
Visceral Leishmaniasis with renal involvement or Systemic lupus Erythematosus: Clinicians dilemma

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Abstract

Indian subcontinent is responsible for the largest proportion of global Visceral Leishmaniasis (VL). 35 year old man watchman by occupation hailing from Nepal came with complaints of high grade fever on and off since two months. He also had pedal oedema, breathlessness, oliguria and distension of abdomen. On examination patient had pallor, pedal oedema, ascites and splenomegaly. His investigations showed proteinuria (1.5 gm/day), raised Creatinine and pancytopenia. Bone marrow aspiration showed multiple *Leishmania Donovanii* (LD) bodies, amastigote form scattered intracellular/extracellular form. Bone marrow Biopsy was suggestive of normocellular marrow with histiocytic infiltration with LD bodies. Patient was treated with Amphotericin B infusions. Patient's condition deteriorated due to amphotericin induced nephrotoxicity. Report of ANA +2 (1:160) nucleolar was then received. Patient was given methyl prednisolone injection 1 gm /day for 5 days. Patient succumbed to hypo-proteinemia, sepsis and renal impairment. Visceral Leishmaniasis and Systemic Lupus Erythematosus (SLE) with flare both can mimic each other due to overlapping clinical features. SLE can have simultaneous infection with VL in endemic areas. A clinician will have to use is detailed history, thorough examination, battery of laboratory investigations and his clinical acumen to arrive at diagnosis and rule out the mimicker.

Keywords: SLE, Lupus nephritis, Kala azar.

1.Introduction

Due to higher suspicion and better diagnostic tools systemic lupus erythematosus (SLE) is getting diagnosed more frequently in urban health care facilities. Mortality in SLE is usually due to infectious diseases in developing country like India. Indian subcontinent is responsible for the largest proportion of global Visceral Leishmaniasis (VL aka Kala Azar) cases, reported case-fatality rates ranged from 1.5% (93 deaths/6224 VL cases from 2004–2008) in Bangladesh to 2.4% (853/34,918) in India and 6.2% (91/1477) in Nepal. However, community-based studies that included active searches for deaths due to kala-azar estimate case-fatality rates of more than 10%, while data from a village-based study in India suggest that as many as 20% of VL patients[1]. We are reporting a case of a man from Nepal having clinical presentation of both these diseases causing diagnostic dilemma to the clinician.

2. Case Report

35 year old man watchman by occupation hailing from Nepal came with complaints of high grade fever on
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and off since two months. Patient also complained of left hypochondrial pain since one month. He had distension of abdomen and pedal oedema since 15 days. He had breathlessness on exertion since 10 days. He also complained of oliguria since one day. There was no history of altered behaviour. No history of any drug abuse or previous blood transfusion. Patient didn't have rash, sore throat or oral ulcers. No history of similar illness past. Patient was chronic alcoholic since last 10 years consuming one quarter (180 ml) of country liquor per day. On examination, he was febrile; pulse–100/min with blood pressure of 110/70mm Hg. Pallor, grade three pitting oedema was present. There was no lymphadenopathy, cyanosis, clubbing. No petechial rash/purpura. Abdomen was distended, tender with splenomegaly and hepatomegaly. Basal crepitations were present bilaterally on auscultation of lungs. Fundus was normal. The following differential diagnoses were thought; Secondary Haemophagocytic lymphohistocytosis (HLH), Alcoholic

liver disease with Hepato-renal syndrome, Visceral Leishmaniasis, Lymphoma or Myelofibrosis He was found to have pancytopenia. Patient’s baseline investigations are shown in Table 1. Peripheral smear showed reticulocyte count 9%, Mean corpuscular volume -76fL, tear drop and fragmented RBCs. To rule out HLH S.Cholesterol-193 mg /dl, Triglyceride-410 mg/dl was done. S.ferritin-816 ng /ml Fibrinogen were done, which was normal. Autoimmune workup DCT / ICT was negative.

G6PD, HIV, HbsAg and Anti-HCV were negative. Malarial antigen test and dengue NS1 was negative. S.Parathyroid Hormone was normal. Urine showed pus cell 4-5/hpf, RBCs-40-50Albumin-3+, 24 Hour urine protein-1.5 gram/24hr. Sonography of Abdomen showed normal liver echo texture splenomegaly, hepatomegaly, ascites, and prominent portal vein. Kidney sizes were right 11.2x5.5 cm, left 11.4x5.4cm, increased echogenicity, cortico-medullary junction maintained. Kidney biopsy was planned but postponed due to ascites. Further autoimmune work up was send, the reports are as follows APLA/ACLA IgG/IgM- Negative, C-ANCA/P-ANCA-Negative, C3/C4 (mg /dl)-31/2. Bone marrow aspiration showed multiple *Leishmania Donovanii* (LD) bodies, amastigote form scattered intracellular/extracellular form, normocellular marrow with myeloid hyperplasia. Bone marrow Biopsy was suggestive of normocellular marrow with histiocytic infiltration with LD bodies. Chest Radiograph and ECG

