



## A Rare Case of Autoimmune Hemolytic Anemia as a Presenting Complaint of HIV Infection

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### Abstract

*HIV patients commonly suffer from haematological complications and it can be because of infection per se or secondary to opportunistic infections and antiretroviral therapy. However overt autoimmune hemolytic anemia (AIHA) is rare although anemia and a positive direct anti-globulin test are each frequently observed in HIV infection. We report a rare case of recently diagnosed HIV infected asymptomatic patient with severe warm type autoimmune hemolytic anemia as a presenting complaint, very few reported from India. The clinical and hematological features were suggestive of autoimmune hemolytic anemia. He was treated with oral prednisolone (1mg/kg/day) and was transfused with 2 unit of packed RBC. At a follow-up visit, he had normal hemogram and liver function test. This case highlights the uncommon presentation of HIV syndrome and illustrates the importance of checking HIV status in patients with autoimmune hemolytic anemia.*

**Keywords:** AIHA (Autoimmune hemolytic anemia), HIV (human immunodeficiency virus), direct antiglobulin test (DAT).

### Introduction

The prevalence of anemia in HIV/ AIDS patients is high, with multiple etiologies like anemia of chronic disease, HIV related myelodysplastic syndrome, iron deficiency anemia, bone marrow suppression due to direct involvement of marrow by some infective process.<sup>[1]</sup> Autoimmune hemolytic anemia (AIHA) is rare and potentially a fatal complication of HIV. A positive direct antiglobulin test (DAT) is found in approximately 20 % of HIV infected patients with

hypergammaglobulinemia.<sup>[2],[3]</sup> Despite high prevalence of direct coombs test positivity in this group, AIHA is rarely seen as an initial manifestation in HIV.<sup>[4]</sup> The following case highlights the uncommon presentation of HIV infection.

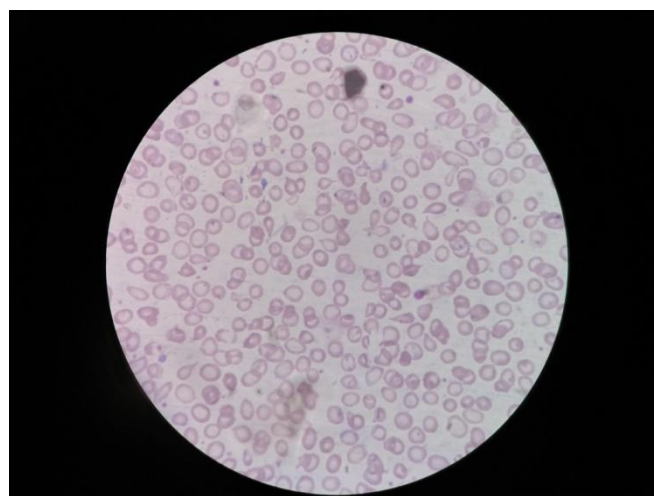
### Case history

A 67 year old male afebrile, non diabetic, normotensive resident of Jaunpur, Uttar Pradesh, India, working as a driver in Kolkata, West

Bengal, 1600 km from his home town, was admitted with complaints of generalized weakness, easy fatigability and jaundice for one month. There was no history suggestive of intravenous drug abuse, alcohol intake, therapeutic drug intake or known allergies, hematemesis, melena, cough with expectoration, hemorrhoid or weight loss. He had no past history of blood transfusion or any other major surgical or medical illness. Family and personal history were noncontributory. On examination he had severe pallor, icterus and splenomegaly of 2 cm. Review of other systemic examinations were unremarkable. Laboratory evaluation revealed haemoglobin 48 g/l with MCV 134 fL, total cell counts  $5.8 \times 10^9$ /l, total platelet count  $120 \times 10^9$ /l, total bilirubin of 109.8 mmol/l, indirect bilirubin of 59.4 mmol/l. Alkaline phosphatase (ALP) is 111 U/L. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) was raised 5.5 and 2.5 times above the normal limit, respectively. Renal function test were within normal limit. Albumin globulin ratio was normal. On further evaluation of anemia, serum iron and total iron binding capacity (TIBC) was found to be 22 mmol/l and 57 mmol/l respectively. Leishman stained peripheral blood smear seen under high power field showed anisopoikilocytosis with presence of microcytes, microspherocytes, and tear drop cells [Fig 1]. The reticulocyte count (RC) was 42% (corrected reticulocyte count – 13.44%). There were no bite cells or Heinz bodies or malarial parasite seen.

