

CASE REPORT

VISCERAL LEISHMANIASIS AND TUBERCULOSIS IN PATIENTS WITH HIV CO-INFECTION

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Abstract. We describe here two cases, one male and one female, both age 40 years, with visceral leishmaniasis and HIV-1 co-infection. The female patient had features of Koch's abdomen. The male patient had features of tuberculous lymphadenitis and bilateral pleural effusion more marked on the right side. Both were treated with highly active antiretroviral therapy, antituberculous drugs, antibiotics, antifungal medicine (fluconazole) and miltefosine. Both patients showed marked improvement with therapy.

INTRODUCTION

Visceral leishmaniasis (VL) is a worldwide disseminated infection transmitted by the bite of infected female sandflies. It is caused by a protozoan *Leishmania donovani*. About 350 million people are at risk, 12 million people are affected worldwide. It is estimated that 500,000 new cases of VL occur annually. About 90% of these are in 5 countries, namely Bangladesh, Brazil, India, Nepal, and the Sudan (WHO, 2000). Host defense against this intracellular infection is T-cell dependent. VL (Kala-azar) has joined the list of AIDS related opportunistic infection in endemic areas. According to the WHO, 42 million people were living with HIV/AIDS at the end of 2002. Recently, HIV-VL, co-infection has increased in prevalence, particularly in India (Thakur *et al*, 2002). Tuberculosis is a very common opportunistic mycobacterial infection, particularly in HIV infection (Sharma *et al*, 2003). Both HIV and tuberculosis are T-cell mediated diseases. The triad of HIV, tuberculosis and VL has been reported (Pandey *et al*, 2005). Pov-

erty, overcrowding, malnutrition, polygamy, illiteracy, and poor domestic conditions facilitate the growth of these diseases.

CASE REPORT

Patient 1

A female patient, age 40 years presented to the out-patient department of Rajendra Memorial Research Institute of Medical Sciences (RMRIMS) with complaints of fever with rigors, loss of appetite and oral thrush for the past 2 months. There was a history of severe abdominal pain with loose stools (5-6 times per day) and generalized weakness. The patient revealed that her husband worked at Kolkata and died one and half years previously due to HIV infection and its complications. An ELISA for HIV-1 was done and found reactive. Her four children, two males and two females, were negative for HIV. This was followed by CD4 and CD8 counts, which showed CD-47.0/ μl (normal range 60-80/ μl), absolute CD4 count 71/ μl (normal range 290-2,600/ μl) absolute CD8 count 179/ μl (normal range 190-120/ μl) and CD4/CD8 ratio 0.40 (normal range 0.6-2.8). The WBC-2,110/ mm^3 (normal range 4,000-11,000/ mm^3), neutrophils 55% (normal range 40-70%), lymphocytes 35% (normal range 15-40%), monocytes 8% (normal range 2-5%), eosinophils 1% (normal range 1-

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6%), hemoglobin-56 g/dl (normal range 11-14.5 g/dl) and ESR 120 mm in the first hour (normal range 1-9 mm/hour). The renal and hepatic profiles were as follows: fasting blood sugar 81 mg/dl (normal range 70-110 mg/dl), blood urea 27.3 mg/dl (normal range 10-50 mg/dl), serum creatinine 0.7 mg/dl (normal range 0.7-1.1 mg/dl), serum bilirubin 0.5 mg/dl (normal range 0.1-1.0 mg/dl) and SGPT 19 μ l (normal range 9-43 μ l). The patient was further investigated for important opportunistic infections associated with HIV. Ultrasonography of the whole abdomen suggested mild multiseptate loculations in the right perihepatic and right lumbar regions with multiple mesenteric lymph nodes and diffusely thickened distal small bowel loops. Chest X ray PA view showed a non-homogenous opaque shadow with infiltration in the right upper lobe of the lungs. Investigation of ascitic fluid demonstrated a protein 5.2 gm/dl, sugar 92.0 mg/dl, and cells being mostly lymphocytes (99%). ELISA for Koch's IgG (241.9 IU/ μ l) and IgM (1.21 IU/ μ l) were positive. *Leishmania donovani* (L.D.) bodies were positive on splenic aspiration (1+). The patient was immediately put on anti-retroviral drugs: a combination of Zidovudine (300 mg) and Lamivudine (150 mg) twice daily; antibiotics, namely ciprofloxacin (500 mg), tinidazole (600 mg) twice daily for 28 days and anti-tuberculous therapy: (rifampicin 450 mg, isonicotinic acid hydrazide 300 mg, ethambutol 1,000 mg, and pyrazinamide 1,500 mg) per WHO protocol. After one month, the oral candidiasis and generalized weakness improved. The anti-retroviral and anti-Koch's therapy is being continued.

