

Leishmanial Hepatitis with Chronic Hepatitis B Infection Treated Successfully with Liquid Form of Liposomal Amphotericin B - A Case Report

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Abstract:

Hepatic involvement either due to leishmaniasis or due to coexisting viral infection sometime poses a problem for the clinicians. Atypical presentation is also challenging for them. We present a case of visceral leishmaniasis (Kala-azar) from a non endemic zone, co infection with hepatitis B virus simulating chronic viral hepatitis successfully treated with liquid form of liposomal amphotericin B.

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Introduction:

Leishmaniasis is an infection caused by a parasite called *Leishmania donovani* complex (comprising *Leishmania donovani*, *Leishmania infantum*, *Leishmania chagasi*) that spread to people through the bite of the female phlebotomine sand fly. The parasite exists in many tropical and temperate countries. Common presentation of visceral leishmaniasis is fever, cachexia, hepatosplenomegaly (predominantly splenomegaly), pancytopenia, and hypergammaglobulinemia. The increasing number of immunocompromised patients has resulted in an increased incidence of visceral leishmaniasis and atypical clinical presentations¹. Though in kala azar splenic enlargement is much common than hepatic enlargement, reverse is also been observed². Kala-azar is an endemic disease. But sporadic cases have also been reported from non-endemic zones and the presentation may vary³. So the clinicians should bear in mind the atypical presentation of Kala-azar when dealing with PUO cases. More over when a kala-azar patient presents with jaundice it is very difficult to say whether the jaundice is due to leishmanial involvement or due to co-existing viral diseases. It was observed that liver function test improved after treatment with sodium stibogluconate in a group of patient with Kala-azar with impaired liver function test possibly due to leishmanial involvement⁴. But when kala azar is associated with hepatitis other than leishmanial involvement we look for a safe anti leishmanial drug. Here we report a case of kala-azar co-infected with HBV with impaired hepatic function treated successfully with amphotericin B.

Case Report:

A 29-year-old man, from Bhola (a south western part of Bangladesh) was admitted into Bangabandhu Sheikh Mujib Medical University (BSMMU) on 7 September, 2011 because of high grade fever and 5 kgs weight loss during the last 5 months. Before coming to BSMMU he was treated by various antibiotics including ciprofloxacin, doxycycline, ceftriaxone and antimalarial without significant improvement. He did not have any history of travelling to malaria or kala azar endemic zone and no history of contact with known case of TB patients. On examination the patient was found febrile, mildly anaemic and mildly icteric and he had signs of generalized muscle wasting. He did not have lymphadenopathy. He had hepatomegaly 6 cm from right costal margin, but no splenomegaly or ascites. Other physical examination was otherwise normal.

His blood picture showed haemoglobin 10mg/dl, ESR 40 mm in 1st hour, platelet count 100000/ml, WBC count 4000/ml. Peripheral blood film showed bicytopenia and reticulocyte count was normal. Serum bilirubin was 3mg/dl with predominantly conjugated bilirubin. Serum ALT 364 U/L, serum ALP 393 U/L, prothrombin time 4 second above the control, routine urinalysis and serum creatinine were normal. ICT for malaria was negative but ICT for kala azar was positive. Bone marrow failed to show presence of LD body. Test for HBs Ag & Anti HBe IgG were positive but HBeAg & Anti HBe were negative. HBV DNA was undetectable. Endoscopy of the upper GIT was normal. Ultrasonography showed enlarged liver with decreased parenchymal echogenicity. We hoped to do a liver biopsy to search for LD bodies as well as to see the hepatic parenchymal status but the patient refused.

On the basis of history of prolonged fever associated with significant weight loss and the result of

immunological tests the patient was diagnosed as a case of visceral leishmaniasis with chronic hepatitis B viral infection. Considering his impaired liver function he was considered a good candidate for liposomal amphotericin B for the treatment of visceral leishmaniasis. When we went for collecting the drug we found that liquid form of liposomal amphotericin B is available from government source. We collected 15 vials for Liposomal amphotericin B, the market price of which was Taka 273,000. For liquid form of amphotericin B sonication is required. So we had to collect sonicator from the same source. Considering patient impaired liver function we initially gave corrected dose of 0.8mg/kg/day (as recommended by the manufacturer) and subsequently when liver function improved we continued with the full dose of 1mg/kg/day. Over the 15 days period the patient received 13mg/kg which is within the recommended cumulative dose for curing visceral leishmaniasis as per the guideline for the treatment of visceral leishmaniasis in Bangladesh (10-15mg/kg)⁵. Over this period of treatment fever subsided, the patient gained 3 kg weight, anemia improved, liver size reduced, liver enzymes became normal and there was significant feeling of well being.

