The hunt for an elusive source of pyrexia in a foreign worker
Lew J W S, Koh C K, Selvan V S, Shen E

ABSTRACT
We report a 23-year-old Bangladeshi man who presented with fever and hepatosplenomegaly. The initial laboratory findings were bicytopenia with elevated serum globulins. The diagnosis of visceral leishmaniasis (Kala Azar) was suspected. The parasite Leishmania donovani was found on bone marrow aspiration. He was treated with liposomal amphotericin B and had a good response to treatment. The case highlights the need to be aware of this disease occurring in a foreign national from an endemic region when he presents with fever and hepatosplenomegaly.

Keywords: Kala Azar, Leishmania donovani, parasitic infection, visceral leishmaniasis

INTRODUCTION
Leishmaniasis is an infection caused by the parasite of the genus Leishmania. The disease may manifest as dermal or visceral leishmaniasis. There was a recent case series of dermal leishmaniasis reported by a tertiary dermatological centre but cases of visceral leishmaniasis are rare. Visceral leishmaniasis is endemic in the northeastern states of India and in Bangladesh. With the large population of foreign workers from these countries now being employed in Singapore, it is necessary to be aware of this disease entity and its protean manifestations.

CASE REPORT
A 23-year-old male Bangladeshi labourer had been working in Singapore for five months prior to presentation. He had no past medical history of note. He presented in December 2005 with fever, chills and loss of appetite. He was febrile and there was no organomegaly found on examination of the abdomen. The full blood count showed thrombocytopenia and leucopenia. Dengue serology was negative, and he continued to have swinging pyrexia. Subsequent examination on the tenth day of admission revealed hepatosplenomegaly (Fig. 1). Computed tomography of the abdomen confirmed the hepatosplenomegaly but there were no enlarged paraaortic lymph nodes. Bone marrow aspiration showed a reactive marrow with lymphocytosis. Cytogenetic study of the marrow did not show any evidence of lymphoproliferative disease. The patient’s temperature settled by the second week of admission and he was discharged.

He presented again in early February 2006 with similar symptoms. Examination of the abdomen showed hepatosplenomegaly. There was also inguinal and cervical lymphadenopathy. The laboratory investigations showed leucopenia and thrombocytopenia, and it was noted that he also had elevated serum globulins (68 g/L). As the patient came from a region where leishmaniasis is endemic and had typical features of visceral leishmaniasis, a repeat bone marrow aspiration was done. This showed Donovan bodies which are consistent with leishmaniasis (Fig. 2). He was treated with intravenous liposomal amphotericin B (Ambisome, Gilead Sciences International Ltd, Foster City, CA, USA). The course of treatment was uncomplicated. After completion of treatment, abdominal examination showed diminishing size of the spleen and resolution of the cervical and inguinal lymphadenopathy. He was followed-up one month later. At this time, the hepatosplenomegaly and lymphadenopathy had resolved (Fig. 3), and he had gained about 10 kg in weight.
**DISCUSSION**

Leishmaniasis is an infection caused by protozoa of the genus *Leishmania*. It is transmitted by the *Phlebotomus* (Old World) or *Lutzomyia* (New World) sandfly. Leishmaniasis presents in three different forms, namely: visceral, cutaneous and mucocutaneous. The visceral form is also known Kala Azar in Asia. It is usually caused by the *L. donovani* complex, which consists of *L. donovani*, *L. chagasi*, and *L. infantum*. *L. donovani* is the causative agent in cases originating from the Indian subcontinent. The incubation period ranges from few weeks to several months. The classic clinical features are fever, weight loss, hepatosplenomegaly and lymphadenopathy. Many patients may have subclinical infections. The laboratory features include pancytopenia and hypergammaglobulinaemia. Untreated, visceral leishmaniasis may be fatal, as patients develop immunosuppression and secondary infections. Post-treatment, patients with visceral leishmaniasis may go on to develop post Kala Azar dermal leishmaniasis (almost 50% in Sudan, 3% – 5% in India). (1)

Cases of dermal leishmaniasis have been reported by a tertiary dermatology centre in Singapore in recent years. (2) There have been cases of visceral leishmaniasis reported in the local medical literature. There was a case reported in 1982, which presented in a similar manner to the case discussed in this report. (3) Subsequent reports involved persons who came from an endemic area as well as locals. (4–6) Visceral leishmaniasis is seen in the Indian subcontinent, parts of Africa, Central Asia, China, the Middle East, and Latin America. There may be up to a million cases per year globally, and 80% of these occur in the Indian subcontinent, primarily in Bangladesh, Bihar and West Bengal. (7,8) The disease is becoming increasingly common due in part to the presence of HIV, a visceral leishmaniasis co-infection and also the failure to control the vector. (9)

The “gold standard” diagnostic test is the demonstration of the presence of the parasite in bone marrow aspirate, splenic aspirate or hepatic biopsy. Where there is massive parasitaemia, the parasite may be demonstrated on a thick blood film with Leishman’s stain. The organism can be cultured on NNN (Nicole, Novy, McNeal) medium. Immunodiagnostic methods and techniques for the identification of parasite DNA in the tissue specimen are available but require skilled personnel and expensive technology to operate. (10,11) Classically, the treatment of Kala Azar would be pentavalent antimonials. However, newer agents like paramomycin, miltefosine and amphotericin B are now being used to treat Kala Azar. There is increasing resistance to antimonials in India. The use of amphotericin B is increasingly common. (12) In this case, a lipid formulation of amphotericin B was used. Liposomal amphotericin B is preferentially taken up by tissue macrophages in the liver, spleen and bone marrow. It is well tolerated and has a 95% cure rate. It has the advantage of being a short course of treatment requiring administration of the drug at 5 mg/kg in divided doses over five days. Side effects include fever, chills, nausea and back pain. (13)

This disease has vague non-specific symptoms and presents like a lymphoproliferative disorder. It is a trap for the unsuspecting physician who may be caught off-guard if the diagnosis of Kala Azar was not considered. (14) In conclusion, the diagnosis of Kala Azar should be considered as a cause of pyrexia of unknown origin in a patient who comes from the...
Indian subcontinent or is a local who has resided in an endemic area, particularly if he presents with fever, splenomegaly and pancytopenia.

REFERENCES