Patient 2

A male patient aged 40 years reported to the out-patient department of RMRIMS with a complaint of fever for the previous two months. This was associated with chest pain, cough, loss of appetite, generalized weakness, and loose stools with mucus (5-6 times per day). The patient had a painless nodule in the posterior triangle of the neck (2 cm) on palpation, which was matted and movable, not fixed to the skin. The patient had lived in Mumbai for the previous ten years and had worked there as a laborer. He had a history of unsafe sex with commercial sex



Fig 1-Ultrasonography of case 1 showing perihepatic fluid collection (attached separately).



Fig 2-Ultrasonography of case 1 showing enlargement of mesenteric lymph nodes (attached separately).

workers in Mumbai for several years. His wife and children were negative for HIV, but ELISA for HIV-1 was done and found reactive in him. CD4 and CD8 counts showed CD4 88.3/ μ l (normal range 60-80/ μ l), absolute CD4 count 08/ μ l (normal range 290-2,600/ μ l), absolute CD count 143/ μ l (normal range 190-2,120/ μ l) and a CD4/CD8 ratio of 0.06 (normal range 0.6-2.8). The total count showed the following: WBC 8,000/ mm^3 (normal range 4,000-10,500/ mm^3), neutro-



Fig 3—Chest X ray PA view of case 2 showing bilateral pleural effusions (attached separately).

phils 64% (normal range 40-70%), lymphocytes 29% (normal range 15-40%), monocytes 0.1% (normal range 2-5%), eosinophils 0.6% (normal range 1-6%), hemoglobin 6.6 g/dl (normal range 11-14.5 g/dl) and ESR 127 mm in the first hour (normal range 1-9 mm/hour). The renal and hepatic profiles were as follows: fasting blood sugar 87 mg/dl (normal range 70-110 mg/dl), blood urea nitrogen 17.0 mg/dl (normal range 5-25 mg/dl), serum creatinine 0.4 mg/dl (normal range 0.7-1.1 mg/dl), serum bilirubin 0.8 mg/dl (normal range 0.1-1.0) and SGPT 21 μ l (normal range 9-43 μ l). The patient was further investigated for opportunistic infections associated with HIV. Ultrasonography of the whole abdomen suggested mild enlargement of the spleen. A chest X ray PA view showed bilateral costophrenic angle obliteration. Two hundred milliliters of pleural fluid was aspirated from the right side. Investigation of the pleural fluid demonstrated: protein 5.2 g/dl, sugar 92.0 mg/dl, cells were mostly lymphocytes (99%). Fine needle aspiration cytology of the cervical lymph node showed whitish caseous material and microscopically acute and chronic inflammatory cells were present in the background of the ne-

crotic field. Few LD spindle shaped epithelioid cells were seen in small granulomatous clusters. Neither AFB nor malignant cells were seen. LD bodies were positive on splenic aspirate (3+). Patient was immediately put on anti-retrovirals the (Zidovudine and Lamivudine) antibiotics (ciprofloxacin) and tinidazole, Miltefosine 50 mg morning and evening and anti-tuberculous four drug regimen per WHO protocol. At one month follow-up the LD body was negative on bone marrow biopsy. The splenic and lymph node enlargement had regressed, and the loose stools and generalized weakness had also improved. Anti-retroviral and anti-Koch's therapy is being continued.

DISCUSSION

These two case reports demonstrate that the triad of HIV-VL and tuberculosis are very difficult to manage. Unfortunately, the number of cases is increasing (Sinha *et al* 2003). There are a lot of shortcomings as far as diagnosis and management are concerned (Pulido *et al* 1998). The Matoux test / Purified protein derivative test may not be positive in cases of HIV infection because of decreased T-cell immunity. As a result, costly tests, like ELISA and PCR, are of utmost importance. However, these are often beyond the reach of the poor in the country.

Highly active antiretroviral therapies and antituberculous drugs are quite costly. There are many drug-drug interactions (Barry *et al*, 1999). Drugs, such as rifampicin, which are metabolized by the CYP P-450 system, are potent enzyme inducers in the liver (Dey *et al*, 2003). They can lead to the metabolism of drugs like protease inhibitors and non-nucleoside reverse transcriptase inhibitors, like Efavirenz and Nevirapine, thereby lowering their serum levels (Dean *et al*, 2002). Similarly, miltefosine a new oral drug for visceral leishmaniasis may have unknown drug interactions. This drug was previously used as an anticancer agent in western countries especially for the breast and gastrointestinal tract. As a result, all these aspects need to be evaluated before a simple, safe and inexpensive regimen for the management of such complicated cases can be undertaken. The Government needs to be involved in this evaluation.

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