VISCERAL LEISHMANIASIS IN TWO CASES OF LEUKEMIA

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Abstract. Two cases of visceral leishmaniasis (VL), one in a 51-year-old man with accelerated-phase chronic myeloid leukemia and another in a 35-year-old woman with acute myeloblastic leukemia, are reported. Incidental finding of Leishman-Donovan (LD) bodies in patients with leukemia highlights VL as a potent opportunistic infection in immunosuppressed patients.

Many opportunistic pathogens have been described in patients with acute myeloblastic leukemia (AML) and chronic myeloid leukemia (CML) (Arrowsmith *et al*, 1999). However, visceral leishmaniasis (VL) has rarely been reported in acute or chronic leukemia (Hauteville *et al*, 1980; Gastaut *et al*, 1981; Aguado *et al*, 1983; Abdeladhim *et al*, 1986; Masseo *et al*, 1989; Mehrotra *et al*, 1995; Di Cataldo *et al*, 1996). We report two cases of VL in leukemia: one associated with AML; one in a patient with CML.

Case 1

A 51-year-old man from Ilam district, eastern Nepal, presented with progressive abdominal distension and an eighteen month history of an abdominal mass. He also complained of intermittent low-grade fever, vomiting, anorexia and weight loss over 3 months. Examination revealed abdominal distension, moderate pallor and a temperature of 38.8ºC; the spleen was huge reaching the umbilicus, and was firm, smooth and non-tender; the liver was also enlarged (4 cm below the costal margin), firm and non-tender. Bilateral axillary lymph nodes were palpable, varying in size from 1.5-2.5 cm in diameter; the glands were non-tender, firm and mobile. Other systems were normal. An initial clinical diagnosis of lymphoma, disseminated tuberculosis or kala-azar (VL) was made even though the patient was not from an endemic VL region.

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Laboratory investigations revealed the following: hemoglobin 7 g/dl; total leukocyte count 320,000/mm^3; platelet count 520,000/mm^3; liver and kidney function tests and chest X-rays were normal. A Mantoux test was negative. Fine needle aspiration (FNA) of the axillary lymph nodes showed features of reactive lymphadenitis. Peripheral blood smear showed a marked leukocytosis characterized by 12% blasts (including promyelocytes); platelets were adequate and occasional giant platelets were seen; red cells were normocytic and normochromic with occasional nucleated RBCs. Myelogram showed myeloblasts 4%, promyelocytes 8%, myelocytes 18%, metamyelocytes 24%, band forms 8%, neutrophils 14%, eosinophils 4%, basophils 10%, lymphocytes 8% and monocytes 2% (Fig 1). Bone marrow smears were hypercellular with marked myeloid hyperplasia; no marrow fragments were seen; blast cells constituted 22% (including promyelocytes) of all cells; a fair number of megakaryocytes were seen; very few erythroblasts were present; the M: E ratio was 15:1; basophils constituted 16% of all cells. Occasional Leishman-Donovan (LD) bodies were seen extracellularly (Fig 2). A diagnosis of accelerated-phase chronic myeloid leukemia (CML) with kala-azar was made.

Case 2

A 35-year-old woman from Morang district, eastern Nepal, presented with an intermittent high-grade fever of six week's standing, gum bleeding for 20 days and discomfort in the left hypochondrium for 15 days. She had been treated with several courses of antibiotics and anti-

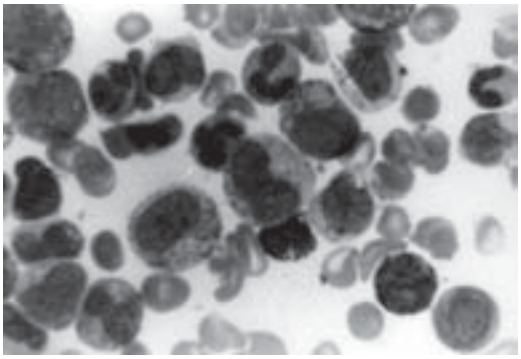

Fig 1–Peripheral blood smear of case 1 showing different forms of myeloid series of cells and 2 myeloblasts (Jenner Giemsa stain, x1,000).

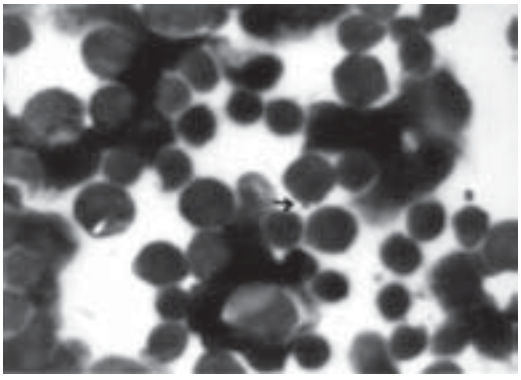

Fig 2–Bone marrow aspirate of case 1 showing a single extracellular LD body (arrow) (Jenner Giemsa stain, x1,000).

