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A Case of African Visceral Leishmaniasis (VL) Treated with a Combination of Liposomal Amphotericin-B and oral Miltefosine

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Abstract A 36-year-old Nigerian man was assessed for chronic recurrent fever, generalized weakness, body aches, epistaxis and bleeding gums of 3-month duration. Despite receiving treatment for suspected malaria twice and undergoing multiple courses of antibiotics for suspected infections, his symptoms persisted. Examination revealed hepatosplenomegaly, lymphadenopathy, and severe pallor. Investigations revealed severe anemia, pancytopenia, raised globulin levels. Bone marrow biopsy revealed Leishmania Donovani (LD) bodies. He received treatment with a short duration of high-dose liposomal Amphotericin B followed by outpatient oral Miltefosine to which he responded successfully.

Keywords: *infections, visceral leishmaniasis, VL, Amphotericin-B, Miltefosine, black fever, Kala-azar*

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1. Background

Visceral Leishmaniasis (VL) is an important differential for chronic febrile illness and should be considered in subjects from endemic areas after the common entities have been excluded. There are no current guidelines on the treatment of African VL. A combination of high-dose short-term liposomal Amphotericin B followed by oral Miltefosine is a safer alternative to conventional treatment with antimonials.

2. Case Presentation

A 36-year-old man from Nigeria presented with a 3-month history of intermittent, low to moderate grade fever, associated with generalized weakness, body aches, and intermittent generalized headaches. He also complained of bleeding from his gums and nose of 3-month duration and had an associated weight loss of 4kg during this duration. He denied any history of chills, altered sensorium, sneezing, rhinorrhoea, cough, expectoration, joint pain, dysuria, abdominal pain, lymphadenopathy or rash anywhere on the body. He had received treatment for suspected malaria for this presentation on two occasions yet the symptoms had persisted. Past medical history was positive for hepatitis B infection detected six months prior in Nigeria during routine blood work as per the patient. Despite seeing multiple caregivers, his symptoms did not improve and the patient traveled to India for further evaluation.

On examination, the patient was alert and cooperative, had a temperature of 100.6°F, heart rate of 102/min, regular, all peripheral pulses were present and symmetrical, blood pressure was 110/80mmHg. He had 3+ pallor and enlarged left supraclavicular and bilateral axillary

lymph nodes, 1-1.5 cm in size, soft, non-tender, discreet and mobile. There was no icterus, cyanosis, clubbing, and edema feet.

Systemic examination revealed soft, non-tender, enlarged liver, 5 cm below the costal margin with a smooth surface and rounded margin, the spleen was also palpable beyond umbilicus, was non-tender with a smooth surface. Rest of the physical exam including respiratory/cardiovascular and nervous system was unremarkable.

2.1. Investigations

Investigations showed a haemoglobin of 5.2g/dl, total leukocyte count of 1200, the differential count showed 74%lymphocytes, 22%neutrophils, 4% monocytes. Platelets were 42,000/µl. Peripheral smear showed pancytopenia, normocytic, normochromic red cells, ovalocytes, and occasional plasmacytoid cells. The malarial parasite wasn't seen. Antigen test for malarial parasite was negative.

Blood investigations revealed urea of 25mg/dl, creatinine 1.0mg/dl, uric acid 7.2mg/dl, sodium 140mEq/L and potassium 3.9mEq/L.

Liver function test revealed total and direct bilirubin of 1.5 and 0.45mg/dl respectively, aspartate and alanine aminotransferase were 26U/L and 18U/L, alkaline phosphatase 121 U/L and gamma glutamyl transferase of

62 U/L. Total protein 10.6g/dl, albumin 2.6g/dl, globulin 8.0g/dl, A/G ratio was 0.3. Prothrombin time 16.2 sec (control 10.7 sec) and INR was 1.6. Activated prothrombin time was 31.7 sec (control 27 sec).

HIV, anti-HCV and HBsAg tests were negative. Blood culture did not show any growth. Serum protein electrophoresis showed thick and dense atypical band in the gamma globulin region. G6PD was normal. Hemoglobin electrophoresis and sickling test were negative.

Routine urine examination was normal. Free kappa in urine was 211.75 mg/l (normal range=3.3-19.4 mg/l), free lambda in urine was 196.44 mg/l (normal range=5.71-26.3 mg/l).

Chest x-ray was normal. Ultrasonography of abdomen confirmed hepatosplenomegaly.

In order to rule out hematologic malignancy, a bone marrow biopsy was performed which revealed numerous LD bodies (Figure 1).

