Visceral leishmaniasis co-infection in people living with HIV/AIDS

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INTRODUCTION

Visceral leishmaniasis (VL) is a worldwide disseminated infection transmitted by the bite of infected female sand flies. It is caused by a protozoan *Leishmania donovani* (LD). About 350 million people are at risk and 12 million people are affected worldwide. Leishmania and human immunodeficiency virus (HIV) co-infection occurs across the world, the situation being particularly alarming in southern Europe, where 50–75% of adult cases of VL are HIV positive.¹ It is estimated that 500,000 new cases of VL occur annually. About 90% of these are in five countries, namely Bangladesh, Brazil, India, Nepal, and the Sudan.² India has the largest number of VL cases, accounting for 40–50% of world disease burden³ and the second-largest HIV-infected population, accounting for approximately 10% of the global disease burden.⁴ The possible overlap in the distribution of VL and HIV in countries where both infections are highly endemic, such as India, may have grave consequences. VL has joined the list of AIDS-related opportunistic infections in endemic areas. Recently, HIV-VL co-infection has increased in prevalence, though tuberculosis is the commonest opportunistic infection in HIV.⁵

The triad of HIV, tuberculosis, and VL has been reported.⁶ A chronic, relapsing course is seen in co-infected patients, VL associated with HIV. These are the first two of the VL cases in people living with HIV/AIDS (PLHA) to be reported from the Armed Forces.⁷

CASE REPORT

Case 1

A male patient, aged 32 years and a resident of Bihar, presented to one of the service hospitals for review medical board in 2009 with major complaints of weakness, easy fatigability,

and breathlessness, with a history of being detected as HIV-1 positive in August 2006, disseminated tuberculosis in June 2008, and on ATT since last one year.

The patient was investigated and was found to have Hb of 10.2 g/dL, TLC of 2000/ μ L, DLC—neutrophils 55%, lymphocytes 35%, monocytes 8%, eosinophils 2%, and a platelet count of $1.5 \times 10^5/\mu$ (SI units). PBS examination revealed normocytic normochromic anaemia. With the diagnosis of bicytopenia, further haematological work-up in the form of iron studies and serum Vit B12 level was carried out, which were within normal limits. The patient was then referred to our centre.

On investigation, the absolute CD4 count was 205/ μ L and ESR 42 mm fall in the first hour. The patient was further investigated for *Pneumocystis jirovecii* and cryptococcal infections, which were found negative. Ultrasonography of the whole abdomen suggested a hepatomegaly of 17.6 cm and splenomegaly of 20 cm. CT scan chest showed hilar lymphadenopathy.

The PBS received along with the bone marrow aspirate showed increased rouleaux formation. The bone marrow study revealed a hyper cellular marrow with a basophilic tinge with increase in plasma cells and macrophages. Numerous extracellular and intra cellular LD bodies were seen (Figure 1). Serological test for antibodies against leishmanial antigen rKE16 was positive.

A detailed past history (which was never elicited earlier) was taken and it revealed that the patient had suffered from Kala-azar 15 years back before recruitment, for which he was treated with some injectables in Bihar, details of which were not known to him. The patient was on HAART and ATT since June 2008. He was treated with liposomal amphotericin B for

Figure 1 Bone marrow aspirate showing presence of *Leishmania donovani* bodies (100 $\times$).

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Figure 2 Bone marrow biopsy showing presence LD bodies (100×).

four weeks. The splenomegaly regressed. Repeat bone marrow revealed complete clearance of LD bodies and the haemogram normalised. The present CD4 count of the patient is 400/ μ L and is on a regular follow-up to look for recurrence of VL.

Case 2

A 40-year-old serving soldier, also a resident of Bihar, under immune surveillance since July 2008 was admitted to CH(SC) for review medical board in December 2009 and was detected to have hepatosplenomegaly and pancytopenia on investigation. In the past, patient was on ATT for presumptive tubercular infection, which he completed in January 2009. However, hepatosplenomegaly persisted.

