Hematological Abnormalities in Early and Advanced HIV Infection Patients

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INTRODUCTION

HIV infection targets mainly the immune system and hence hematological abnormalities are among the most common clinicopathological features. These hematological abnormalities vary from anemia, leukopenia, and thrombocytopenia including bone marrow dysplasia. The pathophysiological basis for these hematological abnormalities may include impaired hematopoiesis, immune-mediated cytopenias, and/or coagulopathies especially in the advanced stage of the disease.¹ ²

HIV destroys the T-cell lymphocytes which in turn disables the immune system to defend the body against diseases and malignancies. This will also lead on to various devastating opportunistic infections paralleling the declining immunity. Peripheral blood picture findings are highly variable depending on the clinical severity of immunodeficient state.³

In general, hematological abnormalities progress in frequency and severity with the progression of the disease from the asymptomatic HIV carrier state to the advanced stage of the disease.⁴ About 15% of asymptomatic HIV
carriers have mild anemia. The prevalence of anemia increases from 30% to 40% in those with the early disease to 75-90% in advanced patients. It may be still higher in HIV-infected infants and children.\textsuperscript{5}

Granulocytopenia with or without lymphopenia occurs in approximately 8% of asymptomatic HIV carriers and as many as 70-75% of children and adults with AIDS. While anemia and granulocytopenia tend to occur concomitantly with a severity that parallels the course of the HIV infection, thrombocytopenia can occur independently of other cytopenias and at all stages of HIV infection. Isolated thrombocytopenia may be the first manifestation of HIV infection.\textsuperscript{6,7}

The accurate measurement of CD4 cell counts is essential for the assessment of immune system of HIV-infected person as the pathogenesis of AIDS is largely attributable to the decrease in CD4 lymphocyte counts. CD4 counts help to categorize the HIV-infected patients from mild to severe form of the disease and in turn guide the treatment. It also depicts the patient's predisposition to various opportunistic infections.

Among the neoplastic complications, Kaposi's sarcoma is the most common neoplasm in patients with AIDS, occurring with a 700 fold increase in HIV-infected patients compared with age-matched, non-infected controls.\textsuperscript{8} Other malignancies commonly seen in patients with AIDS are non-Hodgkin's lymphoma, seminoma, and non-melanoma skin cancer.\textsuperscript{9}

The combined effect of the above alterations in hematological parameters will significantly compromise patient's quality of life who are already overburdened by the treatment of primary viral infection, secondary infections, and neoplastic complications. These hematopoietic abnormalities, in turn, lead to poor tolerance to therapies necessitating dose reductions, alteration of drug regimens, or interruption of therapies.

**METHODOLOGY**

A total of 100 patients detected to be HIV-positive as per the WHO criteria attending the Department of Medicine and Dermatology, JSS Hospital, Mysore during the period of March 2008-April 2010 were enrolled for the study. These patients were assigned into either Group A (HIV-positive patients with CD4 count > 200 cells/cumm) or Group B (HIV-positive patients with CD4 count < 200 cells/cumm).

**Inclusion Criteria**

HIV-positive patients as per the WHO criteria irrespective of their anti-retroviral treatment status, attending the Department of Medicine/Dermatology, JSS Hospital, Mysore.

**Exclusion Criteria**

1. Patients with previously known hematological disorders
2. Congenital hematological disorders
3. Age <18 years
4. Pregnant woman
5. Critically ill patients.

Data were collected using a pre-tested proforma to meet the objectives of the study. The purpose of the study was carefully explained. Informed and written consent was obtained from all the patients prior to the study.

Detailed history, general, and systemic examination was conducted with emphasis on signs suggesting hematological system involvement such as pallor, clubbing, jaundice, edema, glossitis, lymphadenopathy, koilonychias, angular stomatitis, petechiae, and hepatosplenomegaly.

The investigations included complete hemogram with peripheral blood picture, bone marrow cytology, and CD4 cells count by Flow cytometry by a standard technique using Becton-Dickinson FAC Scan.

**Statistical Analysis**

Descriptive statistics was expressed as mean ± SD (range). Results were compared using Chi-square test of significance. A $P < 0.05$ was considered statistically significant.

The study was carried out after obtaining permission from the Institutional Ethics Committee.

**RESULTS**

The patients were divided into two groups according to their CD4 counts: Group A (HIV-positive with CD4 counts >200 cells/cumm) and Group B (HIV-positive with CD4 counts <200 cells/cumm). Out of the 100 patients studied, 50 patients were included in each group.

Age and sex distribution: Most of the patients were males in the age group of 21-40 years (74%). The mean age of the patients in the present study was 33.8 years. In the Group A patients, males were predominant in the age group of 31-40 (50%), whereas females were predominantly in the age group of 21-30 (50%). In Group B patients, most of the patients were males and in the age group of 31-40 years (44.75%), whereas females were predominantly in the age group of 41-50 (66.67%) (Table 1).
Symptoms and Signs: Predominant symptoms in Groups A and B were fever (78% and 80%) and weight loss (62% and 66%). Predominant signs in Group A were pallor (70%) and adenopathy (8%), whereas in Group B was pallor (80%) and oral candidiasis (44%) (Table 2).