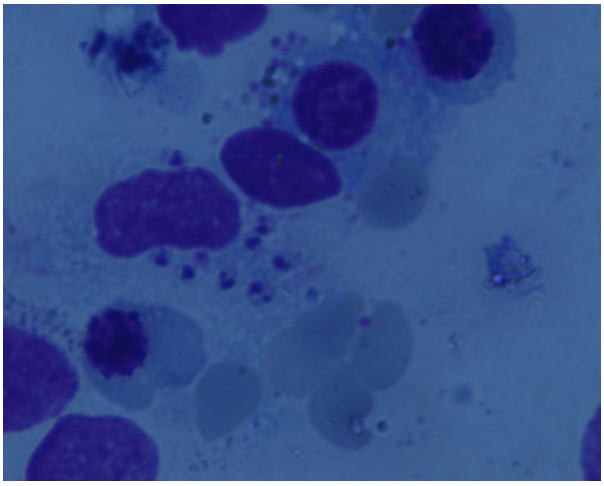

Figure 1. Bone marrow biopsy showing numerous LD bodies

2.2. Differential Diagnosis

1. Infectious aetiology-
   - Chronic Malaria Disseminated Tuberculosis Typhoid fever,
   - Kala Azar (VL),
   - Viral Hepatitis HIV,
   - Other viral infections- EBV
2. Portal Hypertension
3. Haematological Malignancy-leukemia/ lymphomas such as CML.

2.3. Treatment

The patient was transfused 5 units of packed red cells and 6 units of platelets. After bone marrow biopsy findings, Amphotericin B was given intravenously in a dose of 10mg/kg/day for two days. He was subsequently discharged on oral Miltefosine 50mg once daily for 28days.

2.4. Outcome and Follow-up

The patient was scheduled to follow up after one month. His fever had completely subsided; he gained 2.5 kg body weight during this time interval. His hemoglobin was 10.2g/dl and he had a subjective feeling of wellness.

3. Discussion

Visceral Leishmaniasis (VL) is one of the varied manifestations of the affliction with intramacrophage protozoan, Leishmania donovani. Leishmaniasis is endemic in around 88 countries, largely seen in developing and underdeveloped countries in the tropical and temperate regions. It leads to a significant financial burden on these countries [1].

VL is characterized by prolonged febrile illness, enlargement of lymph nodes, hepato-splenomegaly, pancytopenia, and hypergammaglobulinemia [2,3]. Bone marrow is often involved as the reticuloendothelial system is affected by the parasite, which survives and proliferates inside the macrophages. Several diagnostic methods are in use with more being developed for the early identification of the disease, yet bone marrow and splenic aspiration are widely used for the diagnosis of the condition through direct visualization of the parasite [1].

Over the past several decades, pentavalent antimonial has been used effectively for the treatment of VL, however recent trials conducted in India have shown the benefit of short- term high dose treatment with liposomal Amphotericin B to be superior to conventional treatment [4]. Additionally, the cost of such treatment is justified by the advantages such as less adverse effects, better compliance, good cure rate, the susceptibility of the parasite and a short duration of hospitalization.

Considering the capacity of the Leishmanial parasite for resistance, combination therapy, like the one used for tuberculosis and HIV, in endemic areas may be explored for treatment of affected patients [1]. We successfully treated this patient with liposomal Amphotericin B followed by oral agent Miltefosine for 28 days based on recent studies done in Indian subjects with VL [5]. At one-month follow-up, this patient had not displayed any signs of relapse or adverse effects of the treatment.

There are no current guidelines for combination therapy for treatment of VL and further studies are needed before the treatment standards can be established. We provide a case of African VL that was successfully treated with this combination therapy. This combination therapy provides a safer alternative for the current treatment of VL, especially in countries where antimonials are either not available or widespread resistance exists.

4. Learning points

1. Visceral leishmaniasis should be suspected as a differential for chronic febrile illness especially in patients from endemic areas after the common entities have been excluded.
2. Short course, high dose liposomal amphotericin B treatment has been shown to be a safer yet superior alternative to conventional treatment with antimonials.
3. Combination chemotherapy may be beneficial and can be tried in severe cases.
4. This combination therapy provides a safer alternative for the current treatment of VL, especially in countries where antimonials are either not available or widespread resistance exists.

References

[1] Singh, R.K., Pandey, H.P., and Sundar, S., "Visceral leishmaniasis (Kala- azar): Challenges ahead," *Indian J Med Res*, 123. 331-344. Mar.2006

[2] Herwaldt, B.L., "Leishmaniasis," *Lancet*, 354. 1191-1199. Oct.1999.

[3] Murray, H.W., Berman, J.D., Davies, C.R., and Saravia, N.G., "Advances in leishmaniasis," *Lancet*, 366. 1561-1577. Oct.2005.

[4] Sundar, S., Chakravarty, J., Agarwal, D., Rai, M., and Murray, H.W., "Single-Dose liposomal Amphotericin B for visceral leishmaniasis in India," *N Engl J Med*, 362. 504-512. Feb.2010.

[5] Sundar, S., Rai, M., Chakravarty, J., Agarwal, D., Agrawal, N., Valliant, M., *et al.*, "New treatment approach in Indian visceral leishmaniasis: Single dose liposomal amphotericin B followed by short-course oral miltefosine," *Clin Infect Dis*, 47(8). 1000-1006. Oct.2008.