

Case Report



Clinically HIV but negative serology: Think of idiopathic CD4⁺ lymphocytopenia

Vidya Sanjay Nagar, Rahul Kadu, Shamshersingh Gajendra Chauhan, Rudrarpan Chatterjee, Aniruddha Kaushik, Deniskumar Vashrambhai Patel, Ankita Sood

Abstract

Idiopathic CD4⁺ lymphocytopenia (ICL) is a rare disorder characterized by the presence of depleted CD4 cell line without the presence of HIV infection. Slight male preponderance is noticed and is usually seen in the middle age group. Opportunistic infections are the reason for their discovery and here we describe a case where a man was diagnosed as having *Pneumocystis jiroveci* pneumonia and oral candidiasis.

Keywords: idiopathic CD4⁺ lymphocytopenia, immunosuppressed state, *Pneumocystis jiroveci* pneumonia

Access this article online

Website: www.ijccm.org

DOI: 10.4103/0972-5229.183899

Quick Response Code:



Introduction

Since the advent of the HIV-AIDS pandemic across the globe, *Pneumocystis jiroveci* pneumonia has been one of the most common defining illnesses of this condition. Idiopathic CD4⁺ lymphocytopenia is one such condition where the patient presents with such AIDS defining illnesses but with negative serological marker for this dreaded disease. Here, we describe a case where a young man presented with pneumocystis infection but was having negative markers for HIV and thus the diagnosis of ICL was concluded.

Case Report

A 32-year-old adequately nourished male was admitted for complaints of shortness of breath for 1 month which had exacerbated for the past 2 days. No other accompanying complaints were present. He used to work as a tailor with a mixed diet usually on his platter. Examination revealed a well built and nourished

male with a body mass index of 25.3 kg/m² who was tachypneic with the presence of tachycardia and mild fever. Oral thrush was present and scrapings were sent for fungal culture. There were no apparent risk factors for the presence of HIV or any other immunosuppressive states. Chest X-ray revealed few scattered inspiratory crackles and the saturation monitor was showing a SpO₂ of 87%. High flow O₂ was initiated and the patient was then shifted to the Intensive Care Unit for further management. Blood gases showed a PO₂-47 mmHg and PCO₂-24 mmHg. Chest roentgenogram showed bilateral perihilar infiltrates. Given the clinical picture of the patient, *Pneumocystis jiroveci* pneumonia (PJP) was high on cards, given the apparent immunosuppressed state. Empirical antibiotics, fluconazole and oral trimethoprim-sulphomethoxazole [TMP-SMX], was started along with steroids. Lactate dehydrogenase

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

From:

Department of Internal Medicine, Sir JJ Group of Hospitals, Mumbai, Maharashtra, India

Correspondence:

Dr. Shamshersingh Gajendra Chauhan, 703, Ever Top Apartment, Sahakar Nagar, Andheri West, Mumbai - 400 053, Maharashtra, India.
E-mail: dr.sgchauhan@gmail.com

For reprints contact: reprints@medknow.com

How to cite this article: Nagar VS, Kadu R, Chauhan SG, Chatterjee R, Kaushik A, Patel DV, et al. Clinically HIV but negative serology: Think of idiopathic CD4⁺ lymphocytopenia. Indian J Crit Care Med 2016;20:371-3.

was 916 U/L (high) and high-resolution computed tomography of the thorax revealed ground glass opacities in both lung fields, more so being perihilar. Other routine blood work was normal. The patient was tachypneic on high flow O₂ and required noninvasive ventilation intermittently. Bronchoalveolar lavage was done and it revealed pneumocystis organisms. Acid-fast bacteria and routine bacterial and fungal culture were negative. The fungal scrapings yielded a growth of *Candida albicans* sensitive to fluconazole. Thus, the diagnosis of PJP was confirmed.

To identify the cause of the immunosuppressed state, his HIV ELISA was done but was negative. A repeat sample yielded the same result. Since the clinical suspicion of HIV was so high, a Western blot and a HIV-RNA polymerase chain reaction were ordered as well. Both turned out to be negative. Now, it was confirmed that the patient did not have the dreaded disease. CD4 and CD8 counts were ordered, as a suspicion for idiopathic CD4⁺ lymphocytopenia (ICL) was high. The CD4 turned out to be 110/mm³ and the CD4% was 14.3. The CD8 counts were 312/mm³ (normal) with a CD4:CD8 ratio, inverted (0.35; normal: 1.4–1.7). This test was repeated after 6 weeks and the results were the same.

The patient was screened for other causes of immunodeficiencies through history and laboratory reports. He denied any history of immunosuppressive drug intake, did not experience repeated infections in the childhood, his immunoglobulin and sugar levels were normal, and the titers for HTLV1 and 2 were negative. Thus, idiopathic CD4⁺ lymphocytopenia was labeled as the cause of his immunodeficiency and was given a prophylaxis of TMP-SMX and fluconazole post-treatment.

