Original Article

Profile of hematological abnormalities and its correlation with absolute CD4 count and human immunodeficiency virus viral load in human immunodeficiency virus-infected patients in a tertiary care hospital

S. Suja, T. Saravanan, S. Karthikeyan[1]

Departments of General Medicine and [1]Community Medicine, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India

Address for correspondence:
Dr. S. Suja, Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore - 641 004, Tamil Nadu, India.
E-mail: sujasadhasivam@gmail.com

Abstract

Background: A variety of hematological manifestations are seen at every stage of human immunodeficiency virus (HIV) infection, and they often pose a great challenge in the comprehensive management of acquired immunodeficiency syndrome. Anemia is the most common hematological abnormality associated with HIV infection. The severity and the incidence of cytopenia are usually correlated with the stage of the disease and underlying immune status if interpreted cautiously, especially if the patient is on regular follow-up. The primary objective of the present study was to understand the spectrum of hematological abnormalities in HIV-infected patients, whereas the secondary objective was to evaluate the correlation of hematological abnormalities with absolute CD4 count and HIV viral load. **Materials and Methods:** The present cross-sectional descriptive study was conducted on 100 patients, aged 18 years and above, diagnosed with HIV infection and confirmed by Western blot or ELISA method. Both inpatients and outpatients at our tertiary care hospital were included in the study. **Results:** Individuals with high viral load and low CD4 count had a higher prevalence of anemia. There was a statistically significant and directly proportionate decrease in the absolute CD4 count as the hemoglobin levels decreased ($P = 0.004$). In the present study, normocytic normochromic blood picture and anemia of chronic disease blood picture were more prevalent among the study participants. Individuals with high viral load and CD4 count <200 cells/mm^3 had a higher rate of occurrence of coinfections. The correlation of absolute neutrophil count and thrombocytopenia with absolute CD4 count and HIV viral load was not statistically significant. **Conclusions:** Complete blood counts and peripheral smear observations were significantly correlated with high HIV viral load and lower absolute CD4 cell counts and therefore can be suggested as economical alternatives for the evaluation of the status of HIV disease stage and its progression.

Key words: Absolute CD4 count, anemia, cytopenia, hematological profile, HIV viral load

Access this article online

Quick Response Code:

Website:
www.ijstd.org

DOI:
10.4103/ijstd.IJSTD_56_19

INTRODUCTION

A variety of hematological manifestations are seen at every stage of human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS), and they often pose a great challenge in the comprehensive management of AIDS. Hematological abnormalities and their complications are the most common causes of mortality and morbidity in HIV-infected individuals.[1] They hinder the treatment directed at HIV and the opportunistic infections and malignancies of AIDS. The hematological abnormalities have also been reported to augment the risk of bacterial infections and affect the quality of life.

Anemia is the most common hematological abnormality associated with HIV infection. This, in turn, is attributed to the abnormal cytosine expression and alteration in bone marrow microenvironment.[2] On the other hand, thrombocytopenia occurs by immune-mediated destruction of the platelets, in addition to inadequate platelet production. Other causes of cytopenia in these patients include treatment-related adverse events or secondary to the opportunistic infections or neoplasms or preexisting or coexisting medical issues. HIV-infected patients with cytopenia require bone marrow examination to determine the cause of cytopenia and also to direct appropriate therapy. The severity and the incidence of cytopenia are usually correlated with the stage of the disease.[1,3,4] These manifestations also reflect the underlying immune status if interpreted cautiously, especially if the patient is on regular follow-up. Hematological abnormalities can be the initial presentation of HIV infection. Patients might be asymptomatic due to the HIV infection and the reason for referral to a physician is usually the abnormal blood count or lymphoid disorders. By considering the possibility of HIV infection, there is an opportunity to diagnose and treat the patients earlier and prevent the transmission of infection. Hematological abnormalities might be the direct result of HIV infection or due to secondary infections, neoplasms, and side effects of the therapy. Early diagnosis and treatment for hematological abnormalities are key factors that contribute to reduction in the morbidity and mortality. Despite the availability of numerous reports on HIV in India, the focus on the hematological manifestations appeared to be limited. Most of the available data are from the West, which might not be directly applicable to the Indian population. Hence, the present study was conducted with the primary objective to understand the spectrum of hematological abnormalities in HIV patients among the Indian population, whereas the secondary objective was to evaluate the correlation of hematological abnormalities with absolute CD4 count and HIV viral load.

