

Autoimmune Haemolysis in Visceral Leishmaniasis: A Case Report & Review of Literature

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Abstract:

Visceral Leishmaniasis is a very common but neglected disorder in Bangladesh. It can remain subclinical or become symptomatic with an acute, sub acute or chronic course. Atypical presentations can be equally challenging to the clinician. Visceral leishmaniasis is associated with various autoimmune phenomena. Sometimes it can mimic any autoimmune disorders including Autoimmune Hemolytic Anemia (AIHA), SLE, and Rheumatoid Arthritis etc. Here, we describe a case of visceral leishmaniasis with Coombs' positive autoimmune hemolytic anemia.

Key words: Autoimmune Hemolytic Anaemia (AIHA); Kala-azar; Visceral Leishmaniasis; Jaundice; Hepatosplenomegaly; Coombs' Test.

Introduction:

Leishmaniasis is a zoonotic disease having variable clinical presentations in the form of visceral, cutaneous and mucocutaneous types depending upon the Leishmania species and immune responses of the hosts. The classical presentation of kala-azar includes prolonged fever, progressive weight loss, pronounced splenomegaly & hepatomegaly and cytopenia & hypergammaglobinaemia. Splenomegaly appears early and increases gradually in relation to the duration of the disease. The subclinical forms of the disease in the endemic areas remain undiagnosed and can become a clinical challenge to the treating physician. We describe here a case of a 25-year-old young female who came from the endemic area of kala-azar with an atypical presentation.

Case Report:

A 25-year-old housewife hailing from Daudkandi, Comilla, was admitted to Dhaka Medical College hospital with the complaints of fever, loss of appetite, generalized weakness for seven months, weight loss for five months, yellow

discoloration of urine and eye for three months and cough for one month. She had fever which was associated with chills & rigor, persisted most of the time of day but did not completely subside during the initial three months. In later months of her illness, it subsided completely with sweating after taking antipyretic drugs. Sometimes, she became afebrile for four to five days followed by a relapse of fever. Maximum temperature recorded by her was 103⁰F. She also developed loss of appetite. At that time she had no history of nausea and vomiting. She lost weight significantly for last five months despite being good food intake. For the last three months, she developed yellow discoloration of eye and urine, initially gradually progressive, which later became static. There was also mild itching, though not a prominent feature. She had no history of stool colour change & blood vomiting. She also complained of cough, most of the time dry in nature. Occasionally, scanty amount of sputum was produced which white in colour, not foul smelling, not mixed with blood. Her past history was notable for exposure to kala-azar patients seven years back who used to live just beside her house, distance less than fifty meters. But there was no history of contact with patient with TB, of travelling to hill tracts & of blood transfusion. She gave no significant drug history. In her family, no other members were affected by kala-azar. She used to live in a village, no history of sleeping on ground; used net most of the night in all seasons, no history of rearing animals especially cows in the same sleeping room or beside the room.

On admission physical examination disclosed that she was malnourished, having moderate anemia and moderate jaundice. There was no edema, clubbing, leuconychia, koilonychia, scratch marks, flapping tremor or palpable lymphnodes.

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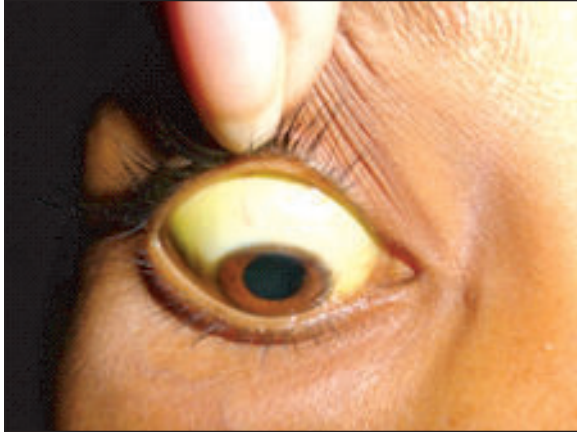


Fig-1: Moderate jaundice of this patient

Liver was palpated fourcentimetre from right costal margin at the mid- clavicular line, Spleen also was palpable, threecentimetre from left anterior axillary line towards the right iliac fossa. There was positive shifting dullness. Examination of other systems revealed no abnormality.

Laboratory investigation confirmed anaemia, leucopenia and thrombocytopenia, high rise of ESR, increased reticulocyte count. There was normochromic normocytic anemia with mild pancytopenia in peripheral blood film. Other laboratory data was as follows: S. bilirubin 9.31 mg/dl, SGPT 171 U/L, LDH 309 U/L. All viral markers were negative. USG of whole abdomen revealed mild ascities with hepatosplenomegaly. Her laboratory investigations were positive for direct Coombs' test & rK39 for kala- azar (ICT). We also did bone marrow examination for parasitological diagnosis that revealed scanty, intracellular (within histiocytes) L.D bodies, confirmatory for visceral leishmaniasis.

