# Profound reduction of CD4+ lymphocytes without HIV infection: two cases from the horn of Africa

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## Abstract

Idiopathic CD4+ lymphocytopenia is a disorder associated with low CD4+ T cell count and opportunistic infections resembling AIDS. Most cases are described in developed countries. We report two HIV-negative patients with idiopathic CD4+ lymphocytopenia and AIDS-defining events diagnosed in Djibouti. The first patient developed lesions of Kaposi's sarcoma and the second one presented with pulmonary tuberculosis. Both patients died with severe immunodepression. In poor resource-areas where HIV testing may not be available it is important to bear in mind that severe immunodepression and a clinical presentation compatible with AIDS do not necessary carry the diagnosis of AIDS.

**Key words:** Human immunodeficiency virus, Acquired immunodeficiency syndrome, Lymphopenia, Kaposi's sarcoma, tuberculosis, Djibouti.

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## Case reports

### Patient 1

A 55-year-old male was admitted with a vesicular rash to the Hôpital Général Peltier in Djibouti. He was married with four children and all were in good health. The clinical history was non contributory and the physical examination revealed several vesicles filled with serous fluid distributed on the trunk and extremities; his weight was 52 kg (body mass index [BMI]: 18.4 kg/m$^2$). Blood analyses and a chest radiograph showed no abnormalities. A skin biopsy demonstrated bullous pemphygoid. The patient was started on oral steroids (30 mg prednisone/day) and was discharged when the vesicles dried up. He was seen twice as an outpatient with marked improvement and then was lost to follow-up after six months.

The patient returned one year later. Multiple bluish nodular lesions covered his eyelids, arms and trunk; he had not lost weight and the rest of the physical examination was normal. He was hospitalized. The hemoglobin was 8.7 g/dL and the leukocyte count 12.7 x 10$^3$/mm$^3$ with 6 % lymphocytes, a CD4+ T cells count of 166/µl (BD FacScount Reagents, BD Biosociences, Becton, Dickinson and Co., San Jose, Ca, USA) and a CD4+/CD8+ ratio of 0.8; ELISA test for HIV and viral load performed twice were all negative (Abbot Lab., Minato-Kuito, Tokyo, Japan and Immunocomb II HIV 1 and 2 Biospot. Orgenics Ltd., Courbevoie, France; Nuclisens, Nasba Diagnostics, Easy Q HIV-1, BioMérieux, Marci L'Etoile, France); a chest radiograph demonstrated an enlarged mediastinum. After three days his family took him home and we learned that he had died a few days later. A skin biopsy obtained from the trunk showed a Kaposi's sarcoma. The immunohistochemical study for Kaposi sarcoma-associated herpes virus (HHV-8) was positive in the nuclei of neoplastic cells (NCL-HHV8-LNA antibody, at 1/25 dilution; Novocastra lyophilized mouse monoclonal antibody human Herpesvirus type 8 [latent nuclear antigen], Leica Biosystems Newcastle Ltd. Newcastle Upon Tyne, United Kingdom).

### Patient 2

A 30-year-old woman was admitted with shortness of breath; her weight was 38 kg (BMI: 14.8 kg/m$^2$). She had suffered from diarrhea and abdominal pain for the past four months and had no history of tuberculosis; she had been treated in a dispensary

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with antibiotics with no relief. Her husband had received treatment for tuberculosis (smear-positive sputum) during four months and was asymptomatic; her four children were in good health. Her weight was 28 kg and she was afebrile; her feet and ankles were edematous and no other abnormalities were noted. The hemoglobin was 10.4 g/dL and the leukocyte count 5.2 x $10^3/mm^3$ with 9.2 % lymphocytes, a low CD4+ count (28 CD4+ T cells/ µl ) and a CD4/CD8+ ratio of 0.9. Tests for HIV infection performed twice were all negative. A chest radiograph revealed bilateral upper lobe infiltrates with multiple cavities in the right upper lobe. The tuberculin test was not available and no sputum could be obtained; she was started on a four-drugs anti-tuberculosis therapy. Her husband was HIV-negative and his chest radiograph was compatible with tuberculosis but was not able to produce any sputum. The patient died three days later.

## Discussion

Idiopathic CD4+ lymphocytopenia has been reported in several areas of the World: Europe[1-5], the Americas[6-8], Australia[9] and West Africa[10-11] with AIDS-defining illnesses and in whom the etiology of the CD4+ T-lymphocyte depletion could not be explained. To our knowledge these cases are the first detected in East Africa. The presenting manifestations are varied: thrombocytopenia, opportunistic infections including tuberculosis and other mycobacterial infections, different types of malignancies, and autoimmune diseases[12].

Our first patient was treated for pemphigus with steroids. He discontinued his treatment after several months and did not return until he had developed new lesions which turned out to be Kaposi's sarcoma. The development of Kaposi's sarcoma after treatment of pemphigus with steroids has already been described in a patient with idiopathic CD4+ lymphocytopenia[13].

The second patient had radiological features suggesting pulmonary tuberculosis but the diagnosis could not be confirmed because on admission she was not coughing and she died shortly after. Her husband had been incompletely treated for tuberculosis and was also HIV-negative. Tuberculosis may reduce the lymphocyte subpopulations[14], although this reduction usually does not reach the dramatic levels observed in our second patient. In Argentina, it was shown that patients with severe tuberculosis and with lower CD4 had a worse prognosis and that the CD4 lymphocytes increased to normal values after the response to treatment[15]. Our patient was severely malnourished and this is also a cause of immunodeficiency. A significant reduction of the CD4 lymphocytes can occur in conditions with no HIV infection[16], including severe wasting, as described in Ethiopia[17].

There is a close and complex relation between tuberculosis and malnutrition (18-20). Several studies suggest that as the BMI decreases, the incidence of tuberculosis increases (21-22) and that malnutrition maybe a predictor of poor outcome[23-24].

Idiopathic CD4 lymphocytopenia was defined in 1992 as a syndrome with <300 CD4+ T cells/µl or <20 % of total T cells with no evidence of infection with HIV-1/HIV-2 and in the absence of any immunodeficiency or therapy associated with reduced levels of CD4 cells[6]. Studies have not observed an epidemiological pattern suggesting a new transmissible agent or an environmental factor[7] contributing to its emergence. It constitutes a very rare syndrome which is probably caused by many factors. Its course seems to be more benign, as many patients do not suffer a progressive worsening of the lymphopenia and in some this reduction even disappears[16]. An explanation of this "new syndrome" could be that it already occurred in the past but that it was not recognized, as T cell phenotyping was not widely applied until recent years.

In conclusion, the detection of a low CD4 does not always imply that the patient is infected with HIV, even when the patient suffers from an AIDS-defining entity and has no history of immunosuppressive therapy. Especially in limited resource areas where HIV testing is not always available such assumption could lead to an erroneous diagnosis of AIDS. We must bear in mind before diagnosing AIDS that the implications of this diagnosis for the patients and their families are severe.

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