MATERIALS AND METHODS

The present cross-sectional study was conducted on 100 patients, aged 18 years and above, diagnosed with HIV infection and confirmed by Western blot or ELISA method. Written informed consent was obtained from all the participants who expressed their willingness to participate in the study. Both inpatients and outpatients at the institution (PSG Institute of Medical Sciences and Research) were included in the study. Patients who refused to give consent and did not have a complete profile of investigations were excluded from the study.

All patients were investigated with a complete hemogram that included estimation of hemoglobin level, red cell indices (mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration), red cell distribution width, total leukocyte count, differential leukocyte count, platelet count, reticulocyte count, and peripheral smear examination. Further to determine the cause of hematological abnormality, indirect bilirubin level, serum iron, total iron-binding capacity, fasting serum Vitamin B12, serum folic acid, stool occult blood, upper gastrointestinal endoscopy, colonoscopy, and bone marrow examination were done accordingly.

Statistical analysis

The data were analyzed using Microsoft Excel 2010 and Statistical Package for the Social Sciences version 19.0 (Armonk, NY: IBM Corp.). A predictive value of <0.05 was considered statistically significant.

RESULTS

Complete hemogram

In the present study conducted on 100 patients, 81 patients were treatment naive and 19 were on antiretroviral therapy (ART). Individuals with high viral load and low CD4 count <200 cells/mm³ had a higher prevalence of anemia. Table 1 shows the comparison of absolute CD4 count and HIV viral load of groups of patients of varying hemoglobin levels. Individuals with high viral load and low CD4 count <200 cells/mm³ had a higher prevalence of anemia. Severe anemia was noted in about 71.4% of individuals with CD4 count <200 cells/μL, 28.6% among CD4 count 200–500 cells/mm³, and 26% among CD4 count >500 cells/mm³ [Table 1]. There was a statistically significant and directly proportionate decrease in the absolute CD4 count as the hemoglobin levels decreased ($P = 0.004$).

Likewise, the comparison of HIV viral load in groups of patients of varying hemoglobin levels showed a statistically significant increase in the viral load as the hemoglobin levels decreased ($P = 0.000$). Severe anemia was noted in about 85.7% of individuals among HIV viral load >1000 copies/ml [Table 1].

In the present study, there were 81 treatment-naive individuals. Hence, the data analysis was done separately

for the treatment-naive patients. Treatment-naive individuals with high viral load and low CD4 count <200 cells/mm³ had a higher prevalence of anemia. Severe anemia was noted in about 66.7% of individuals among CD4 count <200 cells/mm³ and 33.3% among CD4 count 200–500 cells/mm³. Severe anemia was noted in 83.3% of participants with HIV viral load >1000 copies/ml. Severe anemia was not reported in treatment-naive patients with CD4 count >500 cells/mm³ and HIV viral load <200 copies/ml [Table 1]. The differences observed in hemoglobin count in treatment-naive patients between different groups of HIV viral load (P = 0.000) and absolute CD4 count (P = 0.008) were statistically significant.

Comparison of platelet count and absolute neutrophil counts in varying categories of absolute CD4 count and HIV viral load showed insignificant associations in both total study population and treatment-naive patients [Tables 2 and 3].

Type of anemia

In the present study, normocytic normochromic blood picture was noted in majority of the patients. Among the types of anemia, anemia of chronic disease blood picture (35.8%) was more prevalent among the study participants. Iron-deficiency and Vitamin B12-deficiency anemia were noted in about 8.6% and 2% of the study participants, respectively. Hemolytic anemia was not observed. Nearly ten patients presented with pancytopenia. Among the individuals on ART, the patients who were on zidovudine-based therapy had normocytic normochromic anemia with macrocytosis.

Bone marrow biopsy

In the current study, bone marrow biopsy was done among five patients. The bone marrow picture in three participants was erythroid hyperplasia with mild dyserythropoiesis, megakaryocytic hyperplasia, and mild increase in plasma cells which were suggestive of HIV infection. In the other two participants, immune thrombocytopenia was observed.

Coinfections

Comparison of occurrence of coinfections in various categories of absolute CD4 count and HIV viral load showed statistically significant differences (P = 0.000). In individuals with high viral load and low CD4 count <200 cells/mm³, a higher rate of occurrence of coinfections was observed.

