

Journal of Coastal Life Medicine

Journal homepage: www.jclmm.com



Document heading

doi:10.12980/JCLM.2.20143D181

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Recurrent visceral leishmaniasis in a HIV positive patient—a case report

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PEER REVIEW

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Comments

This work reports a very important case of leishmaniasis and HIV co-infection, which is very common in leishmania endemic countries. Generally the work is well reported. The work had very good results. Details on Page 48

ABSTRACT

Current treatment options for visceral leishmaniasis (kala-azar) are pentavalent antimony, amphotericin B, liposomal amphotericin B and miltefosine, which achieve long term clinical relief in the majority of HIV patient. Disease relapse is usually provoked by T-cell number or function impairment (corticosteroid or cytotoxic therapy, transplant recipient, advanced human immunodeficiency virus disease). We report a case of visceral leishmaniasis with multiply relapses in a 45 year old Indian HIV positive man. The disease was diagnosed with rK-39 test and confirmed by spleen aspiration test (presence of *Leishmania donovani* bodies). These findings demonstrate that human immune deficiency virus-positive with visceral leishmaniasis was caused by dissemination of viscerotropic *Leishmania donovani* parasites as a consequence of immunosuppression.

KEYWORDS

Visceral leishmaniasis (Kala-azar), HIV, Recurrent, Amphotericin B

1. Introduction

Leishmaniasis is endemic in 88 countries, 72 of which are developing countries. The worldwide prevalence of the disease is estimated at 12 million cases with 400 000–600 000 new cases per year for visceral form (kala-azar)[1]. Leishmaniasis is a parasitic disorder transmitted by bite of infected female *Phlebotomus* sand fly in developing countries. In human beings, the disease present in four different forms with a broad range of clinical manifestation: visceral leishmaniasis, or kala-azar, cutaneous leishmaniasis, mucocutaneous leishmaniasis, and diffuse cutaneous leishmaniasis. Leishmaniasis and human immunodeficiency virus (HIV) co-infection is very common in leishmania endemic countries[2]. In India, it is endemic

in Bihar, West Bengal, Orissa, and some parts of Rajasthan. Leishmaniasis emerges as the third most common opportunistic infection. The genus *Leishmania* causes a wide spectrum of human diseases ranging from self-limited cutaneous to the more severe diffuse cutaneous and visceral forms[1,2].

India, Nepal, Bangladesh and East African countries develop post kala-azar dermal leishmaniasis[3]. This manifestation is a form of cutaneous leishmaniasis characterized by maculopapular or nodular lesions on the face, limbs or trunk, which appear after a symptom free period following the end of visceral leishmaniasis treatment. The interval between kala-azar and post kala-azar dermal leishmaniasis is estimated as being months to years in India but considerably shorter in Africa (0–6 months)[4].

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Article history:

Received 2 Jan 2014

Received in revised form 9 Jan, 2nd revised form 13 Jan, 3rd revised form 20 Jan 2014

Accepted 22 Jan 2014

Available online 28 Jan 2014

2. Case report

A 45 years old man was referred to Rajendra Memorial Research Institute and Medical Sciences, Bihar, India. He had complaints of fever for 45 d, loss of appetite, diarrhea, and indigestion for 15 d. On examination the patient was conscious, oriented, pulse (96 beats/min), blood pressure (110/76 mm Hg) and pallor (+++). Icterus, cyanosis and clubbing were absent. No venous engorgement was found. Chest and cardiovascular examination was found to be normal.

He had previous history of two episodes of visceral leishmaniasis, pulmonary tuberculosis and family history of kala-azar (visceral leishmaniasis). First episode of leishmaniasis occurred and he took sodium antimony gluconate injection for one month. First relapse (after six months) was treated with miltefosine (150 mg/d for 28 d). After 4 months the second relapse occurred and the physical examination revealed palpable enlarged spleen reached up to umbilical cord and palpable two finger enlarged liver.

Laboratory investigation showed leucopenia (leukocytes: 1700/ μ L), erythrocytopenia (red blood cell: 2.71 million/ mm^3), thrombocytopenia (platelets: 106 000/ μ L), and normocytic anemia (haemoglobin B: 7.3 g/dL). The biochemical test was normal except serum creatinine (1.8 mg/dL) and albumin: globulin ratio (1.15:1). Liver function test showed normal (serum glutamic-oxaloacetic transaminase: 24 IU/L, serum glutamic pyruvic transaminase: 21 IU/L, and alkaline phosphatase: 224 IU/L). K-39 antigen was found to be positive by performing rK-39 strip test and spleen aspiration test showed the presence of *L. donovani* (*Leishmania donovani*) antibodies (4+) in the spleen.

Even after diagnosing *L. donovani* antibodies, the treatment of leishmaniasis was not yet started. Sodium antimony gluconate and miltefosine were not prescribed due to its resistance to the parasite. In this case fungizone (amphotericin B) is the choice of drug but it cannot be prescribed after diagnosing because his serum creatinine level was above the normal (1.6 mg/dL). The laboratory tests were performed after 7 d of admission and serum creatinine was found to be in normal range (1.3 mg/dL). At this stage antileishmanial therapy was started with fungizone (amphotericin B 0.5 mg/kg) infusion 15 doses in alternative days.