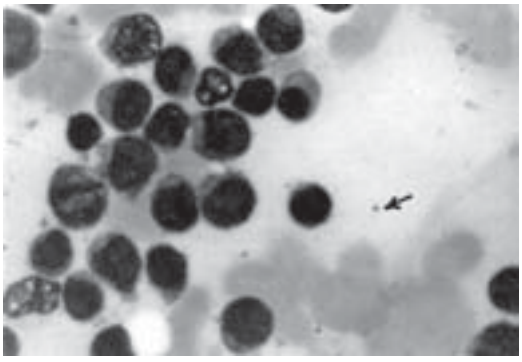

Fig 3–Bone marrow aspirate of case 2 showing multiple promyelocytes and blast cells. A single extracellular LD body is seen (arrow) (Jenner Giemsa stain, x1,000).

malarials with no response. On examination, the patient was dehydrated, febrile and moderately pale; hepatomegaly (2 cm below costal margin) and splenomegaly (4 cm below costal margins) were found. Other systems were normal. A clinical diagnosis of acute leukemia was made.

Investigations revealed: hemoglobin 5.6 g/dl; total leukocyte count 120,000/mm^3; platelet count 60,000/mm^3. Peripheral blood smear showed marked leukocytosis characterized by the presence of 81% blasts, a few of which showed granules and Auer rod; red cells were normocytic and normochromic to hypochromic with occasional macrocytes; there were 3 nucleated RBC/100 WBC; platelet numbers were markedly reduced. Bone marrow smears were hypercellular and characterized by presence of 80% promyelocytes and blast cells; some of these promyelocytes showed Auer rods; few maturing myeloid cells were seen; reaction was normoblastic and very few megakaryocytes were seen; plasma cells constituted 6% of all cells. Occasional extracellular LD bodies were seen (Fig 3). A diagnosis of acute myeloid leukemia (AML - M3) with kala-azar was made.

Visceral leishmaniasis (kala-azar) caused by *Leishmania donovani* is an important public health problem in Nepal and is of particular concern in the southern central areas of the country and in the region that borders the Indian state of Bihar (Karki *et al*, 1998). Both of our patients were from the eastern region of Nepal: the first patient, from a non-endemic region, had a history of visiting VL endemic districts; the second patient was from an area endemic for VL.

VL is a systemic disease characterized by fever, hepatosplenomegaly, weight loss, pancytopenia, hypergammaglobulinemia and positive serology for leishmanial antibodies. The importance of VL as an opportunistic infection has only recently been recognized (Fernandez-Guerrero *et al*, 1987), particularly in association with HIV infection (Albrecht *et al*, 1996). While reviewing the literature, we found 7 reports on VL associated with leukemias (Hauteville *et al*, 1980; Gastaut *et al*, 1981; Aguado *et al*, 1983; Abdeladhim *et al*, 1986; Masseo *et al*, 1989; Mehrotra *et al*, 1995; Di Cataldo *et al*, 1996): 6 in acute leukemia and one in CML (Abdeladhim *et al*, 1986). There is one report of asymptomatic VL in a child from the Indian subcontinent with

ALL in remission (Mehrotra *et al*, 1995). Both of our patients had fever; their marked leukocytosis was attributed to their leukemia.

Opportunistic infections in hematological neoplasia are caused by the impairment of phagocytosis (mainly neutropenia), the defective production of circulating antibody (humoral immunity), or impaired cellular immunity, or a combination of these defects. Neutropenia is a common complication of acute leukemias: in patients with CML neutropenia occurs only with blast crisis, in the face of developing myelofibrosis, or with therapy; neutrophils from untreated patients with CML may be mildly defective with respect to phagocytosis, oxygen consumption, and bactericidal capacity and tend to have decreased concentrations of lactoferrin, elastase, collagenase, and peroxidase (Olofsson *et al*; 1976); lysosomal enzymes of possible importance in bacterial killing, such as lysozyme, lactoferrin, and peroxidase, have been found in reduced concentrations in neutrophils of some patients with AML (Catovsky *et al*, 1972). Immunoglobulins tend to be toward the lower limit of normal in ALL but are normal or increased in AML and CML (Dupuy *et al*, 1971). Unless extensive therapy has been employed immunity is usually intact in patients with AML or CML. Our patient with CML and VL was put on Busulphan but left against medical advice; our second patient left before treatment could be started.

Although there was indirect evidence for global impairment of immunity in our patients, *in vitro* tests to confirm these observations could not be performed. VL may be coincidental findings in both of our cases. In conclusion, VL should be considered as a possible potent opportunistic infection in immunocompromised patients from endemic and non-endemic areas of countries in which the disease in prevalent.

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