Table 1: Comparison of absolute CD4 count and human immunodeficiency virus viral load in groups of patients with varying hemoglobin level

Hemoglobin count	Absolute CD4 count (%)				HIV viral load (%)			
	>500 cells/mm³	200-500 cells/mm³	<200 cells/mm³	P	>200 copies/ml	200-1000 copies/ml	<1000 copies/ml	P
Treatment naïve (g/dl)								
>12	17 (39.5)	13 (30.2)	13 (30.2)	0.008**	29 (67.4)	1 (2.3)	13 (30.2)	0.000**
10-12	3 (15.8)	3 (15.8)	13 (68.4)		6 (31.6)	0	13 (68.4)	
8-10	0	3 (23.1)	10 (76.9)		0	0	13 (100.0)	
<8	0	2 (33.3)	4 (66.7)		0	1 (16.7)	5 (83.3)	
On HAART (g/dl)								
>12	21 (39.6)	14 (26.4)	18 (34.0)	0.004**	38 (71.7)	1 (1.9)	14 (26.4)	0.000**
10-12	5 (22.7)	4 (18.2)	13 (59.1)		9 (40.9)	0	13 (59.1)	
8-10	0	3 (16.7)	15 (83.3)		1 (5.6)	0	17 (94.4)	
<8	0	2 (28.6)	5 (71.4)		0	1 (14.3)	6 (85.7)	

**P<0.05 is considered to be statistically significant. HAART=Highly active antiretroviral therapy; HIV=Human immunodeficiency virus

Table 2: Comparison of absolute CD4 count and human immunodeficiency virus viral load in groups of patients with varying platelet level

Platelet count	Absolute CD4 count (%)				HIV viral load (%)			
	>500 cells/mm³	200-500 cells/mm³	<200 cells/mm³	P	>200 copies/ml	200-1000 copies/ml	<1000 copies/ml	P
Treatment naïve (cells/mm³)								
50,000-100,000	20 (25.0)	21 (26.3)	39 (48.8)	0.595	35 (43.8)	2 (2.5)	43 (53.8)	0.653
20,000-500,000	0	0	0		0	0	0	
<20,000	0	0	1 (100.0)		0	0	1 (100.0)	
On HAART (cells/mm³)								
50,000-100,000	26 (27.7)	22 (23.4)	46 (48.9)	0.511	47 (50.0)	2 (2.1)	45 (47.9)	0.560
20,000-50,000	0	0 (o)	1 (100.0)		0	0	1 (100.0)	
<20,000	0	1 (20)	4 (80.0)		1 (20)	0	4 (80.0)	

HAART=Highly active antiretroviral therapy; HIV=Human immunodeficiency virus

Table 3: Comparison of absolute CD4 count and human immunodeficiency virus viral load in groups of patients with varying absolute neutrophil count levels

Absolute neutrophil count	Absolute CD4 count (%)				HIV viral load (%)			
	>500 cells/mm³	200-500 cells/mm³	<200 cells/mm³	P	>200 copies/ml	200-1000 copies/ml	<1000 copies/ml	P
Treatment naïve (cells/mm³)								
1000-1500	20 (27.0)	20 (27.0)	34 (45.9)	0.345	35 (47.3)	2 (2.7)	37 (50.0)	0.168
500-1000	0	1 (16.7)	5 (83.3)		0	0	6 (100.0)	
<500	0	0	1 (100.0)		0	0	1 (100.0)	
On HAART (cells/mm³)								
1000-1500	26 (28.3)	22 (23.9)	44 (47.8)	0.266	48 (52.2)	2 (2.2)	42 (45.7)	0.069
500-1000	0	1 (16.7)	5 (83.3)		0	0	6 (100.0)	
<500	0	0	2 (100.0)		0	0	2 (100.0)	

HAART=Highly active antiretroviral therapy; HIV=Human immunodeficiency virus

Among the coinfections, pulmonary tuberculosis was predominant and it was about 25% of the total infections. The other coinfections observed were extrapulmonary tuberculosis (11%), central nervous system toxoplasmosis (4 individuals), oral candidiasis (8%), and esophageal candidiasis (5%). Other coinfections (<5%) noted were *Pneumocystis jiroveci* infection, nocardiosis, and herpes simplex infection. Hepatitis B coinfection was noted in about 2% of the total population.

