Case Report

Efavirenz induced haemolytic anaemia : A rare case report

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ABSTRACT

HIV infection/ AIDS is a global pandemic, with its prevalence in almost every nation. The mainstay of management in patients with HIV infection is the highly active anti-retroviral therapy (HAART). Anaemia is a known toxicity with nucleoside reverse transcriptase inhibitor, Zidovudine. We report here a rare side effect of efavirenz causing haemolytic anaemia which subsided after withholding the drug.

Keywords: Antiretroviral therapy, hemolysis

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is caused by the RNA virus, Human immunodeficiency virus (HIV). The HIV infection has spread across the globe affecting almost every society. The highly active antiretroviral therapy was commenced in 1995-96[1] which resulted in marked decline in the AIDS incidence. Efavirenz was known to cause dermatological manifestations, hepatic and lipid abnormalities. Efavirenz causing haemolytic anaemia is rare and not many cases were reported. We would like to report this case to create awareness to the care providers regarding this unusual manifestation of efavirenz.

CASE REPORT

A 38 year old lady was admitted to the hospital with two months history of intermittent fever with significant weight loss and decreased appetite. She had history of tuberculoma in January 2016 (diagnosed elsewhere). She received category-1 anti-tubercular therapy and the course was completed uneventfully. Generalised lymphadenopathy was present. She was diagnosed to have HIV disease. Absolute CD4 count was 139cells/mm^3. Anti-retroviral therapy with Lamivudine (300mg/day), Tenofovir (300mg/day) and Efavirenz (600mg/day) was started along with Cotrimoxazole [Trimethoprim/Sulfamethoxazole] (160/800 mg/day) for prophylaxis of Pneumocystis carinii pneumonia (PCP).

Three weeks later, she presented with severe anaemia in congestive cardiac failure. On examination, she had pallor, bilateral basal crepitations, functional systolic murmur in pulmonary area, bilateral pitting pedal oedema, tachycardia (110 beats/min) and hypotension (90/60 mm of Hg). Her haemoglobin was 2.2g/dl, total leucocyte count was 5,100 cells/mm^3 and platelet count was 2,80,000/mm^3. Peripheral smear showed severe degree of anisopoikilocytosis, spherocytes with extensive clumping and rouleaux formation of red blood cells. Leucocytes and platelets were normal in number and morphology. These features were suggestive of haemolytic anaemia. Corrected reticulocyte count was 2.5% (normal 1.5% to 2.5%). She was transfused with two units of packed red blood cells. Lactate dehydrogenase (LDH) was 1,210 U/L (normal < 250 U/L). Direct coombs test was positive. Liver function tests were deranged with high aspartate transferase 152 U/L (normal < 40 U/L) and alanine transferase 73 U/L (normal <40 U/L). Total bilirubin was 1.3mg/dl (direct bilirubin 0.5mg/dl and indirect

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

bilirubin 0.8mg/dl). Alkaline phosphatase was 63 U/L (normal 60-170 U/L). Renal function testes were normal. Drug induced haemolytic anaemia was considered at this stage. As Cotrimoxazole was known to cause haemolytic anaemia[2], it was stopped and patient was started on steroid therapy with prednisolone at 40mg/day. She was transfused with two more units of packed red blood cells. Her haemoglobin was 7gm/dl after transfusions and steroids. She was discharged with plan to taper the steroids slowly over 3 months. Advised to continue the medications and review with haemoglobin report.

She came for follow-up after 2 weeks with severe anaemia. Haemoglobin was 4gm/dl with normal total leucocyte and platelet count. Steroids were continued at same dose. An extensive literature search was done and efavirenz was withdrawn as it causes haemolytic anaemia[3]. Nevirapine was administered at 200 mg/day dose with initial dose of lamivudine and tenofovir. She was transfused 2 units of packed red blood cells. She was symptomatically better and was discharged with steroids and anti-retroviral therapy (lamivudine, tenofovir and nevirapine). She came for follow-up after fifteen days. Haemoglobin was 10gm/dl and she was doing well. Lactate dehydrogenase was 950 U/L. Later, steroids were tapered and stopped over a month. She was followed-up regularly every month for 6 months. Repeat haemoglobin after 2 months was 12gm/dl. Her absolute CD4 count after 6 months of anti-retroviral therapy was 454. Lactate dehyrogenase was 240 U/L. Haemoglobin was 12.5gm/dl.

DISCUSSION

This middle aged lady with history of tuberculoma in the past was diagnosed with stage 4 HIV infection at admission and anti-retroviral therapy with lamivudine, efavirenz and tenofovir was commenced with cotrimoxazole. She had hemolytic anaemia 2 weeks later. Cotrimoxazole was stopped and she was transfused 4 times. However, her anaemia didn't improve. After a thorough review of literature, we found that efavirenz can cause haemolytic anaemia. We discontinued efavirenz and Nevirapine was introduced with lamivudine and tenofovir. Hemolysis was resolved and she was clinically better. However, we hadn't done a rechallenge with efavirenz for definite proof for the haemolytic anaemia due to efavirenz.

Various factors contribute to anaemia in patients with HIV infection[4]. (1) It may be nutritional as the patients have anorexia which improves with initiation of anti-retroviral therapy. (2) Anaemia can be due to opportunistic infections. (3) The anti-retroviral therapy suppressing bone marrow leads to anaemia. (4) Haemolysis secondary to drugs causes anaemia.

Drugs are a rare cause of immune haemolytic anaemia. The drugs can cause hemolysis by one of them mechanisms. (1) Drug-dependent antibodies which are seen only when there is drug. (2) Drug independent antibodies where autoantibodies are produced against red blood cells as the immune system is effected by the drugs. (3) Drugs bind to the proteins on the red blood cell membrane; the entire complex is phagocytosed. This is the most widely accepted mechanism[5]. Many drugs are known cause haemolytic anaemia. This is observed even in patients without Glucose 6 Phosphate Dehydrogenase deficiency. This is similar to auto-immune haemolytic anaemia in presentation. Various drugs were implicated in this category. Common anti-retroviral agent to cause haemolytic anaemia is Zidovudine.

Similar case was reported where the patient first developed hypersensitivity to nevirapine; haemolytic anaemia when nevirapine was switched with efavirenz; she was better once efavirenz was withdrawn and lopinavir was started[4]. Efavirenz is a non-nucleoside reverse transcriptase inhibitor. Its toxicity is usually associated with skin rash, mood disturbance, raised hepatic enzymes and lipid abnormalities. We report this case as efavirenz

induced haemolytic anaemia is unusual. It has to be brought to the knowledge of the practitioners for early diagnosis and effective management. It should be looked for when a HIV patient is started on efavirenz.

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