3. Discussion

Leishmaniasis is a group of disease caused by several species of genus *Leishmania*. Each species leads to occupying a particular geographical zone. It has been estimated that 1.5 million new cases of cutaneous leishmaniasis occur annually and more than 80% of cases affect individual in developing countries. Brazil, Iran, Afghanistan and Sudan suffer the highest prevalence and are the hyper endemic regions of the world[4]. In India, Bihar, Orissa, West Bengal, and northern part of Rajasthan have high prevalence. In old world countries such as India, Bangladesh, Burma, Middle-East and Central Asia, Sudan, and Kenya *L. donovani* is a causative organism whereas in

new world countries, *Leishmania braziliensis*, *Leishmania chagasi* and *Leishmania amazonensis* are the causative organisms. In 5% of East African patients and 20% of Indian patients, a rash develops after visceral disease has been healed, either spontaneously or following treatment[5–8]. Usually the rash comprises of papules, plaques, and nodules resembling leprosy[7]. Diagnosis may be clinical, but parasite can be seen by microscopy in smears with limited sensitivity. Polymerase chain reaction and monoclonal antibodies may detect parasite in more than 80% cases. Serological test and leishmanin test are of limited value[9]. The aspirates of bone marrow and spleen show extremely heavy parasitization. Spleen aspiration technique (sensitivity: 99.5%) has high sensitivity than bone marrow aspiration (sensitivity: 60%). Leishmaniasis may be acquired before or after HIV infection. In some patients, typical characteristics of fever and splenomegaly have not been present and serological tests have been negative.

Co-infection of leishmania and HIV produces cumulative deficiency of cell mediated immunity, a key factor for primary protection against infection, recurrences of metastasis of parasites. Co-infection may amplify the immune defect against both leishmaniasis and HIV, and increase disease severity and morbidity. Visceral leishmaniasis, 100–1000 times more common in HIV, is a major fatal outcome of co-infection[10]. Treatment is always needed in Indian patients. Sodium stibogluconate is given at 20 mg/kg for 2 months in Sudan and for 4 months in India. Liposomal amphotericin B is found to be effective. Newer compounds such as miltefosine can be administered orally or topically[4].

Current therapies for visceral leishmaniasis such as pentavalent antimony, amphotericin B, liposomal amphotericin B and miltefosine lead to clinical cure in the majority of immunocompetent patients. Recurrent infections occur within a period of six months, commonly in patients with impaired cellular immunity such as individuals with HIV disease or immune-suppressed transplant recipients[11]. In this case we report on multiple episodes of relapsing visceral leishmaniasis in a patient with HIV positive. Beyond the known decreased capacity of cytotoxic responses during senescence no other immune-suppressing factor was identified in our case.

Initially, our patient was treated with sodium antimony gluconate. However, this treatment option fails to succeed in chronic suppression of the disease. Miltefosine, an alkyl phosphocholine with antileishmanial activity was used as an alternative treatment in his first episode of relapse. Studies in immunocompromised patients (HIV seropositive) have shown that the antileishmanial activity of the drug is retained in this special population, suggesting that miltefosine might be a useful option in preventing relapses of the disease. Unfortunately, even after miltefosine therapy, our patient had a new episode of visceral leishmaniasis. In order to eradicate the infection, we decided to administer amphotericin B (0.5 mg/kg) infusion 15 doses in alternative days. During the amphotericin B therapy, after the 8th dose treatment was withheld due to increase in serum creatinine level. Rests of the doses were continued after 15 d as serum creatinine level reached normal.

4. Conclusion

An unusual case of recurrent visceral leishmaniasis in a HIV patient was effectively treated with amphotericin B and there is no evidence of relapse after 6 months of follow up. Maintenance therapy may be needed in some cases in order to prevent visceral leishmaniasis relapse. As the incidence of HIV increases in areas in which *Leishmania* species are endemic, visceral leishmaniasis is being recognized more frequently as a opportunistic infection in patients with AIDS. This case also emphasizes the potential use of polymerase chain reaction to confirm the diagnosis, the *Leishmania* species genotyping, and for clinical evaluation and follow up of HIV patients undergoing antiretroviral therapy who have previously had leishmaniasis or patient living in leishmaniasis endemic areas.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

We express our gratitude to Dr. Pradeep Das (Director) and Dr. Krishna pandey (Scientist D) Rajendra Memorial Research Institute and Medical Sciences, Patna, India for permitting us to take cases from the hospital, and also express our gratitude to our faculty at National Institute of Pharmaceutical Education and Research, Hajipur, Bihar, India for their constant support and encouragement.

Comments

Background

Leishmaniasis is a very important neglected tropical disease. Leishmaniasis and HIV co-infection is very common in leishmania endemic countries. This co-infection further compromises the patients' immune system and therefore increasing disease severity and morbidity. Knowing the outcome of such co-infections is important in the management process.

Research frontiers

This case report emphasizes the use of confirmatory diagnosis of leishmaniasis and genotyping of the *Leishmania* species, and for clinical evaluation and follow up of HIV patients undergoing antiretroviral therapy who have previously had leishmaniasis or patient living in leishmaniasis endemic areas.

Related reports

Diffuse cutaneous leishmaniasis/kala-azar dermal leishmaniasis in HIV-positive patients have previously been reported elsewhere. The extent of such co-infection and the severity of the diseases vary from one setting to another.

Innovations & breakthroughs

This report has shown that amphotericin B (0.5 mg/kg) infusion 15 doses in alternative days can be used to treat leishmaniasis in HIV-positive patients.

Applications

The report on co-infection is important in understanding the diseases that can occur together and devising the management process that will not increase the severity of the other.

Peer review

This work reports a very important case of leishmaniasis and HIV co-infection, which is very common in leishmania endemic countries. Generally the work is well reported. The work had very good results.

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