number of patients for whom the scan was appropriate or not in terms of the diagnostic algorithm. It can be seen that the number of scans could have been reduced to 6. Two of the 16 negative scans could have been avoided if a policy was in force of only scanning patients with anaemia (a surrogate marker of dissemination).

In conclusion, there is a limited role for ultrasound in the diagnosis of TB. However, at a time of crisis in academic and rural medicine in South Africa, calls for use of existing investigations in new ways should be qualified by careful cost-benefit analysis. We should also point out that our study was performed in an HIV-positive population at very high risk of TB.[4] Experience elsewhere may differ, possibly resulting in ultrasound being even less useful.

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1. Emby DJ, Hunter M. The value of ultrasound in the HIV-infected patient with a fever of undetermined origin. *S Afr Med J* 2002; **92:** 566.
2. Hudson CP, Wood R, Maartens G. Diagnosing HIV-associated tuberculosis: reducing costs and diagnostic delay. *Int J Tuberc Lung Dis* 2000; **4:** 240-245.
3. O'Keefe EA, Wood R, Van Zyl A, Cariem AK. Human immunodeficiency virus-related abdominal pain in South Africa. Aetiology, diagnosis and survival. *Scand J Gastroenterol* 1998; **33:** 212-217.
4. Wood R, Maartens G, Lombard C. Risk factors for developing tuberculosis in HIV-1 infected adults from communities with a low or very high incidence of tuberculosis. *J AIDS* 2000; **23:** 75-80.

Massive hepatomegaly due to visceral leishmaniasis

To the Editor: In 1908 Leishman and Donovan[1] described the protozoan *Lesishmania donovani* in splenic tissue. Almost a century later leishmaniasis has emerged in new regions and new settings.[1] Recent interest in the disease has been prompted by recognition of cases in returning US Gulf War veterans and people with HIV infection.[2] We describe a case of visceral leishmaniasis diagnosed on bone marrow aspirate in a patient presenting to a tertiary hospital in KwaZulu-Natal.

A 42-year-old Mozambican national, who works as a marine merchant, was referred from a local hospital with fever, hepatosplenomegaly and pancytopenia. He had a 6-month history of gradual weight loss of approximately 10 kg with intermittent fever and rigors. He was treated for hepatic tuberculosis in a Mozambican hospital. A liver biopsy was not done before commencement of antituberculosis therapy and the patient did not improve after completion of this treatment.

He had been treated for malaria several years previously while living in Mozambique. He travelled to Brazil, Argentina, Italy and Portugal between 1995 and 1998.

On examination, the patient was febrile (39.8°C). He was pale and had no lymphadenopathy. He had a hepatomegaly that extended 10 cm below the costal margin and a 3 cm splenomegaly.

The full blood count showed haemoglobin 8 g/dl (normochromic, normocytic anaemia), platelets 132 × 10^9/l and white blood cell count 1.8 × 10^9/l. Liver function tests revealed a hyperglobulinaemia. He had an erythrocyte sedimentation rate (ESR) of 113 mm/h, and his urea and electrolytes were normal. HIV and hepatitis screens were negative. The chest radiograph was normal. Ultrasound of the abdomen detected no additional abnormalities. A bone marrow aspirate and trephine were done in the first instance to investigate the pancytopenia. A liver biopsy was scheduled, but this was deferred when the results of the bone marrow aspirate and trephine were received. Fig. 1 is a photomicrograph of the marrow aspirate showing the characteristic intracellular amastigotes of leishmaniasis.This was confirmed on the trephine biopsy.

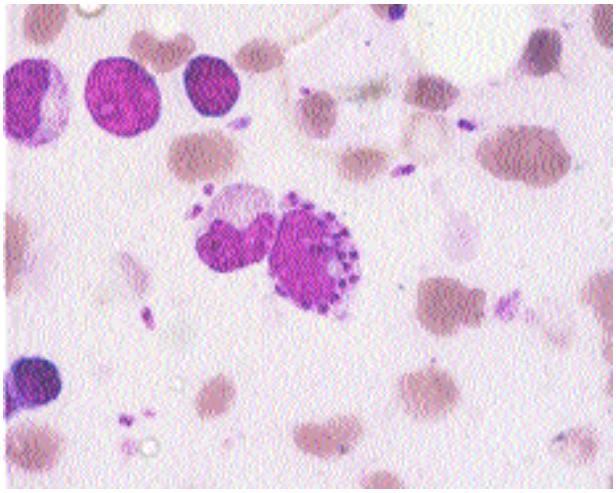

Fig. 1. Bone marrow aspirate — Gram stain showing intracellular 'dot-like' microorganisms (magnification 1 000). Courtesy of Dr P Sturm.

The patient was treated with intravenous amphotericin B (60 mg/kg/day) for 20 days. Renal impairment and thrombophlebitis complicated his therapy. The renal function improved when amphotericin B was stopped. At 3 months after treatment the hepatosplenomegaly had resolved and a repeat bone marrow aspirate was normal.