DISCUSSION

Many studies have been conducted across India on HIV manifestations and various aspects have been addressed. However, the focus on the hematological manifestations was very limited. Most of the available data are from the Western studies and may not be directly applicable to the Indian population. Hence, the present study was an attempt to understand the profile of hematological abnormalities in HIV infection in a South Indian population. The study looked into the hematological manifestations and their correlation with viral markers.

HIV is a retrovirus affecting immunity, impairing the immune function, thereby resulting in opportunistic infections and malignancies. The hallmark of HIV infection is decreasing the activity and number of CD4+ T lymphocytes. Furthermore, it impedes other cell lineages and tissues. Cytopenias have been noted even without highly active antiretroviral therapy (HAART) or opportunistic infections and malignancies, proving that HIV infection is directly associated in causing these hematological derangements.

The present study among HIV-infected individuals from South India showed the prevalence of anemia to be 47%. The incidence and severity of anemia, thrombocytopenia, and neutropenia reflect the underlying immune status, if interpreted cautiously. It will be of great benefit, especially if the patient is on regular follow-up. Cytopenias are the leading cause of morbidity and mortality in HIV patients. Hence, it is necessary to identify and treat for hematological abnormalities to reduce the morbidity and mortality.

Studies done worldwide reveal that the prevalence of anemia in HIV-infected persons has been found to be as high as 63%–95%; they also reveal that anemia is more common than thrombocytopenia or leukopenia. In a US-based study, Mildvan *et al.* noted the prevalence of anemia in 9690 HIV-infected individuals and showed that 39.5% (1721) of patients receiving no ART and 35.5% (7252) of patients receiving HAART were anemic. They found that anemia was more prevalent among men and patients with CD4 <200 cells/mm³.[5] Reasons for anemia were found to be decreased production because of associated infections, ART drugs, low erythropoietin levels, or HIV infection *per se*. Furthermore, red blood cell lysis due to autoimmune hemolytic anemia, disseminated intravascular coagulation or thrombotic microangiopathy, and nutritional deficiencies were causes for anemia.[6] The most common reason for anemia in HIV patients is the anemia of chronic disease. In the Multistate Adult and Adolescent Spectrum of HIV Disease Surveillance Project, Sullivan *et al.* analyzed cytopenia in 32,867 individuals affected by HIV infection. They showed that anemia occurrence increased with the clinical severity of the disease.[7] About 3% of HIV patients developed anemia at 1-year follow-up, compared to 12% among those who had immunologic AIDS that is CD4 count <200/mm³ and 37% among those with clinical AIDS.[8] Among cytopenia, anemia in an HIV-infected individual was significantly correlated with higher mortality.[1] However, on the contrary, decreased risk of death was noted in those who recovered from anemia. Although the levels of serum erythropoietin may be high in these patients, the response to anemia was blunted compared to those with uncomplicated iron-deficiency anemia of comparable severity.[9]

Drug treatment and the subsequent complications were also the common reasons for anemia among HIV patients. Zidovudine is the most common among the ART drug to cause anemia. It inhibits the *in vitro* erythroid colony

formation. It does it in a dose-dependent manner.[10] Following zidovudine intake, macrocytosis develops within weeks. Macrocytosis in these patients also acts as a useful marker of drug compliance. It was noted that serum Vitamin B12 levels were often low in HIV-infected patients. However, only few patients presented with true Vitamin B12 deficiency. *Mycobacterium avium* complex, *Mycobacterium tuberculosis*, and *Histoplasma capsulatum* caused anemia in AIDS patients by bone marrow infiltration.

In the current study, anemia was more prevalent in individuals with high HIV viral load and low absolute CD4 count. The present finding was concurrent with numerous studies conducted globally.[5,11,12] Low hemoglobin count was observed in both treatment-naive HIV patients and patients on HAART therapy.[11,12] Low hemoglobin levels were also found to correlate significantly with the increased severity of the disease and poor prognosis as in other studies.[1,3,4,13] Normocytic normochromic anemia was the common finding among the blood picture of HIV patients in the present study and was concurrent with the report of Evans and Scadden.[14] The severity of anemia was significantly correlated with high HIV viral load and low absolute CD4 count. The abovementioned findings were consistent with the study done by Volberding *et al.*, who reported that more severe levels of anemia are found among HIV-positive patients presenting with low CD4 counts.[15]

