CLINICAL NOTES

In an effort to increase the utility of the JOURNAL in continuing medical education, in this section we welcome contributions dealing with practical problems in leprosy work. Submissions to this section will undergo minimal editorial changes and may well contain controversial points. Letters to the Editor pointing out other viewpoints are welcome.

Renal Transplantation in Leprosy Patients

Leprosy is an endemic disease which represents an important public health problem in Brazil. According to the National Leprosy Service of the Brazilian Health Department, leprosy prevalence in Brazil is 2.0 to 4.9 cases/1000 inhabitants. Brazil is one of the countries of high endemic occurrence of the disease since, according to the World Health Organization (WHO), the world rate is 1.0/1000 inhabitants. In the Ribeirão Preto region of Brazil, the prevalence is 1.84/1000 inhabitants. Some of these patients, especially those with complications due to the course of the disease or to treatment, are followed up at the University Hospital of the Faculty of Medicine of Ribeirão Preto, University of São Paulo.

The disease presents a broad spectrum of clinical manifestations ranging from a pole of high resistance to bacillary multiplication (tuberculoid leprosy, TT) to a disseminated form with systemic involvement (lepromatous leprosy, LL).

Three types of renal involvement not specific for the disease are frequently described in lepromatous leprosy: renal amyloidosis, glomerulonephritis, and interstitial nephritis, generally associated with circulating immune complexes such as erythema nodosum leprosum (type 2 reaction) whose course involves sudden relapses which, in some cases, lead to renal failure as a final consequence.[1, 2] In the past, renal transplantation was not indicated for leprosy patients for fear of involvement of the transplanted organ or of the probable risks of immunosuppression in a patient with lepromatous leprosy.

The first report of a renal transplant in a patient with leprosy was published in 1973, and the procedure has been encouraged ever since.[3]

The first renal transplantation performed at the University Hospital of the Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil, dates back to 14 February 1968, and 520 transplants have been performed since then up to 2 October 1992. Two of these transplantations involved patients with a history of leprosy. The series also includes two patients who presented no manifestations of leprosy before transplantation but who developed the disease during the postoperative period. We describe here these four cases.

CASE REPORTS

Case 1. Case 1 was a white married housewife. Leprosy of the indeterminate form was diagnosed when she was 10 years old, and she was treated with sulfones for 17 years. At 27 years of age she underwent renal transplantation due to end-stage chronic renal failure and was treated with prednisone and azathioprine for immunosuppression. The renal history of the patient involved generalized edema when she was a child (nephritis?) and repeated infection of the urinary tract since 18 years of age, as well as a congenitally hypoplastic kidney. No manifestation of leprosy occurred during the 14-year period after renal transplantation. The patient died on 28 March 1991

[1] Drutz, D. O. and Gutman, R. A. Renal manifestations of leprosy: glomerulonephritis, a complication of erythema nodosum leprosum. Am. J. Trop. Hyg. **22** (1973) 496–502.

[2] Jopling, W. H. and McDougall, A. C. In: *Manual de Hanseniase.* 4th edn. Rio de Janeiro: Livraria Atheneu Ed., 1991, pp. 36–37.

[3] Adu, D., Evans, D. B., Millard, P. R., Calne, R. Y., Shwe, T. and Joplingy, W. H. Renal transplantation in leprosy. Br. Med. J. **2** (1973) 280–281.

due to uncontrollable high digestive tract hemorrhage as a consequence of esophageal varices caused by portal hypertension which, in turn, was caused by active chronic hepatitis (positive EIE test for HBc Ag IgM). At autopsy, the transplanted kidney presented rare glomeruli with increased segmental mesangium, tubuli and interstitium with acute tubular necrosis, and large vessels with paucicellular thickening indicating incipient chronic vascular rejection.

Case 2. Case 2 was a white 53-year-old male with a diagnosis of end-stage renal failure and arterial hypertension who had been on hemodialysis for 1 year. He had no history of renal pathology. Lepromatous leprosy was diagnosed when he was 12 years old, and the patient has been treated ever since, most recently with rifampin, dapsone and clofazimine, except for rare periods of interruption. The time of use of each drug or drug combination was not reported. On the occasion of renal transplantation with an organ from a related donor (sister) in March 1991, the patient was prescribed prednisone, azathioprine and cyclosporine, as well as maintained on 100 mg/day clofazimine. A slit-skin smear for acid-fast bacilli (AFB) performed on that occasion was negative. Six months after transplantation, the patient was given a new dermatological evaluation which did not show any active lesions, but simply ichthyotic and hyperchromic skin due to clofazimine. An earlobe slit-skin test was negative. The dose of clofazimine was changed to 100 mg on alternate days.

Case 3. Case 3 was a white male who was seen at the urology outpatient clinic at the age of 37 with end-stage, chronic renal failure due to chronic diffuse glomerulonephritis confirmed by biopsy. The patient presented hepatomegaly (positive test for the Australia antigen), and had been on hemodialysis for 1 year and 5 months. Two years later (November 1983) he received a kidney from a related living donor (sister). Five months after the renal transplant, he began to complain of numbness of his hands and feet. He was taking prednisone and azathioprine, as well as furosemide on occasion and Sandoz calcium. His wife had been under treatment for leprosy with dapsone and thalidomide for 3 months. A dermatological examination of the patient was compatible with lepromatous leprosy, and this was confirmed by a positive slit-skin test for AFB from the elbow. Treatment with 600 mg/day of rifampin and 100 mg/day of dapsone was started. Rifampin was maintained for 2 months, and dapsone alone was administered thereafter. Five months after treatment for leprosy was started, there was an increase in bilirubin levels which worsened over the following 2 months and was accompanied by increased transaminases. Dapsone was discontinued because of suspected drug-induced liver disease. Eight months after transplantation, 100 mg/day of clofazimine was begun. The patient continued to have active leprosy lesions. Two years after transplantation he continued to have high bilirubin levels, and azathioprine was replaced with cyclophosphamide. On that occasion, the slit-skin smear continued to be positive, the patient started to gain weight, and routine urinalysis repeatedly revealed the presence of hematuria and proteinuria. Despite these findings, the patient continued to be normotensive. Two years and 7 months after transplantation, a bacilloscopy was positive, bilirubin levels were increased, hematuria persisted, and weight increased; renal function was under control with creatinine = 1.0 (normal: 0.7 to 1.4 mg/dl) and creatinine clearance = 86.8 ml/min/1.73 m^2. Dapsone was reintroduced at this point but the patient died outside of the hospital of an unknown cause.

