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General Medicine

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CASE REPORT : LEISHMANIASIS (KALA AZAR) IN MUMBAI

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ABSTRACT

Leishmaniasis is caused by the infection of haemoparasite 'Leishmania donovani'. Clinically it can present as Cutaneous Leishmaniasis (CL), Mucocutaneous Leishmaniasis (MCL) and Visceral Leishmaniasis (VL). In India it is a major health problem in the North & Central regions of India and is infrequently reported from western India. However, we encountered a clinically suspected case of Leishmaniasis in Mumbai. The case presented with Visceral Leishmaniasis. Laboratory diagnosis was made by demonstration of LD bodies on histopathological examination. Patient recovered with treatment with Liposomal Amphotericin B. The reason for the emergence of the disease in Mumbai could be due to migration of people from areas where the disease is endemic to hubs of development in urban areas for their livelihood.

INTRODUCTION

Leishmaniasis is a disease caused by parasites of the genus Leishmania. Several clinical syndromes are subsumed under the term leishmaniasis: most notably visceral, cutaneous, and mucosal leishmaniasis, which result from replication of the parasite in macrophages in the mononuclear phagocyte system, dermis, and naso-oropharyngeal mucosa, respectively. These syndromes are caused by a total of about 21 leishmanial species, which are transmitted by about 30 species of phlebotomine sandflies.[1–3] If clinically evident but untreated, visceral leishmaniasis (also known as kala-azar, Hindi for black sickness or fever) causes life-threatening systemic infection; cutaneous leishmaniasis can cause chronic skin sores ; and mucosal leishmaniasis (also known as espundia), a dreaded metastatic complication of new-world cutaneous leishmaniasis, causes facial disfigurement . Thus, the primary goals for clinical management are straightforward—to prevent death from visceral leishmaniasis and morbidity from cutaneous and mucosal leishmaniasis. However, even tropical medicine clinicians are often baffled by the complexities of leishmaniasis: by the apparently innumerable possible combinations of different leishmanial syndromes, species, and geographical areas of acquisition of infection, each combination varying by clinical presentation, ease of diagnosis, natural history, and response to therapy.

CASE

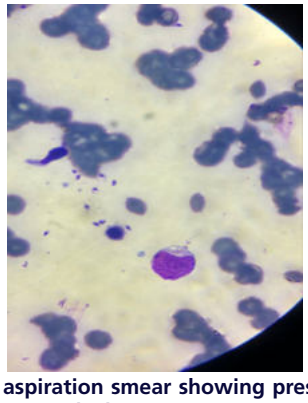
A 53 year old female, migrated from Madhavpur district of Bihar 2 years back, came to our hospital with complaints of abdominal pain since 1 year, loss of weight 8 kgs over 1 year, low grade fever on & off since 1 year, dry cough since 1 year. On examination, her general condition was poor, pulse 90/min, Blood pressure 90/60 mm Hg, Respiratory System examination was Normal, Per Abdomen examination revealed hepatosplenomegaly. She was investigated and treated profusely by multiple places over the year but still her complaints persisted. Her symptoms mimicked Tuberculosis so she was started on Anti Tuberculous Treatment prophylactically previously but she stopped on her own. On hematological examnination, CBC revealed pancytopenia with Hb : 5.7 g%, Total Leucocyte Count :2,900/cu.mm ; Platelet 1,29,000 / cumm; ESR was raised 146 mm/hr ; LDH 190 IU/L. Peripheral smear showed microcytic normochromic picture and was negative for malaria parasite. The results of serial hemogram are shown in [Table 1]. Blood glucose and renal function were normal. Hepatitis B surface antigen, anti-hepatitis C virus, and human immunodeficiency virus serology were negative. Chest X-ray was normal. Ultrasound of the abdomen showed hepatosplenomegaly . Bone marrow aspiration and biopsy were performed. Bone marrow morphology was normocellular with normoblastic erythropoiesis. M:E ratio was 1.5:1. Myeloid and megakaryocytic series were normal in maturation and morphology. There was a marked increase in histiocytes with a prominent hemophagocytosis. Amastigote forms of *Leishmania donovani* were seen both intracellularly and extracellularly [Figure 1]. The final diagnosis of Visceral Leishmaniasis was made. The patient was started with amphotericin liposomal B 3 mg/kg/day on day 1 to 5, day 14 and day 21. At discharge, spleen was 16 cm and liver was 17 cm in size which was less than that on admission. Hematological and biochemical parameters at discharge are shown in [Table 1]. The patient remained asymptomatic and improved at the end of 1 month and follow-up. Bone marrow aspiration and biopsy was done on follow up and reports showed no evidence of haemoparasite.