Neutropenia was also found in majority of patients with high viral load and low CD4 count.[16] Among leukopenia, neutropenia was more prevalent in HIV patients, ranging from 10% to 30% at later stages of the disease. HIV infection leads to bone marrow suppression causing decreased granulocyte colony-stimulating factor levels, thereby causing low granulocyte–macrophage lineage. This resulted in leukopenia and neutropenia in HIV patients. Bone marrow suppressive drugs or opportunistic infections might also contribute to leukopenia. Moreover, HIV infection *per se* results in lymphopenia at later stages of disease, causing low CD4+ lymphocytes. In HIV patients, lower values of absolute neutrophil counts were due to granulopoiesis inhibition by the HIV virus itself or by bone marrow infiltration by infections. Leukopenia was also attributed to malignancies, adverse drug reactions, autoimmunity, and hypersplenism.

Various studies from developing nations showed a marked decline in mortality in HIV patients following HAART therapy. An Indian study showed a dramatic decline in mortality from 25 to 5 deaths per 100 person years in HIV patients between 1997 and 2003 after starting HAART therapy.[16] Factors such as older age, baseline low CD4 counts, tuberculosis infection at any point of time, and ART-naive status had significant associations with mortality.

Thrombocytopenia was noted during the early stages of the disease and it was not associated with poor prognosis. Thrombocytopenia in HIV infection is due to immune complex-mediated peripheral destruction and antiplatelet antibodies. Interestingly, thrombocytopenia is noted as the first clinical manifestation in otherwise asymptomatic HIV-infected individuals, whereas neutropenia and anemia were mostly noted in the later stages of HIV disease. The possible mechanisms considered for thrombocytopenia are increased destruction of platelets by immune complexes in circulation which nonspecifically get deposited on the platelets. Furthermore, thrombocytopenia can be attributed to the existence of specific antiplatelet antibodies, as well as direct action on megakaryocytic by HIV *per se* causing ineffective platelet production. The incidence of thrombocytopenia among HIV patients was about 40%, and in 10% of HIV patients, it might be the first sign of AIDS. Thrombocytopenia was related to increased morbidity and mortality, by accelerating the deterioration of CD4 counts and leading to progression to AIDS.

Among all the study participants, anemia was more common than thrombocytopenia or neutropenia. In treatment-naive individuals and individuals on ART, thrombocytopenia and neutropenia were more prevalent among high HIV viral load and low CD4 count <200 cells/mm^3. Immune thrombocytopenic purpura remains the most common cause of low platelet count in HIV patients.[17]

Abnormalities in the bone marrow were noted at various stages of the HIV disease and more during the later stages of the disease. HIV infection in the mesenchymal stem cells of bone marrow leads to various bone marrow abnormalities.[2] HIV infection leads to a histiocytic reaction and further resulting in hemophagocytic syndrome and severe pancytopenia. HIV also causes decrease in progenitor cells in the bone marrow.[18] As per Paradela *et al.*'s study, it was reported that bone marrow defects in HIV-infected individuals mainly showed features of increased cell counts, granulomatous changes, and some amount of dysplasias.[19] Studies conducted *in vitro* showed the direct influence of HIV on mesenchymal cells and hematopoietic cell activity.[2]

India has the third largest HIV population with 2 million people affected, more than 60,000 deaths due to AIDS-related illnesses, and only about 43% receiving proper HAART from health sectors. The government spends a huge sum of its health budget over HIV treatment and prevention. Our study can be considered as a pilot study and should be extrapolated to a larger study with case and control group selected within the sample, for instance with low and high absolute CD4 count and HIV viral load.

CONCLUSIONS

Most of the available data on HIV infections and hematological profiles are from the Western studies, which might not be directly applicable to the Indian population. The present study looked into the hematological manifestations and their correlation with viral markers of HIV patients from South India. HIV viral load and absolute CD4 count are the most essential biomarkers to identify the stage of HIV disease and its progression. However, these tests are expensive in both developed and developing countries. The results of the present study suggest that complete blood counts and peripheral smear can be economical alternatives to HIV viral load and absolute CD4 cell counts in staging the disease and assessing the prognosis.

Financial support and sponsorship

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Mocroft A, Kirk O, Barton SE, Dietrich M, Proenca R, Colebunders R, *et al*. Anaemia is an independent predictive marker for clinical prognosis in HIV-infected patients from across Europe. EuroSIDA study group. AIDS 1999;13:943-50.