In this patient, an accurate diagnosis is very much difficult for a clinician because of presentation. At last, this case was diagnosed as Visceral Leishmaniasis with Autoimmune Hemolytic Anemia.

Discussion:

Leishmaniasis is a disseminated intracellular parasitic disease caused by *Leishmania* transmitted to human by sandflies in endemic zones & fatal if untreated. It can be transmitted by blood transfusion, sharing of needles by intravenous drug abusers, occupational exposures, congenital transmission and rarely sexual transmission.¹ Human is the only reservoir for kala- azar in Bangladesh.^{1,2} After inoculation by a sand fly, promastigotes are phagocytosed by macrophages and transformed into amastigotes having the capacity to resist intracellular digestion. It then invades the whole reticulo-endothelial system causing hyperplasia of the parasitized

cells in the liver, spleen, bone marrow, lymph nodes & mucosa of small intestines and other lymphoid organs.^{1,2,3} In the immunological response to *Leishmania*, there is evidence of both protective and disease enhancing immune response. Malnutrition is a recognized risk factor for progression of disease in Bangladesh. However it depends on parasite factors including invasiveness, tropism, pathogenicity & host genetically determined cell mediated immune response & environmental factors.¹ The suspicion of kala- azar should be high when a patient presents with prolonged fever, progressive weight loss, weakness, pronounced splenomegaly, hepatomegaly, cytopenias and hypergammaglobulinemia from a known endemic area.¹ Our patient came from a kala- azar endemic zone of Bangladesh, having prolonged fever, progressive weight loss, splenomegaly & hepatomegaly, and pancytopenia. Therefore, it was highly suspicious of kala- azar. The anemia is almost always present and sometimes very severe. The cause of anemia is multifactorial including hemolysis, marrow replacement with leishmania infected macrophages, hemorrhage, splenic sequestration of erythrocytes, hemodilution and marrow suppressive effect of cytokines such as TNF – alfa.¹ In our case, there was moderate normocytic normochromic anemia and moderate jaundice & a not hugely distended spleen. So, there was a probability of autoimmune hemolysis though it is very rare in kala- azar. Positive direct Coombs' test indicates that there is an autoantibody IgG against antigen of RBC membrane and/or complement component coated with RBC's membrane.⁴ The presence of autoantibody to host suggests the role of polyclonal B cell stimulation.¹ *Leishmania donovani* infection induces a non-specific, as well as a specific antibody production, much of which is probably due to the parasite-released substances, which act as B cell mitogens. As a consequence of the B cell hyperactivity, *Leishmania donovani* may cause hyper gammaglobulinaemia and the production of autoantibodies.^{3,5,6,7}

But Most of the time, hemolysis occurs due to macrophages in the liver and spleen without immune complexes.¹ Sometimes, the presentation of visceral leishmaniasis due to polyclonal B cell stimulation can mimic or exacerbate AIHA, autoimmune hepatitis, primary biliary cirrhosis, SLE, Rheumatoid arthritis and even Felty's syndrome. Thus, positivity of one or more of antibody tests with vague clinical presentations may be misinterpreted as autoimmune disorders. Kala- azar should be considered and rule out in case of autoimmune disease with atypical presentation or not responding to immunosuppressive drug.^{8, 9, 10, 11, 12,13} Treatment with immunosuppressive drugs for autoimmune disease may deteriorate the disease process¹¹. Sometimes it causes a fatal outcome in the absence of specific treatment

of Visceral Leishmaniasis. But treatment with anti-leishmanial drug without any immunosuppressive agent causes the disappearance of all antibodies after completion of treatment in visceral leishmaniasis.³ This patient requires follow up with immunological reports at six months after completion of treatment. Visceral leishmaniasis can occur as an opportunistic infection in immunocompromised state of any autoimmune diseases.^{1, 14, 15} Our patient had a positive direct Coombs' test. At six months of completion of treatment with anti leishmanial drug, persistent hemolytic disease should be checked with a Coomb's test. Our patient also had jaundice & mild ascites. The uncommon findings of jaundice, ascites even with pleural effusion is more common in case of Indian kala-azar in Bangladesh.³ So, in hepatosplenomegaly with jaundice or ascites, kala-azar is one of the most important differential diagnoses in Bangladesh.

Conclusion:

When a patient of kala-azar presented with jaundice, it is very difficult to reach a final diagnosis for a clinician. So, high suspicion is required to treat this fatal disease. This case is probably the first diagnosed case of autoimmune hemolysis developing in a patient of Leishmania infection in Bangladesh.

Conflict of Interest: None

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