Discussion

This case highlights the importance of considering exotic diseases associated with common clinical presentations, given

the movement of people within sub-Saharan Africa. The diagnosis was not suspected clinically but established by a stepwise approach to investigation. Secondly, this case highlights the pitfalls of the all too frequent use of empirical antituberculosis therapy without establishing a microbiological diagnosis or setting goals for the empirical therapeutic trial.

Leishmaniasis is endemic in areas of the tropics, subtropics and southern Europe, in settings ranging from rain forests in the Americas to deserts in Western Asia and from rural to peri-urban areas.[1] A total of 200 million people are at risk and an estimated 500 000 new cases occur worldwide each year.[1]

The protozoan is an obligate intracellular organism of the genus *Leishmania* (order *Kinetoplastida*). *Leishmania* is a vector-borne parasite transmitted by the bite of a female phelobotomine sandfly. Parenteral and congenital transmission also occur. In most cases, humans are the incidental host of infection, but in India and East Africa humans appear to be the major reservoir where peripheral parasites are taken up via the bite of sandflies.[3]

Several clinical syndromes are described. These include visceral, cutaneous and mucosal leishmaniasis. Visceral leishmaniasis is caused by infection with *L. donovani* or *L. infantum*, which is increasing in incidence and causing major epidemics and high mortality.[1] Visceral leishmaniasis encompasses a wide range of manifestations and can follow an acute, subacute or chronic course. The classic kala-azar syndrome (Hindi for black sickness or fever) is exemplified by a life-threatening disease after an incubation period of weeks to months. Features include fever, cachexia, hepatosplenomegaly, pancytopenia, and hypergammaglobulinaemia with hypoalbuminaemia, all of which were present in our patient. The differential diagnosis includes malaria, schistosomiasis, cirrhosis with portal hypertension, African trypanosomiasis, miliary tuberculosis, typhoid fever, bacterial endocarditis, histoplasmosis, lymphoma and leukaemia.

The diagnosis depends on demonstrating the intracellular amastigote in infected tissue (spleen, lymph node, and bone marrow) using Giemsa's stain. Other methods of parasitological diagnosis include culture of infected tissue or animal inoculation, e.g. hamster. Molecular-based applications are currently being tested in order to avoid invasive methods. These include the detection of immunoglobulin G (IgG) antibody to *Leishmania* antigen or for parasite DNA.[4]

While our patient was HIV-negative, it is worth noting that visceral leishmaniasis is an emerging opportunistic infection in HIV-infected patients.[5] A major surface molecule, the lipophosphoglycan of *L. donovani*, induces HIV transcription in CD4 cells.[1] *Leishmania* may be newly acquired via vector-borne transmission or contaminated syringe transmission and may reactivate after years of latency.[1]

There is a high mortality rate if untreated.[1] Pentavalent antimony compounds (sodium stibigluconate, meglumine antimonate) are the mainstay of therapy.[1] These agents are unavailable in South Africa. Lipid formulations of amphotericin B represent a recent advance in the therapy of visceral leishmaniasis. In India, the use of conventional amphotericin B has been almost 100% effective.[1] Patients with visceral leishmaniasis should be monitored for bleeding and intercurrent infections, such as pneumonia, tuberculosis and dysentery.[1] Response to therapy can be monitored by resolution of fever, haemoglobin level and decrease in spleen size.[1]

Splenomegaly and biochemical abnormalities resolve weeks to months later.[1] Freedom from clinical relapse for at least 6 months is the best indicator of cure.[1] The absence of parasites does not preclude relapse until 12 months after therapy. Relapse rates are less than 5% except in HIV-infected individuals in whom the relapse rate is as high as 60% in the first year.[6]

Leishmaniasis has protean clinical manifestations and is difficult to diagnose without tissue diagnosis. This infection should be suspected in patients with unexplained systemic illness who have travelled to areas of the world where leishmaniasis is endemic.

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1. Herwaldt BL. Leishmaniasis. *Lancet* 1999; **354:** 1191-1199.
2. Magill AJ, Grogl M, Gasser RA, Sun W, Oster CN. Visceral infection caused by *Leishmania tropica* in veterans of Operation Desert Storm. *N Engl J Med* 1993; **328:** 1383-1387.
3. Eddleston M, Pierini S. Leishmaniasis. In: *Oxford Handbook of Tropical Medicine*. Oxford: Oxford University Press, 2000: 228.
4. Phillipe JG, Olliaro P, Sundar S, *et al.* Visceral leishmaniasis: current status of control, diagnosis, and treatment, and a proposed research and development agenda. *Infectious Diseases* 2002; **2:** 494-501.
5. De La Rosa R, Pineda JA, Delgado J, *et al.* Influence of highly active antiretroviral therapy on outcome of subclinical visceral leishmaniasis in human immunodeficiency virus-infected patients. *Clin Infect Dis* 2001; **32:** 633-635.
6. Laguna F, Lopez-Velez R, Puledo F, *et al.* Treatment of visceral leishmaniasis in HIV-infected patients: a randomised trial comparing meglumine antimonate with amphotericin B. *AIDS* 1999; **13:** 1063-1069.