

## A case of kala-azar diagnosed by bone marrow aspiration

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### Abstract

A 35-year-old man from Bangladesh, who had been in Malaysia for approximately a year, was extensively investigated for more than two months in a state hospital for pyrexia with hepatosplenomegaly. However, no obvious cause of his illness was found. He was treated with multiple antibiotics with no resolution of pyrexia and hepatosplenomegaly. He was later referred to the Haematology Unit, Universiti Kebangsaan Malaysia for further assessment as a case of lymphoma. On carefully reviewing his bone marrow aspirate smears, the diagnosis of leishmaniasis (kala-azar) was finally made. The patient responded to treatment with pentamidine.

**Key words:** Pyrexia, bone marrow biopsy, leishmaniasis, kala-azar.

### INTRODUCTION

Visceral leishmaniasis or kala-azar is caused by an intracellular protozoa *Leishmania donovani* and is transmitted through the bite of sand flies belonging to the genus *Phlebotomus*. Kala-azar is endemic in India, northern South America and the Mediterranean area.<sup>1</sup> An epidemic of kala-azar was reported in Bihar, Bangladesh in 1977.<sup>2</sup> However, kala-azar is not an endemic disease in Malaysia. Kala-azar can cause prolonged fever and can cause difficulty and delay in diagnosis.<sup>3-5</sup> We describe a patient with kala-azar who was investigated for fever of unknown origin and whose diagnosis was made on bone marrow examination.

### CASE REPORT

A 35-year-old man from Bangladesh, who had been working for almost a year in Malaysia, presented to a state hospital with complaints of fever of two weeks duration associated with anorexia and malaise. There was no chills or rigors. Physical examination then revealed a hepatomegaly of 3cm below the right subcostal margin and splenomegaly of 16cm below the left subcostal margin. There was no lymphadenopathy. He was extensively investigated but no obvious cause of his illness was found. His haematological profile showed pancytopenia. Blood smears for malaria were negative. Erythrocyte sedimentation rates were elevated (105, 120 mm/hr). Bone marrow aspirations were performed twice and were non-diagnostic on both occasions. He had hyperglobulinaemia of 40.0 g/l. General bacterial cultures of the blood, stool and urine were also negative. Serology tests for serum hepatitis antigen

and human immunodeficiency virus (HIV) were negative. Additional negative tests included antinuclear antibody, lupus erythematosus anticoagulant, Widal-Weil-Felix reaction (WWF), VDRL test, echocardiography, electrocardiogram, renal function, serum bilirubin and chest X-ray. There was no paraproteinaemia and urine for Bence Jones protein was negative. Ultrasound and computerised tomography of the abdomen showed hepatosplenomegaly without portal hypertension, and there was no paraaortic lymph node enlargement or any focal lesion in the spleen. Because the pyrexia persisted, he was treated with multiple antibiotics which included penicillin, ampicillin, gentamycin, vibramycin, cefoperazone and amikacin but there was no resolution of pyrexia and hepatosplenomegaly persisted. Owing to pancytopenia and persistence of his condition despite therapy with multiple antibiotics, he was referred to the Haematology Unit, Universiti Kebangsaan Malaysia more than two months later, for further assessment with a presumptive clinical diagnosis of a lymphoma.

On admission into our Unit, he was noted to be pale. He was still febrile and abdominal examination confirmed the hepatosplenomegaly. His full blood picture revealed a pancytopenic profile; haemoglobin being 7.4 g/dl, total white cell count was  $1.4 \times 10^9/l$ , and thrombocytopenia of  $39.0 \times 10^9/l$ . However he had no bleeding problems. There was also hyperglobulinaemia (45.0 g/l), elevated alkaline phosphatase (222 u/l) and lactic dehydrogenase activity (1339 u/l). Several investigations were repeated, including serological tests for toxoplasmosis, malaria, fungal, HIV, WWF, VDRL, blood smears for malaria parasites, general bacterial and fungal

blood cultures, serum immunoglobulin quantitation and electrophoresis. He was also investigated for tuberculosis. The results were all negative. Bone marrow examination was repeated because a trephine biopsy had not been done in the previous hospital. Both recent and previous bone marrow aspirate specimens stained with May-Grunwald-Giemsa (MGG) stain were reviewed and they showed hypercellular trilineage haemopoiesis with increase in macrophages. Numerous tiny intracellular inclusion bodies were seen in the macrophages and some were extracellular. They were typical of *L. donovani* amastigotes (Fig. 1). The bone marrow trephine biopsy also showed macrophages filled with these basophilic bodies.