was normal. Patient was given haemodialysis due to fluid overload and oliguria. He was infused with two units of packed cell volumes. Four bags of platelets were infused on alternate days. Patient was put on conventional Amphotericin B 1mg/kg (correction done according to Creatinine clearance) for 24 days. Liposomal Amphotericin could not be given due to financial constraints. Total 850 mg of cumulative dose conventional amphotericin-B was given. Patient started having symptomatic improvement after two weeks of Amphotericin administration. Then the Creatinine started to rise, renal adjustment of dose was done for Amphotericin. Reports of ANA-Positive 2+ (1:160) nucleolar, dsDNA-negative were received at this point of time. Then the differential diagnosis lupus nephritis was strongly suspected. Patient was started on Methyl Prednisolone intravenous infusion at 1 gm. / day for 5 days and hydroxychloroquine. Angiotensin-converting enzyme inhibitors could not be given due to rising Creatinine. Patient’s vitals deteriorated due to secondary infection, persistent hypoalbuminemia and Amphotericin induced nephrotoxicity. The Plan was to start on oral Miltefosine or repeat amphotericin B and cyclophosphamide after repeat bone marrow culture. But patient succumbed to his illness on day 40 of hospital stay due to secondary sepsis. Post-mortem renal biopsy was sort but relatives denied permission for the same.

Table 1: Biochemical investigations

Parameters	Day 1	Day 3	Day 9	Day 20	Day 35
Haemoglobin(mg/dl)	8.1	7.9	7.8	10.5	9.0
CBC (cumm)	900	1500	1800	2200	1900
Platelet (lacs/cumm)	78000	1.lac	1 lac	90000	70000
Creatinine /BUN (mg /dl)	2.2/32	2.0/40	2.1/ 45	1.2/12	1.3/14
T. Protein/albumin (g/ L)	5.5/2.5	4.7/2.2	5.7/ 3	-	4.5/2
Calcium/ Phos (mg /dl)	7.5/3.5	-	-	-	-
ALT/AGT(U/L)	88/92	78/48	88/56	110/67	96/65
Alk Phosphatase (U/L)	1646	1281	1068	-	-
24 Hr urine protein (gm/day)	-	1.5	-	3	-

3. Discussion

Visceral Leishmaniasis is a chronic, lethal, parasitic disease, caused by the Leishmania parasite. Symptoms range from irregular and recurrent fever to pancytopenia, haemorrhagic spells, and liver and spleen enlargement. Kidney involvement in chronic leishmaniasis is frequent when untreated; its mortality rate can reach 95%. There is B cell hyperactivity, resulting in production of autoantibodies such as ANA and others [2]. Hypoalbuminemia, hypergammaglobulinemia and increased plasma levels of both IgG and b2-IJBR (2016) 7(09)

microglobulins were found in a group of 55 patients with visceral Leishmaniasis. Renal proximal tubular damage with alterations in the reabsorption of proteins and light chains with characteristics of a tubular proteinuria[6]. Histopathology Tubular and interstitial lesion is the most frequently seen kala-azar-associated kidney lesion. Amyloid deposits and rapidly progressive glomerulonephritis with nephrotic syndrome have been reported in human leishmaniasis. On immunofluorescence IgG, IgM, IGA and C3 deposits in the mesangial matrix seen. Rk39 is rapid immunochromatographic test based on

the detection of antibodies to a recombinant antigen (rK39). This test is used in endemic states of India namely Bihar, Uttarpradesh, Jharkhand, West Bengal sensitivity 98% and its specificity is 90%. Liposomal Amphotericin B, Miltefosine with Amphotericin B or Paromomycin is very efficient. Our patient had history of chronic alcoholism but there were no signs of alcoholic liver disease. It was thought to be cause of oedema at the onset. Patient was fulfilling the ACR 2012 criteria for SLE with lupus nephritis i.e. leukopenia, thrombocytopenia, 24 hour urine protein 1.5 gm /day, low complements and ANA positive 2+ (1:160). Therefore fulfilling 3 clinical and 2 laboratory criteria. It was not proved on renal biopsy. He had ANA positive 2+ (1:160) but dsDNA was negative. Leishmaniasis was proved on bone marrow aspiration and patient came from Nepal which is endemic for VL. Pancytopenia was explained on the basis of hypersplenism. Patient responded to Amphotericin therapy and there was no improvement after steroid therapy pointed towards VL. Renal involvement in VL is membranous nephritis [7]. There are cases reported in literature VL mimicking SLE flare. Garget *al* reported VL in a diagnosed biopsy proven case of SLE [3].

Presentation with massive ascites is uncommon in SLE, through Hammami *et al* have reported successful treatment of 72 year old presenting with massive ascites[4]. Voulgari PV reported a case similar to ours were VL mimicked as SLE [5].

To summaries VL and SLE with lupus flare both can mimic each other due to overlap clinical features. There will be fever, malaise, and pancytopenia in both. Lupus nephritis and renal involvement in VL will have nephrotic range proteinuria, RBC in urine. Presence of proteinuria is bad prognostic factor for VL Antibody positivity can be present in VL due to B cell activity [8]. SLE can have simultaneous infection with VL in endemic areas. A clinician will have to use is detailed history, thorough examination, battery of laboratory investigations and his clinical acumen to arrive at diagnosis and rule out the mimicker.

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