Visceral Leishmaniasis-Like Cause of Unexplained Fever in a Reno-Pancreatic Graft Recipient

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Dear Sir,

Recently, Moulin et al. [1] described a case of visceral leishmaniasis in a renal graft recipient. Here we report a similar case of nonfatal visceral leishmaniasis in a reno-pancreatic graft recipient.

Visceral leishmaniasis is an opportunistic protozoal subacute infectious disease, endemic in many underdeveloped countries around the world, and is also present in some Mediterranean countries such as Spain.

Visceral leishmaniasis is infrequently reported in immunocompromised hosts [2-5] and has occasionally been described in renal transplant recipients, often with a fatal course [6-9].

A 45-year-old man with chronic renal failure, secondary to diabetic nephropathy, on hemodialysis treatment since April 1990, was submitted to a cadaveric renal and pancreatic transplant on October 1991. The patient had a 20-year history of diabetes mellitus.

After initial immunosuppressive therapy with prednisone (1 mg/kg/day), azathioprine (2 mg/kg/day), cyclosporin A (8 mg/kg/day) and a 14-day course of antilymphocyte globulin, basal immunosuppression consisted of low doses of prednisone (0.25 mg/kg/day), azathioprine (0.75 mg/kg/day) and cyclosporin A (4 mg/kg/day).

The patient's postoperative course was uneventful and he was discharged on the 36th posttransplant day with normal renal (serum creatinine 114 mmol/l) and pancreatic function. Three months later he had a urinary infection (*Escherichia coli*) which responded to Ciprofloxacin therapy.

In June 1992, the patient was readmitted to the hospital because of nocturnal fever (38.5°C) 7 days prior to admission. Physical examination was unrevealing. Renal, pancreatic and hepatic function was normal, but pancytopenia was detected (WBC 2,730/mm³, platelet count 91,000/mm³, Ht 25%, Hb 6.9 g/l). Urine culture remained positive for enterococci. Chest X-ray film showed a cavitation in the apical area of the right lung. Sputum, Ziehl-Neelsen and Löwenstein-Jensen cultures were positive for *Mycobacterium tuberculosis*. The patient was treated with isoniazid,

rifampin and pyrazinamide. Rifampin was suppressed cholestasis and pyrazinamide hyperuricemia. Ofloxacin and ethambutol were added.

After 12 days of TBC treatment, the patient remained febrile. CMV serology and blood cultures were positive and he received antiviral treatment with Foscarnet. Consecutive blood cultures were negative.

Forty-five days after admission, the patient remained febrile and his general condition was deteriorated: hematocrit 26%; hemoglobin 8.6 g/l; WBC 990/mm³ and platelet count 48,000/mm³. Abdominal ultrasound showed only a homogenous splenomegaly. Bone marrow aspirate revealed moderate intra-medullary destruction and numerous *Leishmania donovani* amastigotes.

The patient received pentavalent anti-monials (Glucantime) in a modified dosage of 10 mg/kg/day for a total of 3 weeks. Rapid remission of the febrile syndrome with improvement of the patient's general condition was obtained.

One month later, WBC was 4,010/mm³, hematocrit 32%, hemoglobin 9.4 g/l and platelet count 161,000/mm³. Bone marrow aspirate was normal and leishmania organisms were not identified. The renal and pancreatic function has since remained stable.

Infections represent an important cause of morbidity and mortality in allograft recipients. Their incidence and severity are modified by immunosuppressive therapy.

Mediterranean visceral leishmaniasis (*Kala-Azar*) is a protozoal acute or subacute infectious disease of children, endemic in the Mediterranean area. Clinical manifestations include a prolonged febrile syndrome with hepatosplenomegaly, pancytopenia and hyperglobulinemia which is almost invariably fatal in untreated patients. Latent infection could progress to acute disease under immunodeficiency conditions. In contrast to the non-immunodeficient patients, immunosuppression may transform classic leishmaniasis into a fulminant disease, poorly responsive to antiparasitic therapy [2-5, 9].

Although a variety of serum factors may play a role in the pathogenesis of the disease and in protection against reinfection, the resolution of leishmaniasis is primarily dependent on cell-mediated immune response [3, 10]. The present patient, in spite of exhibiting severe cellular immunodeficiency, manifest-

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ing as pulmonary tuberculosis and cytomegalovirus infection, developed subacute visceral leishmaniasis symptomatology.

Few cases of leishmaniasis in renal transplant patients have been reported in the literature. The present case represents the first in a reno-pancreatic graft recipient. Five of the nine described cases had a fatal evolution secondary to superinfection and/or hemorrhage [3, 6, 7, 9], and 4 survived after anti-protozoal therapy [3, 11, 12]. The patient reported here had complete remission without reappearance of symptomatology 3 months after treatment. The renal and pancreatic function was stable during Glucantime treatment, and no changes in the cyclosporin A blood levels were detected.

Visceral leishmaniasis should be considered in the differential diagnosis of renal transplant recipients with prolonged febrile syndrome and pancytopenia, especially in endemic areas. Antiprotozoal pentavalent anti-monial therapy represents the first line in the treatment of visceral leishmaniasis in these patients.

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