The patient was treated with intravenous pentamidine at a dose of 150 mg three times per week. His constitutional symptoms improved after the treatment and he regained his appetite. He became afebrile by the fourth dose of pentamidine. Hepatomegaly resolved after the sixth dose and the splenomegaly also regressed by 6 cm after the tenth dose of pentamidine. As he insisted on being transferred back to his working area, he was referred back to the state hospital for continued management after completing the fourteenth dose of treatment. He was reported to be well after that.

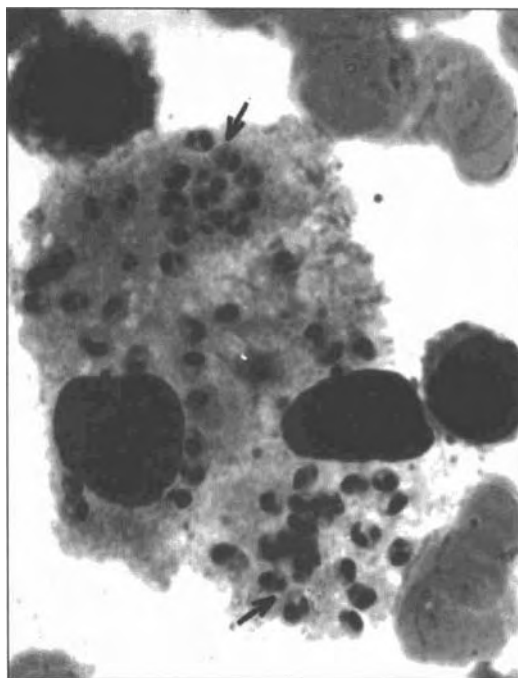


FIG. 1: Leishman-Donovan bodies (arrows) within macrophages from bone marrow aspirate specimen. MGG x 100.

## DISCUSSION

**Kala-azar**, the visceral form of leishmaniasis is characterised by irregular fever, hepatosplenomegaly, anaemia, leucopenia, hyperglobulinaemia, thrombocytopenia, and progressive emaciation of the host, usually resulting in death if untreated. Generalized lymphadenopathy may also occur. The differential diagnosis in visceral leishmaniasis includes lymphoproliferative disorders, malaria, typhoid fever, tuberculosis, brucellosis, histoplasmosis, liver abscess and leukaemic reticuloendotheliosis which were all considered in this patient. The diagnosis of visceral leishmaniasis requires visualization of the intracellular, non-flagellated amastigote stage in the host tissue or of the extracellular, flagellated promastigote stage in culture.<sup>6</sup> However, parasitologic diagnosis can be difficult especially in cases with low parasitic burden.

The patient was a young man from Bangladesh, which is an endemic area for kala-mar. Because of his prolonged pyrexia, hepatosplenomegaly and negative investigations for the usual causes, we were alerted to the possibility of the diagnosis of kala-mar. Thus this prompted us to review carefully the bone marrow aspirate biopsy specimens that were done on his first admission into the state hospital. On careful study of those that were stained with MGG, typical *L. donovani* bodies were seen in abundance in the macrophages intracellularly and also extracellularly. The repeated bone marrow aspirate biopsy and trephine biopsy done here also showed similar findings. Reviewing the Literature, we believe that this is the first case reported in Malaysia.

Pentavalent antimonials are highly effective against leishmania and has been the reference treatment of kala-azar. The alternative second-line therapy, pentamidine and amphotericin B are used in antimony resistant kala-azar cases.<sup>1,7-10</sup> Badaro *et al* reported that a combination of pentavalent antimony and interferon gamma can cure seriously ill patients with refractory kala-azar.<sup>11</sup> Pentavalent antimonial drugs were not available in this country and the alternative albeit more toxic drug, pentamidine, was given. The duration of treatment with pentamidine should be guided by the disappearance of parasites from splenic or marrow aspirates, and not simply by a fixed number of injections or duration of treatment and it should be continued for sometime following parasitological cure.<sup>1,9,12</sup>

With the increasing numbers of foreign workers in Malaysia, it is important to be aware of the

endemic diseases peculiar to other countries. Thus the possibility of kala-azar in this patient with prolonged fever associated with hepatosplenomegaly who comes from an endemic area, should be considered. In view of this, careful study of the bone marrow biopsy specimen, would have aided the physicians in early diagnosis and management of this patient.

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