Discussion:

According to national guide line of Bangladesh an individual in an endemic area who has fever for more than 2 weeks, splenomegaly and rK39 test positive may be labeled as a case of visceral leishmaniasis (kala-azar)⁵. Splenomegaly appears early and is almost invariably present. Spleen size increases gradually in relation to duration of disease⁶. But a large cohort study in Brazil^{7,8} demonstrated that sub clinical form of kala azar is not associated with splenomegaly. The cohort study also demonstrated that combination of fever, hepatomegaly, hypergammaglobulinemia and increased blood sedimentation rate can predict the subclinical form of visceral leishmaniasis. The occurrence of splenomegaly and leucopenia distinguished the acute form from subclinical form. As the patient was from non endemic area and had no splenomegaly nobody initially thought of kala-azar.

After getting admission in BSMMU during evaluation of prolonged fever rK39 test was done and it was positive. We found he had hepatomegaly along with impaired liver function. Subsequently we got HBsAg positive, anti HBcIgG positive and HBeAg negative. So we advised him for HBV DNA study and labeled him as a case of visceral leishmaniasis with chronic hepatitis B infection. Hence, we started to treat him with liposomal amphotericin B and

patient started to improve significantly. Within two weeks all liver enzymes came within normal limit. In the meantime the DNA report was available and it was undetectable. This indicates that hepatic involvement was not due to HBV infection but due to leishmanial hepatitis^{6,9,10}.

The exact pathology and aetiology of hepatic damage in leishmaniasis is unclear but may have an immunologic basis; more so since leishmaniasis has been reported to cause vasculitides and mixed cryoglobulinemia in endemic areas¹¹.

This reported case reminds us that kala azar should be considered when evaluating fever of unknown origin whether the patient comes from an endemic or non endemic zone. Also leishmanial involvement of the liver can be well managed by anti leishmanial therapy. In case of suspicion or coinfection of kala azar with HBV or HIV a less hepatotoxic drug like liposomal amphotericin B is a good choice.

References:

1. Rosenthal E, Marty P, Del Giudice P. HIV and Leishmania coinfection: A review of 91 cases with focus on atypical locations of Leishmania. *Clin Infect Dis* 2000; 31(4):1093–1095.
2. Chowdhury MAJ, Alam MN, Rafiqueuddin AKM, Hussain A, Rahman H, Siddiqui AB, Nazir MFH, Rahman KM, Biswas A. Clinical profile of Kala azar in Rajshahi: A prospective study of 273 Hospitalised patients during one year. *Journal of Bangladesh College of Physicians and Surgeon* 1990; 8(1):18-28.
3. Alam MN, Chowdhury MAJ, Rafiqueuddin AKM, Hussain A, Rahman MH, Siddiqui AB, Nazir FH and Rahman KM. Kala azar in Bangladesh. *Bangladesh journal of Medicine* 1990; 1:5-8.
4. Mishahuddin M, Jahan K, Chowdhury MAJ, Absar N. Stibogluconate for Leishmaniasis. *Lancet* 1993; 342:804.
5. National Guideline for Diagnosis and treatment of Kala azar and PKDL in Bangladesh July 2010(In Press).
6. Ahsan HAMN, Chowdhury MAJ, Azhar MA, Rafiqueuddin AKM. Correlation between duration of fever and splenic enlargement in kala Azar. *Bangladesh Medical Journal (Khulna Branch)* 1993; 26:1-2.
7. Gulati S, Paljor HP, Pandit S, Jindal R. Kala Azar without splenomegaly. *Ann Trop Med Public Health* 2009; 2:57-60.
8. Carvalho EM, Barral A, Pedral-SampaioD, Barral-Netto M, Badaro R, Rocha H, et al. Immunologic markers of clinical evolution in children recently infected with *Leishmania donovani* chagasi. *J Infect Dis* 1992; 165: 535–540.
9. Azhar MA, Ahsan HAMN, Chowdhury MAJ, Mahmood TAK, Rafiqueuddin AKM, Rahman F. Liver pathology in kala-azar. *Specialist: Pakistan's J Med Science* 1997; 13:249-251
10. Aggarwal P, Wali J, Chopra P. Liver in kala Azar. *Ind J Gastroenterol* 1990; 9: 135-36
11. Casto M, de Rosa FG, Pucillo LP. Mixed cryoglobulinemia secondary to visceral leishmaniasis. *Arth Rheuma* 1999; 42:2007-11.