Visceral leishmaniasis: A case report

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Visceral leishmaniasis or Kala Azar, an infectious disease caused by leishmania donovani, has never been reported in Thailand. This condition is prevalent in certain parts of the world especially around the Mediterranean basin, the Middle East, South America, East Africa and at the junction of Northeast India and Bangladesh in Asia,\(^1,2\) where sandflies, the vectors that are responsible for transmission of this disease, are commonly found.

Our institute, Chulalongkorn hospital, is one of the referral centers for neighbouring countries in Asia such as Laos, Burma, Bangladesh, Pakistan etc. Referred patient, sometime, presents with unusual or rare disease which has never been encountered before in Thailand. So it is the role of the attending physician to become aware of its possibility or else the diagnosis can be missed.

We describe here a patient referred from Bangladesh whose presenting symptoms were prolonged fever, hepatosplenomegaly, anemia and malnutrition. The diagnosis of visceral leishmaniasis was established by bone marrow aspiration, demonstrating the parasite. A review of this disease with special focus on the pathogenesis of hematological changes including platelet survival study is presented.

**Report of the case**

A Bangladesh girl aged 7 years was referred to Pediatric Department, Chulalongkorn Hospital, Bangkok, with the problem of prolonged fever of 2\(\frac{1}{2}\) months prior to admission. The girl came from a poor family who lived in a remote rural village in the western part of Bangladesh. Two years prior to admission she was brought by her relatives to Dhaka to have a tibial osteotomy on her fractured right knee. Investigation at that time revealed tuberculosis in her chest and she was treated for a complete one year course. She stayed in the city for one year then went back to live with her family in the village for 5 months before coming back to stay with her foster-mother in Dhaka again.

Three months prior to admission she began to have gastrointestinal symptoms: vomiting, loss of appetite and diarrhea with mucous bloody stool. She was diagnosed as having amoebic dysentery and was treated with metronidazole. Half month later, she developed high fever with dry cough. Several kinds of antimicrobial treatment, which included ampicillin, amoxycillin and cotrimoxazole were administered without any improvement. She was found to have obvious hepatosplenomegaly, and was admitted to PG Hospital in Dhaka for complete investigation. Results of the laboratory tests were insignificant including a leishmanin skin test. Bone marrow aspiration showed erythroid and myeloid hyperplasia suggestive of myeloproliferative reaction, but negative for the parasite. The patient had blood transfusion twice during her hospital course.

At the Pediatric department, Chulalongkorn Hospital, on initial examination the patient looked toxic, pale, weak, and
emaciated. Her weight was 16 kgs and her height was 117.5 cms. The pulse rate was 100/minute, respiratory rate 20/minute, temperature 39°C and blood pressure 100/60 mm.Hg. Her skin was dusky dark with hyperpigmentation. The liver was enlarged 5 cm. below the right costal margin and the spleen was 9 cm. below the left one (Fig. 1). Examination of the right knee revealed medial angulation of the joint with surgical scar from previous operation. There were some small lymph glands about 0.5 cm. in diameter palpable at both axillary and groin regions.

Laboratory investigations (Table 1) revealed pancytopenia. The peripheral blood smear showed hypochromia, anisocytosis of RBC with some rouleaux formation. The thick and thin blood films for malaria were negative. Bone marrow aspiration revealed panhypercellular marrow with eosinophilia. Moderate increase in plasma cells and histiocytes were also noted. Numerous amastigote form of L. donovani bodies were found both intracellular and extracellular of the RE Cells. (Fig. 2). Bacterial culture of the blood and urine were also negative. Other negative or normal tests included urinalysis, chest X-ray, BUN, creatinine, widal agglutination test, liver function test and prothrombin time. ESR was elevated to 57 mm. per hour. Strongly positive tuberculin test was also noted. There was a reverse ratio of the albumin and globulin fraction. Immunelectrophoresis showed marked increase in IgG class. Hook worm eggs were found in the stool. X-ray of the right leg showed sclerotic bony fragments in upper tibia with deformed epiphysis compatible with osteochondritis from old trauma. Platelet survival study was done and showed slight shortening of survival time (Fig. 3) without definite evidence of sequestration of platelet in liver or spleen (Fig. 4).

Therapy was initiated with pentamidine isethionate at a dosage of 50 mg intramuscularly on alternate days for 3 doses and then shifted to daily dose for another 9 doses for the total 12 doses. The patient tolerated the administered medication very well. Other treatment included oral mebendazole for hook worm and vitamins combined with ferrous sulfate for nutritional supplement. The fever gradually declined and reached base line after the fifth dose of pentamidine. (Fig. 5). The patient remained afebrile throughout the hospital course. The examination of the bone marrow aspiration performed on day 10th of pentamidine treatment was negative for leishmania bodies although the cellularity remained unchanged. The follow-up CBC showed only slight improvement of pancytopenia. The patient was discharged from the hospital after 17 days of admission due to socio–economical factor. She and her foster–mother went back to Bangladesh with our advice to be followed by her consulting physician. There is no subsequent clinical information received.