Peripheral blood picture: Anemia was the most common sign, about 77% of them had hemoglobin below 13 g% and about 6% had hemoglobin below 6 g%. Cytopenias of all peripheral blood cells have been observed in patients with HIV infection (Table 3).

The most common type of anemia in Group A (CD4 counts > 200 cells/cumm) was normocytic normochromic anemia and normocytic hypochromic anemia, while in Group B (CD4 counts <200 cells/cumm) it was normocytic normochromic anemia and pancytopenia.

Leukopenia was seen in 10% cases of Group A and 60% cases of Group B patients. Thrombocytopenia was seen in 32% and 78% cases of Groups A and B, respectively.

Bone marrow cellularity: Bone marrow picture was hypercellular in 64% and 68% normocellular in 36% and 20% of Groups A and B patients, respectively, while it was hypocellular in 12% of Group B patients. In addition, megakaryocytic dysplasia was seen 2 cases of Group A and 7 cases of Group B patients. Marrow eosinophilia was seen in 2 cases (4%) of Group A and 4 cases (8%) cases of Group B (Table 4).

**DISCUSSION**

Hematological abnormalities and impaired immune status represent one of the common causes of mortality in HIV-infected patients. This hematological status worsens with the progression of the disease.

In the present study, the age of the patients ranged from 19 to 62 years. 60% of these patients were in the highly productive age group of 21-40 years. There was an overall male predominance (78%) which is in accordance with a study done by Sharma et al. (79.7%). Females were much younger with 54% of them in the age group of 21-30 years.

The most common symptoms were fever (79%), weight loss (64%) followed by fatigue (41%). The most common signs were pallor (75%) and oral thrush (24%). The increased frequency of these symptoms and signs could possibly be due to the severity of the illness, and the majority of patients were in WHO clinical Stages III and IV.

The anemia was the most common hematological finding, about 77% of them had hemoglobin below 13 g% and about 6% were having hemoglobin below 6 g%. This incidence was in accordance with previous studies of Rajeev et al. (75%). When hemoglobin (Hb)% is correlated to CD4 counts, in the Group A patients, about 70% of cases had Hb% <13 g%, whereas in Group B, 84% of cases had Hb% <13 g%. Morphologically the most common type of anemia was normocytic normochromic
type followed by normocytic microcytic and the least being pancytopenia.\textsuperscript{11}

Leukopenia was prevalent in 35\% of the patients. Leukopenia was seen in 10\% cases of Group A and 60\% cases of Group B. Lymphocytopenia was seen in 26\% cases of Group A and 50\% cases of Group B. Neutropenia was seen in 6\% of cases of Group A patients and 8\% cases of Group B. According to Zon et al., the incidence of leukopenia range from 57\% to 85\% in patients with fully developed AIDS, whereas it was <5\% in asymptomatic seropositive patients presenting with leukopenia.\textsuperscript{12}

However, according to Castella et al., the incidence of granulocytopenia was around 75\% probably because of influence from anti-retroviral therapy along with the disease itself.\textsuperscript{13}

The prevalence of thrombocytopenia (platelet count below 1.5 lakhs/mm\(^3\)) was 24\%. This is in accordance with studies of Murphy et al. (30\%) and Zon et al. (40\%). In a multi-centric AIDS cohort study of 1500 HIV-positive individuals, 6.7\% had platelet counts <1.5 lakhs/mm\(^3\) on at least one semiannual visit. In the present study, thrombocytopenia was seen in 36\% cases of Group A patients and 78\% cases of Group B patients.\textsuperscript{14,15}

Bone marrow study in Group A cases showed hypercellularity in 64\% and was normocellular in 36\%. Whereas in Group B, 68\% were hypercellular, 20\% normocellular, and 12\% were hypocellular. In number of earlier studies bone marrow is hypercellular in early stages of the disease and hypocellular later on as disease advance. In addition, there were 2 cases of megakaryocytic dysplasia in Group A and 7 cases in Group B. Megakaryocytic dysplasia has become increasingly recognized in patients with fully developed AIDS patients and also in isolated thrombocytopenia according to van der Lelie et al.\textsuperscript{16} Furthermore, in the present study, marrow eosinophilia was seen in 4\% cases of Group A patients and 22\% cases of Group B patients. However, according to Zon et al. and Delacrétaz F et al., marrow eosinophilia is common and has been reported in 9\% and 61\% of patients with AIDS.\textsuperscript{17,18}

\section*{CONCLUSION}

In the present study, the most common hematological manifestations found were anemia, leukopenia, and thrombocytopenia. The frequency and severity of these hematological manifestations increased with the decline in CD4 counts and have got a significant impact on clinical outcomes and patients quality of life. Hence, all patients should be investigated for hematological abnormalities and treated accordingly to reduce the morbidity and mortality.

\section*{REFERENCES}

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