The patient was investigated and found to have a Hb of 11 g/dL, TLC of 1300/ μ L, DLC—neutrophils 56%, lymphocytes 40%, monocytes 01%, eosinophils 03%, and a platelet count of $0.67 \times 10^5/\mu$ (SI units). PBS examination revealed normocytic normochromic anaemia and leucopenia with thrombocytopenia. The bone marrow examination was done to find the cause of pancytopenia and revealed a hypercellular marrow with increased plasma cells and macrophages studded with LD bodies (Figure 2). The serological test to detect antibodies against leishmanial antigen rKE16 was also positive even though the absolute CD4 count was 51/ μ L. The stool examination of the patient revealed cysts of *Cryptosporidium*.

The patient was on treatment for HIV since February 2009 with HAART. Inj amphotericin B and tab nitazoxanide were added and continued for four weeks. The patient's splenomegaly regressed and the peripheral blood counts normalised over six weeks. The patient's CD4 counts increased to 550/ μ L after which he was sent on sick leave and regular follow-up has been planned.

DISCUSSION

These two cases demonstrate that the triad of HIV-VL and tuberculosis presents interesting diagnostic and therapeutic problems. Unfortunately, the numbers of these cases are increasing.⁸ There are a lot of shortcomings as far as the diagnosis and

management of these cases are concerned.⁹ Serological tests for the detection of antibodies against leishmanial antigen rKE16 done using Signal-KA spot/immunodot test kit may be falsely negative in patients with low CD4 counts due to the lack of immune response. However, this test was positive for these patients, even in the patient with CD4 count of 51/ μ L. Therefore this case report highlights that in HIV positive patients belonging to a region endemic for VL, with hepatosplenomegaly, a high index of suspicion for VL is required and bone marrow aspirates or splenic aspirates must be examined to detect these cases early. In both these cases there was no clinical suspicion of VL but they were detected on bone marrow examination for cytopenias. The immunodot test for anti-leishmanial antibody must also be performed upfront if the patient is from an endemic region. Patients who have previously had VL are known to have high resistance to antimonials and pentamidine, and hence have to be treated aggressively with Amphotericin B.¹⁰ The study conducted by Mathur et al on 104 patients of VL over a period of two years showed that four of the six (67%) VL and HIV co-infected patients had a chronic relapsing course, not responding to anti-leishmanial treatment.¹¹ A chronic, relapsing course is seen in co-infected patients, which is the most outstanding feature of VL associated with HIV infection and hence regular monitoring of patient is required. However, in these two cases there has been no relapse till now and the patients are on regular follow-up.

REFERENCES

1. Pintado V, Martin-Rabadan P, Rivera M, Moreno S, Bouza E. Visceral leishmaniasis in human immunodeficiency Virus(HIV)-infected and non-HIV infected patients. *Medicine* 2001;80:54–73.
2. World Health Organization. WHO Fact sheet. May 2004:116.
3. Bora D. Epidemiology of visceral leishmaniasis in India. *Natl Med J India* 1999;12:62–68.
4. USAID, Fact Sheet. 2003:215.
5. Sharma SK, Aggarwal G, Seth P, Saha PK. Increasing HIV seropositive among adult tuberculosis patients in Delhi. *Indian J Med Res* 2003; 117:239–242.
6. Pandey K, Sinha PK, Das VNR, et al. Nexus of infection with human immunodeficiency virus, pulmonary tuberculosis and visceral leishmaniasis. A case report from Bihar, India. *Am J Trop Med Hyg* 2005; 72:30–32.
7. HIV registry Indian Armed Forces. 2009.
8. Sinha PK, Das VNR, Pandey K, et al. Visceral leishmaniasis and HIV co-infection in Bihar, India. *J AIDS* 2003;32:115–116.
9. Pulido F, Iribarren JA, Kindelan JM, et al. Diagnosis and treatment of mycobacterial infections in patients with HIV/AIDS. *Enferm Infectet Microbiol Clin* 1998;16:20–28.
10. Murray HW. Current treatment of leishmaniasis. *Am J Trop Med Hyg* 2004;71:787–794.
11. Mathur P, Samantaray JC, Vajpayee M, et al. Visceral leishmaniasis/human immunodeficiency virus co-infection in India: the focus of two epidemics. *J Med Microbiol* 2006;55:919–922.