TABLE 1

CBC	On Admission	On Discharge
Hb (g %)	5.7	9.0
TLC (cells/mm3)	2900	4600
PLATELETS (/mm3)	1,29,000	1,98,000

Hb : Haemoglobin ; TLC: Total Leucocyte Count

FIGURE 1



Bone marrow aspiration smear showing presence of two *Leishmania donovani* (LD) body

DISCUSSION

Clinical manifestations

Visceral leishmaniasis encompasses a broad range of manifestations of infection. Infection remains asymptomatic or subclinical in many cases, or can follow an acute, subacute, or chronic course. The classic kala-azar syndrome is exemplified by patients such as those in Sudan[4] who are heavily infected throughout the mononuclear phagocyte system; develop life-threatening disease after an incubation period of weeks to months; and have fever, severe cachexia, hepato-splenomegaly (splenomegaly usually predominates), pancytopenia (anaemia,

thrombocytopenia, and leucopenia, with neutropenia, marked eosinopenia, and a relative lymphocytosis and monocytosis), and hypergammaglobulinaemia (mainly IgG from polyclonal B-cell activation) with hypoalbuminaemia.

Differential diagnosis and diagnosis

The differential diagnosis includes malaria, tropical splenomegaly syndrome, schistosomiasis or cirrhosis with portal hypertension, African trypanosomiasis, miliary tuberculosis, brucellosis, typhoid fever, bacterial endocarditis, histoplasmosis, malnutrition, lymphoma, and leukaemia. Leishmanial parasites can be seen on stained slides or in cultures of a biopsy sample or tissue aspirate (eg, of spleen, bone marrow, lymph nodes). The sensitivity is highest for splenic aspiration (as high as 98% compared with <90% for other organs). Whereas in most cases leishmanial-specific cell-mediated immunity becomes detectable only after recovery, high titres of non-protective antileishmanial antibody can typically be detected (eg, with the direct agglutination test) during the illness and can persist for years afterwards. A serological assay for IgG antibody to K39 (a recombinant leishmanial polypeptide), which uses antigen-impregnated nitrocellulose paper strips,35 looks promising for diagnosis of visceral leishmaniasis under field conditions; but additional field testing is needed.

Treatment

Use of highly effective, rapidly active therapy is important, as is monitoring for bleeding and intercurrent infections, such as pneumonia, tuberculosis, and dysentery. Pentavalent antimony is still commonly used outside of India, with response rates averaging 90%.[5]. Treatment of cases in India is particularly challenging because of their sheer abundance and their refractoriness to antimony (and pentamidine12) therapy. Currently, up to 50% or more of previously untreated cases in the state of Bihar are unresponsive to, or relapse after, conventional antimony therapy,[6] perhaps largely because of inappropriate use of antimony by local practitioners.

In Bihar, many practitioners have turned to conventional amphotericin B for first-line therapy, which remains almost 100% effective. The newly available lipid formulations of amphotericin B, in which various lipids have replaced the component deoxycholate, are also highly effective and offer added benefits: passive targeting of drug to macrophage-rich organs decreases nephrotoxic effects and allows higher daily doses of the drug and shorter courses of therapy [7'8]. Lipid formulations of amphotericin B include liposomal amphotericin B, amphotericin B lipid complex, and amphotericin B cholesteryl sulphate. The US Food and Drug Administration recently licensed liposomal amphotericin B for treatment of visceral leishmaniasis and recommended treating immunocompetent patients with 3 mg/kg daily on days 1–5, 14, and 21 (total 21 mg/kg) and immunosuppressed patients with 4 mg/kg daily on days 1–5, 10, 17, 24, 31, and 38 (total 40 mg/kg)[9].

Other parenteral alternatives that have merit in some settings include pentamidine (limitations include suboptimal effectiveness in India and toxic effects, especially with long courses of treatment), and paromomycin (currently not commercially available). Adjunctive interferon-gamma therapy may accelerate or improve the response to antimony therapy in some difficult cases.[6'10] An effective oral agent would be a major advance. Therapy with the oral agent miltefosine (100–150 mg daily for 28 days) has been virtually 100% effective and acceptably tolerated in phase I/II studies of adult patients in Bihar[11] .

To summarize, this patient is migrant from endemic area of Bihar. Mumbai has a large migrant population, hence we should always consider Kala Azar as a differential diagnosis. This case, according to literature and other case reports, is the third such case reported in Mumbai. This case is also different as lipid formulation Inj. Amphotericin Liposomal B was used instead of the Inj. Amphotericin B. Thus, the occurrence of such cases seems to be an indication of reemergence of Leishmania in the sub-continent.

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