2. Wang L, Mondal D, La Russa VF, Agrawal KC. Suppression of clonogenic potential of human bone marrow mesenchymal stem cells by HIV type 1: Putative role of HIV type 1 tat protein and inflammatory cytokines. AIDS Res Hum Retroviruses 2002;18:917-31.

3. Moyle G. Anaemia in persons with HIV infection: Prognostic marker and contributor to morbidity. AIDS Rev 2002;4:13-20.

4. Mekonnen Y, Dukers NH, Sanders E, Dorigo W, Wolday D, Schaap A, *et al*. Simple markers for initiating antiretroviral therapy among HIV-infected Ethiopians. Ethiop Med J 2003;41 Suppl 1:61-5.

5. Mildvan D, Creagh T, Leitz G; Anemia Prevalence Study Group. Prevalence of anemia and correlation with biomarkers and specific antiretroviral regimens in 9690 human-immunodeficiency-virus-infected patients: Findings of the Anemia Prevalence Study. Curr Med Res Opin 2007;23:343-55.

6. Antelman G, Msamanga GI, Spiegelman D, Urassa EJ, Narh R, Hunter DJ, *et al*. Nutritional factors and infectious disease contribute to anemia among pregnant women with human immunodeficiency virus in Tanzania. J Nutr 2000;130:1950-7.

7. Sullivan PS, Hanson DL, Chu SY, Jones JL, Ward JW. Epidemiology of anemia in human immunodeficiency virus (HIV)-infected persons: Results from the multistate adult and adolescent spectrum of HIV disease surveillance project. Blood 1998;91:301-8.

8. Remacha AF, Cadafalch J. Cobalamin deficiency inpatients infected with the human immunodeficiency virus. Semin Hematol 1999;36:75-87.

9. Spivak JL, Barnes DC, Fuchs E, Quinn TC. Serum immune reactive erythropoietin in HIV-infected patients. JAMA 1989;261:3104-7.

10. Dainiak N, Worthington M, Riordan MA, Kreczko S, Goldman L. 3'-Azido-3'-deoxythymidine (AZT) inhibits proliferation *in vitro* of human haematopoietic progenitor cells. Br J Haematol 1988;69:299-304.

11. Abrams DI, Steinhart C, Frascino R. Epoetin alfa therapy for anaemia in HIV-infected patients: Impact on quality of life. Int J STD AIDS 2000;11:659-65.

12. Grossman HA, Goon B, Bowers P, Leitz G; 010 Study Group. Once-weekly epoetin alfa dosing is as effective as three times-weekly dosing in increasing hemoglobin levels and is associated with improved quality of life in anemic HIV-infected patients. J Acquir Immune Defic Syndr 2003;34:368-78.

13. Mofenson LM, Harris DR, Moye J, Bethel J, Korelitz J, Read JS, *et al*. Alternatives to HIV-1 RNA concentration and CD4 count to predict mortality in HIV-1-infected children in resource-poor settings. Lancet 2003;362:1625-7.

14. Evans RH, Scadden DT. Haematological aspects of HIV infection. Baillieres Best Pract Res Clin Haematol 2000;13:215-30.

15. Volberding PA, Baker KR, Levine AM. Human immunodeficiency virus hematology. Hematology Am Soc Hematol Educ Program 2003;1:294-313.

16. Kumarasamy N, Solomon S, Chaguturu SK, Cecelia AJ, Vallabhaneni S, Flanigan TP, *et al*. The changing natural history of HIV disease: Before and after the introduction of generic antiretroviral therapy in southern India. Clin Infect Dis 2005;41:1525-8.

17. Nardi M, Karpatkin S. Antiidiotype antibody against platelet anti-GPIIIa contributes to the regulation of thrombocytopenia in HIV-1-ITP patients. J Exp Med 2000;191:2093-100.

18. Leiderman IZ, Greenberg ML, Adelsberg BR, Siegal FP. A glycoprotein inhibitor of *in vitro* granulopoiesis associated with AIDS. Blood 1987;70:1267-72.

19. Paradela A, Rivas C, Fernández-Guerrero M, Román A. Histopathology of bone marrow biopsy in patients with human immunodeficiency virus infection. Rev Clin Esp 1996;196:9-15.