Visceral Leishmaniasis: A Rare Cause of Unexplained Pyrexia in a Renal Allograft Recipient

R.	Ravindra	Mittal ^a
S.	Sanjiv	Saxena ^a
S.	Sandeep	Guleria ^b
S.K.		Mittal ^a
S.K.		Agarwal ^a
S.C.		Tiwari ^a
S.C.		Dash ^a

Departments of ^aNephrology and ^bSurgery, AIIMS, New Delhi, India

Dr. Sanjiv Saxena, Assist. Prof., Department of Nephrology, AIIMS, New Delhi (India)

Dear Sir,

Visceral leishmaniasis or kala-azar has not been recognised as a common infection in renal allograft recipients. However, immunodeficiency states can facilitate the reactivation of a dormant illness in infected patients or predispose such patients to infection in endemic areas. Indeed, following its first description in renal transplant recipients in 1979 [1], in recent years more case reports have described such an association [2-5]. In contrast to the non-immunodeficient patients, the disease is often more fulminant and poorly responsive to therapy in these high risk patients [3]. We report here a case of visceral leishmaniasis in a renal allograft recipient who presented with pyrexia of undetermined origin and showed an excellent response to pentavalent antimonials.

A 23-year-old young male, resident of Bihar, India, underwent a one-haplotype-matched live related renal transplantation for Alport's syndrome with end stage renal disease at our centre in December 1992. Immunosuppression given comprised three drugs – azathioprine, prednisolone and cyclosporine, with a gradual tapering off from cyclosporine from 3 months onwards so as to be completely weaned off by 9 months. The early posttransplant period was uneventful.

In June 1993 the patient was admitted for evaluation of his pyrexia of unknown origin of 3 weeks duration. The fever was high grade and remittent in nature without any localising symptoms. He had received an empirical course of antimalarials twice (chloroquine followed by a sulphamethoxazole and pyrimethamine combination) and also broad-spectrum antibiotics (ampicillin and norfloxacin) for his pyrexia in Bihar without response. Physical examination revealed a pale, anicteric, febrile patient with no significant peripheral lymphadenopathy. He was normotensive and the cardiovascular and respiratory systems were normal. Abdominal examination showed a 2-cm hepatomegaly and a firm 3-cm splenomegaly with the allograft being normal and non-tender.

Investigations on admission revealed a haemoglobin of 6.4 g/dl, reticulocyte count 1%, total leucocyte count 3,200/mm³, platelet count of 90,000/mm³ and ESR of 33 mm in the 1st h. Blood urea was 30 mg/dl, serum creatinine 1 mg/dl, serum bilirubin 0.9 mg/dl, SGOT 86

IU/ml, SGPT 93 IU/ml and an alkaline phosphatase of 86 IU/ml. The total proteins were 7.1 g/dl with the serum albumin being 3.2 g/dl and the globulins 3.9 g/dl. The rest of serum biochemistry was normal. A routine urinalysis and 24-hour urine examination were normal. Radiography of the chest was normal. Peripheral smears for malarial parasites were negative on three occasions and repeated blood, urine and throat cultures were sterile. Widal test was negative and showed no increase in titre serially. Serology for cytomegalovirus was negative for both IgM and IgG antibodies. Mantoux test was negative. Abdominal ultrasonography showed hepatosplenomegaly but no retro-peritoneal lymph nodes or masses. The patient was initially treated with ciprofloxacin 500 mg b.d. for 2 weeks without response. A repeat empirical course of antimalarials was also administered without success. In view of leucopenia, the patient was restarted on cyclosporine at a dose of 2 mg/kg/day and azathioprine was discontinued.

A bone marrow examination was done subsequently and the smears were full of amastigote forms of *Leishmania donovani*. Definitive therapy was then instituted in the form of sodium antimony gluconate started in a dose of 8 mg/kg/day in view of deranged LFTs and then stepped up to a dose of 15 mg/kg/day. The patient showed an excellent response with amelioration of toxemia and became afebrile after 7 days of therapy. The therapy was, however, continued for a total of 2 weeks. A repeat bone marrow examination done after 4 weeks was reported negative for Leishman-Donovan bodies. The patient was discharged with normal counts, normal renal parameters and normal LFTs at completion of therapy. The patient has been under follow-up for the last 6 months without recurrence of the disease. Visceral leishmaniasis or kala-azar is endemic in several parts of India with 30 of the 39 districts of Bihar having been identified as currently endemic areas by the WHO [6]. To the best of our knowledge, only 12 cases, including this report, of visceral leishmaniasis in renal allograft recipients have been described so far [2-5]. Four of these patients (33.3%) had a fatal outcome mainly due to superinfection, most often *Pseudomonas* septicemia, or disseminated intravascular coagulation [2, 3], and only 8 patients (66.6%) have survived after antiprotozoal therapy [4, 5]. The outcome depends on early diagnosis and treatment – which may be delayed because this diagnosis is often not considered in the first place and secondly because of a misleading presentation of the disease in such immunocompromised hosts. The optimum dosage and duration of treat-

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0028-2766/95/0701-0123
\$8.00/0

ment in such patients is also not clearly defined as is demonstrated by the various treatment schedules and outcome reported in the literature [2-5]. However, a close follow-up is essential after effective treatment since relapses have been described occurring even after 1 year of apparent cure, necessitating successful retreatment with either pentavalent antimonials again or with other antileishmanial drugs, like allopurinol and amphotericin [3]. In conclusion, visceral leishmaniasis should be considered as an opportunistic infection in the differential diagnosis of the febrile renal allograft recipients residing in or having visited an endemic area.

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