Case 4. Case 4 is a white 49-year old male who had been presenting with end-stage chronic renal failure for 1 year and was on hemodialysis. He reported a history of nephritis at 11 years of age with anasarca, for which he was treated with remission of symptoms. One year later he received a kidney from a related living donor (brother) and was maintained on prednisone, azathioprine and insulin NPH-100, 50 U/day. Five years after transplantation he presented with burning pain and edema in the upper and lower limbs. A diagnosis of borderline (dimorphous) leprosy was made and confirmed by positive skin smears for AFB from the earlobe and elbow and by skin biopsy. He had no previous history of leprosy. Treatment with dapsone 100 mg/day was started; 6 months after the diagnosis of leprosy the patient presented with only residual lesions. He is regularly seen for check-

up visits and has now completed 7½ years post-transplantation. Dapsone is being maintained, and the patient does not present any specific leprosy lesions.

DISCUSSION

The first case described here is that of a woman with the indeterminate form of leprosy who was treated with sulfone for a period of 18 years from diagnosis to renal transplantation. This case demonstrated that during the 14 years between transplant and death the patient did not suffer a relapse of the disease, and an autopsy did not reveal any signs of kidney involvement by leprosy. The clinical form of the disease presented by this patient may possibly justify the expected favorable course when compared to a case of tuberculoid leprosy reported in 1982.[4]

The second case involved a lepromatous patient under treatment for 40 years and whose disease led to renal failure. Since the patient did not have a history of renal disease, this was probably renal amyloidosis. Although this is a short period of time, 6 months after transplantation there were no signs of a relapse of the disease and bacilloscopy continued to be negative. Prophylactic treatment with clofazimine is being maintained despite the negative results of bacilloscopy and the absence of lesions, since two cases of untreated lepromatous leprosy reported in the literature suffered relapses 14 and 23 months after renal transplantation, respectively.[3, 5] On the other hand, another case of lepromatous leprosy maintained without specific treatment showed no signs of relapse 30 months after renal transplantation.[6] Thus, although the maintenance of specific therapy is debatable, we believe this approach is more cautious and, in addition, provides greater peace of mind for the patient.

The last two cases are of the lepromatous and borderline forms with onset at 5 months and 5 years after renal transplantation, respectively. The first was a contact of a lepromatous patient (his wife) who had been under treatment for 3 months, a fact that might explain the onset of the disease. However, we believe that the time of evolution to the lepromatous form was too rapid, probably suggesting that the patient might have had subclinical disease which became manifest after renal transplantation due to the therapeutic immunosuppression. Another possibility is that this suppression was responsible for the accelerated course of the disease. The last case had no epidemiological history of leprosy. Both patients were treated with dapsone, and the last still is being followed up with no complications. The patient who died of an unknown cause, since death did not occur in our hospital, probably suffered an accelerated course of the disease due to previous hepatic involvement (Australia antigen+) which impaired handling of the immunosuppressive drugs and of the specific leprosy drugs. The hematuria of the final months may be attributed to cyclophosphamide (hemorrhagic cystitis) or to glomerulonephritis caused by leprosy, although the patient was not hypertensive.

Our observations confirm previously reported results,[4, 5] indicating that leprosy is not a contraindication for renal transplantation. Even in cases who presented with the disease after transplantation, the disease in these patients could be controlled even though they received immunosuppressive drugs concomitantly.

SUMMARY

We report four cases of leprosy in renal transplant recipients, two of whom had the disease before transplantation and no signs of relapse even in the presence of immunosuppressive drugs. The other two cases presented with lepromatous and borderline (dimorphous) leprosy 5 months and 5 years after transplantation, respectively. The disease of the last patient was controlled with sulfone even in the presence of immunosuppressive drugs, but the mechanism whereby the first patient rapidly developed lepromatous leprosy is unclear, even though

[4] Date, A., Mathai, R., Pandey, A. P. and Shastry, O. C. M. Renal transplantation in leprosy. Int. J. Lepr. **50** (1982) 56–57.

[5] Teruel, J. L., Liano, F., Hoyo, M., Rocamora, A., Gomes Mampaso, E., Quereda, C. and Ortuno, J. Successful kidney transplantation in leprosy and transitory recurrence of the disease. Int. J. Lepr. **53** (1965) 410–411.

[6] Mocelin, A. J., Ajzen, H., Ancao, M. S., Stabile, N. C., Sadi, A., Maluli, A. M. and Ramos, O. L. Kidney transplantation in leprosy. Transplantation **28** (1979) 260.

he was a home contact of a patient with lepromatous leprosy (his wife). In view of the data presented here, we do not contraindicate renal transplantation in patients with leprosy who frequently suffer changes in renal function. We believe that renal function should be periodically evaluated in patients with borderline and lepromatous leprosy.

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