,3,4].

Case Report:

A 27 year old female was referred to us on account of severe anaemia and had received seven units of whole blood over a period of two months in a private hospital. She was started on antiretroviral therapy with Duovir® (combination of Zidovudine and Lamivudine) 10 months earlier by a family doctor in the same private hospital after diagnosing the patient with HIV infection. Her husband died two months earlier due to HIV infection.
No other ancillary investigations were carried out prior to commencement of the antiretroviral agents in the private hospital.

Examination revealed severe pallor, mild pitting pedal oedema, pulse rate of 124/min a third heart sound and a haemic murmur.

The haemogram showed a packed cell volume of $0.5^{L}/_{L}$, total white cell count of $4.4x10^{9}$/L and a platelet count of $202x10^{9}$/L. The $CD4^{+}$ lymphocyte cell count was 280 cells /μL of blood. The serum urea, electrolytes and liver function test were within normal limits. Stool microscopy revealed no ova or parasite. A repeat HIV test confirmed the patient as HIV 1 positive.

The bone marrow aspirate showed adequate fragments with a grossly hypocellular marrow with paucity of erythroid precursors but with sparing of other cell lineage.

Trephine biopsy of the bone marrow also confirmed the hypocellular marrow with paucity of erythroid precursors.

A diagnosis of Zidovudine induced pure red cell aplasia with hypocellular bone marrow was made.

Correspondence to ***Dr. Abdul-Aziz HASSAN,*** *Email- hassanyola@yahoo.com*

The patient was then transfused with four (4) units of packed red cells. and based on these findings the patient was commenced on Highly Active Anti Retroviral agents (HAART) according to the Nigerian National Guidelines[5] with Stavudine (d4T) 30mg twice daily, Lamivudine (3TC) 150mg twice daily and Nevirapine (NVP) 200mg once daily for the first two weeks then 200mg twice daily for the next two weeks. She was also placed on haematinics.

Post transfusion haematocrit was 0.21L/L .Repeat complete blood count at two weeks showed a haematocrit of 0.26L/L and reticulocyte count was 5%. She was then discharged home and followed up in the clinic. Six months later her haematocrit was 0.35L/L and at twelve months it was 0.38L/L.

Discussion

Zidovudine was the first antiretroviral agent that was licensed for the treatment of HIV/AIDS in 1989, however it was soon to be discovered that it has the major side effect of severe anaemia and possibly pancytopenia.[2, 3, 4] In patients with HIV infection there are numerous causes of anaemia which range from the viral infection of progenitor cells to the cytokines produced by the virus. [2, 3, 4] Patients are also prone to anaemia of chronic disorder and reduced intake of nutrients[2, 3, 4]. In this patient anaemia resolved with discontinuation of the drug and Zidovudine was thus implicated although the patient was not re-challenged as was done in studies by **Cohen H** et al.[5]

In the index patient it is clearly seen that inadequate evaluation and the use of inappropriate antiretroviral agents, in this case a two drug combination (ZDV & 3TC) was responsible for the anaemia. The Nigerian national antiretroviral guidelines recommended the use of triple therapy, which was not used for this patient and this led to the pure red cell aplasia.[6]

Conclusion

Antiretroviral treatment guidelines should be made available to all medical practitioners. Treatment of HIV/AIDS requires that the patient be adequately evaluated to assess the suitability of commencing antiretroviral agents and the choice of the agent to be used. Careful and detailed history taking, full clinical examination and laboratory investigations are mandatory.

References

1. Grossman H. AIDS at 25: A Quarter of Medical Miracles. The Dramatic Impact of Highly Active Antiretroviral Treatment 2006. Also available at URL: http://www.medscape.com
2. Crumpacker C (ed). Antiviral therapy. In: Fields Virology. 4th ed. London: Lippincott Williams & Wilkins; 2001. p. 672-675. 3. Costello C (ed). Haematology in HIV disease. In: Postgraduate Haematology. 5th ed. Philadelphia: Blackwell Publishing; 2005. p. 380-394.
4. Lee GR, Foerster J, Lukens J, Paraskevas F, Greer JP, Rodgers GM (eds). Wintrobe's Clinical Haematology. 10th ed. London: Lippincott Williams & Wilkins; 1998. p. 3526-3529.
5. Cohen R, Williams I, Matthey F, Miller RF, Machin SJ, Miller IV. Reversible Zidovudine induced pure red aplasia anaemia. AIDS 1989 3(3)177-8.
6. Guidelines for the use of Antiretroviral Drugs in Nigeria. Federal Ministry of Health, Nigeria. 2005.