Lactate dehydrogenase (LDH) was 620 IU/L (normal value 230-460 IU/L) at the time of admission which raised to 3855 IU/L the following day. Stool for occult blood was negative. Ultrasound abdomen was suggestive of moderate splenomegaly with normal liver echo structure and bilateral kidney size with absence of abdominal lymphadenopathy and ascites. Routine microscopy of urine and chest X ray was normal. Bone marrow examination showed erythroid hyperplasia. DAT was positive for warm antibodies (IgG type). The profound anemia,

jaundice and splenomegaly with reticulocytosis, raised LDH and positive DAT confirmed the diagnosis of autoimmune hemolytic anemia. Screening for secondary causes for autoimmune hemolysis was done. Serology for viral infections (Hepatitis A, B, C) was negative. A normal CT scan, negative collagen profile and rheumatoid factor excluded underlying malignant condition and connective tissue disorders. There was no evidence of acute infection with Syphilis. Serological tests for cytomegalovirus, Epstein-Barr virus, Chlamydia pneumoniae, Mycoplasma pneumonia and parvovirus B19 was negative. He was tested for HIV as per NACO protocol and found to be reactive. CD4 cell count is  $812 \times 10^6$ /l. HIV induced AIHA was considered as the final diagnosis. He was treated with oral prednisolone (1 mg/kg/day). The patient received a transfusion of 2 units packed red blood cells. There was a dramatic improvement with a rise in hemoglobin to 9.2 g/dl and a reduction in reticulocyte count to 20% (corrected reticulocyte count – 9.33%). There was a concurrent reduction in polychromasia and microspherocytes on the peripheral smear. As per recent NACO guidelines 2011, antiretroviral therapy will be commenced if CD4 cell count falls below  $350 \times 10^6$ /l or when patient is in stage III or IV. After 6 months of follow up, he was asymptomatic and currently doing well on maintenance doses of steroids.



**Fig. 1** Leishman stained peripheral blood smear seen under high power field showed anisopoikilocytosis with presence of microcytes, microspherocytes, and tear drop cells

### Discussion

In this case AIHA was the presenting manifestation of HIV infection which is unusual. The patient is asymptomatic, has normal CD4 count with no evidence of any other opportunistic infections and is in stage I. The diagnosis of AIHA in previously diagnosed HIV infected patient has been described in only 22 cases in the literature till 2010.<sup>[5]</sup> Average age was 36.8 years and all of them had low CD4 count with reticulocytopenia in most of the cases. Among them only one case of AIHA was diagnosed during HIV seroconversion illness. It was observed that mixed direct antiglobulin pattern (IgG and C3b positive) was more common around 75%. The majority of patients were treated with corticosteroids either alone or in combination with other modalities like intravenous immunoglobulin and splenectomy. However a few died of causes like pulmonary embolism, disseminated intravascular coagulation.<sup>[5]</sup> A considerable number of reports<sup>[6]</sup> describe that clinically significant autoimmune haemolytic anaemia can occur in HIV patients with or without reticulocytosis.<sup>[7]</sup> However the frequent lack of reticulocytosis and presence of bone marrow erythroid hyperplasia lead to the risk of under diagnosis of AIHA in HIV-infected patients.<sup>[8]</sup> In our case, the retroviral infection may play a role in the pathogenesis of AIHA as the initiator of the disease by directing the auto antibodies against the red blood cells. Since HIV testing in this patient was not done before, we cannot say whether AIHA occurred during HIV seroconversion illness. Several studies have demonstrated the high incidence (i.e.21%) of direct Coomb's test positivity in patients with HIV infection though frank hemolysis being reported very infrequently.<sup>[7]</sup> Since CD4 count was on the higher side, we can easily say that it was an earlier manifestation of HIV making this case significant and it is really important to check for HIV status in patient of AIHA.

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