Discussion

Visceral leishmaniasis is usually not included in differential diagnosis of
unremitted febrile illness in Thailand. However, for those who come from endemic area of the disease, physicians should be alert for its possibility. The disease is characterized by a latent period varying from 1 month to several years. The time of inoculation of organisms in our patient was suspected to be during her last visit to the rural village 7 months PTA. The location of the village is in a short distance from Bihar in India; where recent epidemic spread of Kala azar was reported.(3)

The onset of symptoms depend on the time of invasion of RE system and may be of two types. One is the acute type with chills, double febrile spikes each day. The patients usually look well and mostly ambulatory. The other type is insidious and characterized by chronicity, weight loss, weakness, low grade or recurrent fever and left upper gradrant pain from enlarged spleen.(1,5,4) This patient’s presentation replicates the second type of clinical manifestation.

Constant physical findings usually show progressive splenomegaly and hepatomegaly. Purpura, gingivitis, conjunctivitis are common but not found in this case. Generalized lymphadenopathy may occasionally be seen. Diarrhea, and at times dysentery, are not uncommon during the acute stage. This was also present in the patient’s history but was diagnosed as amoebic dysentery. Cutaneous manifestation such as dry brittle hair, dark dusky grey pigmentation of skin are characteristic evidence of chronic form as exemplified in this case.

The most common laboratory change is pancytopenia of varying degree. The cause of pancytopenia was previously explained by many mechanisms.(5,6,7) Firstly, an ineffective hematopoiesis from proliferated and parasitized macrophages replaces the normal bone marrow in combination with nutritional deficiency of iron, protein and folic acid. Secondly, the hypersplenism increases the destruction of blood cells through sequestration and phagocytosis. The third mechanism is an autoimmune process which could be demonstrated by the evidence of antibodies against RBC, WBC and platelets. In this case the peripheral blood showed pancytopenia without evidence of overt hemolysis. The bone marrow showed the same feature as had been described before.(5,6) However, the platelet survival study, which was done simultaneously during the drug administration, showed only slight shortening of platelet survival time without definite evidence of organ sequestration. The finding is suggestive of the major defective mechanism within the bone marrow that produces the pancytopenia—the ineffective hematopoiesis.

Other laboratory investigations revealed hyperglobulinemia with marked elevation in IgG class. Immunological studies in Kala azar so far carried out demonstrated impairment of cell-mediated immune function with exaggerated humoral response during active stage of disease.(6,9,10) This may explain the negative skin test recently performed at Dhaka, but the tuberculin test was
strongly positive in this patient, indicating that the T lymphocyte function was intact.

The diagnosis of Kala azar can be made by two methods. The direct method is by demonstrating L. donovani bodies is the RE cells from stained smear or culture on Novy–MacNeal–Nicolle medium. Bone marrow aspiration is the most suitable way to demonstrate the organisms and is also the clue to the diagnosis in this patient. Other tissues likely to yield organisms are spleen, liver and lymph nodes. Indirect method for diagnosis are skin test and serological test for liehmania. Indirect hemagglutination test using soluble leishmanial antigen appears to be the most sensitive serodiagnosis for early detection of the disease.\(^{(1)}\)

Clinically, Kala azar rationally responds to the pentavalent antimonial such as Stibogluconate sodium (Pentostam) which is the usual drug of choice. In resistant case, pentamidine isethionate and amphotericin B are the alternatives.\(^{(1,4)}\) In this case pentamidine isethionate was administered for its availability. The drug was given intra-muscularly at the dosage of 3.5 mg/Kg/day for 12 doses without any complication. A single course is reported to cure 90% or more of cases. Clinical relapse may occur up to one year after the completion of treatment.

**Summary**

The first case report of visceral leishmaniasis seen in Thailand is presented. The disease should be included in the differential diagnosis of patients who have evidence of prolonged fever with history of residing or travelling through the endemic area of the disease. Pancytopenia and hyperglobulinemia are frequently found. Bone marrow aspiration, if carefully examined, will be the most effective method for the organism demonstration. Early and proper treatment can cure the disease more effectively.

**Acknowledgement**

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Table 1 Laboratory data

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Urinalysis pH6, Albumin, Sugar-negative RBC, WBC 0–2/HD
Stool Exam hook worm eggs.
Thick & Thin Film for Malaria negative
Widal Agglutination Test negative
Hemo Culture and Urine Culture negative
Tuberculin Test 2 cm. after 48 hours
Bun 14 mg% Creatinine 1.1 mg%
Liver Function Test Total bilirubin 0.4 mg% direct bilirubin 0.05 mg%  
SGOT 36 units SGPT 38 units alkaline phosphatase 65 I.U.  
albumin 1.9 gm% globulin 5.45 gm%
Serum Immunoelectrophoresis IgM 272 mg% IgA 71 mg% IgG 3900 mg%  
Prothrombin Time 13.9 seconds (control 11.5 seconds)
Fig. 1 The patient after Treatment

Fig. 2 Bone marrow smear showing amastigote form of leishmania donovani bodies both intracellular and extracellular of RE cells.
Fig. 3 $^{51}$Cr–Platelet survival graph
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Fig. 4 Organ surface count of $^{51}$Cr-Platelet

Fig. 5 Temperature curve and treatment