Discussion

The Centre for Disease Control in the USA in 1993 defined a new entity in the ever expanding world of immunology, known as the idiopathic CD4⁺ lymphocytopenia. The HIV-AIDS pandemic had just began to shape in those days and defining a disease, so close and yet so far from it, was a challenge that the Centers for Disease Control and Prevention had to face. They defined this entity as the presence of CD4 counts <300/mm³ or <20% of the total lymphocyte count on more than one occasion, at least 6 weeks apart, with the absence of HIV infection or any other condition that might cause CD4 cytopenia.

ICL is a heterogeneous condition which is usually diagnosed in middle age and has a slight male

preponderance.^[1] The spectrum of the presence of opportunistic infections in ICL is the same when compared to a patient with HIV infection.^[2] Cryptococcosis is the most common infection associated with this disease, but candida, cytomegalovirus, nontuberculous, and tuberculous infections are common.

ICL appears to be due to a physiological response where there is an altered environment of cytokines and inflammation that leads to decreased production of T-cell precursors and clonogenic capacity of the bone marrow. This appears due to decreased interleukin-2 and increased tumor necrosis factor alpha in the internal milieu.^[3] In addition, decreased T-cell response and increased T-cell activation have been noted.^[2,4]

One study had found that there is a profound defect in CXCR4 expression on CD4 cells and an abnormal intracellular accumulation of CXCR4 and its ligand CXCL12. CCR5 remained normal. Loss of this CXCR4 was postulated to cause disturbance in the priming of T-cells in the secondary lymphoid organs and its improper antigen reception and subsequent activation.^[5]

Conditions such as hepatitis B, hepatitis C, Epstein-Barr virus, adenovirus, parvovirus B19, and some other viral infections can cause lymphopenia in their acute stages, but it is highly unusual for them to cause an exclusive isolated CD4 cytopenia-like syndrome.

There are not any published guidelines for managing these cases, and most centers advocate using a CD4 cell count level of below 200/mm³ to start antimicrobial prophylaxis. This is in accordance with the guidelines published for HIV-infected patients. However, few case reports do suggest that ICL may not be at an identical risk of infection as a patient with HIV at the same CD4 count,^[6] these data are too less to refute such claims and deny the patient of these measures.

If the CD4 cytopenia is very low, i.e. below 100 and there is a presence of recalcitrant infections, then treatment with interleukin-2 is warranted;^[7] however, this therapy has its own set of side effects and needs an informed written consent, depicting the investigational nature of the treatment protocol. Hematopoietic stem cell transplant also has shown promise in some reports to be an effective mode of treatment for this condition.^[8]

PJP is regarded as an AIDS-defining illness, but its presence in our patient without the serological evidence

of HIV in any form leads us to investigate for this rare but important disorder.

Conclusion

ICL is a rare disease which warrants a high index of suspicion to be diagnosed. It can come with the same opportunistic infections as in a HIV patient, but the negative serology gives way the diagnosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. DeHovitz J, Feldman J, Landesman S. Idiopathic CD4+ T-lymphocytopenia. *N Engl J Med* 1993;329:1045-6.
2. Walker UA, Warnatz K. Idiopathic CD4+ lymphocytopenia. *Curr Opin Rheumatol* 2006;18:389-95.
3. Sharma A, Lal V, Modi M, Khurana D, Bal S, Prabhakar S. Idiopathic CD4+ lymphocytopenia presenting as refractory cryptococcal meningitis. *Ann Indian Acad Neurol* 2010;13:136-8.
4. Netea MG, Brouwer AE, Hoogendoorn EH, Van der Meer JW, Koolen M, Verweij PE, *et al.* Two patients with cryptococcal meningitis and idiopathic CD4 lymphopenia: Defective cytokine production and reversal by recombinant interferon-gamma therapy. *Clin Infect Dis* 2004;39:e83-7.
5. Scott-Algara D, Balabanian K, Chakrabarti LA, Mouthon L, Dromer F, Didier C, *et al.* Idiopathic CD4+ T-cell lymphocytopenia is associated with impaired membrane expression of the chemokine receptor CXCR4. *Blood* 2010;115:3708-17.
6. Zonios DI, Falloon J, Bennett JE, Shaw PA, Chaitt D, Baseler MW, *et al.* Idiopathic CD4+ lymphocytopenia: Natural history and prognostic factors. *Blood* 2008;112:287-94.
7. Zonios D, Sheikh V, Sereti I. Idiopathic CD4+ lymphocytopenia: A case of missing, wandering or ineffective T cells. *Arthritis Res Ther* 2012;14:222.
8. Hamidieh AA, Pourpak Z, Hamdi A, Nabavi M, Ghavamzadeh A. Successful fludarabine-based hematopoietic stem cell transplantation in a pediatric patient with idiopathic CD4+ lymphocytopenia. *Pediatr Transplant* 2013;17:E109-11.