MEDICAL MEMORANDA

Renal Transplantation in Leprosy

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This is the first report of renal transplantation in a patient with lepromatous leprosy although renal failure is an important cause of death in these patients (Brusco and Masanti, 1963; Desikan and Job, 1968; Hart and Rees, 1967).

The deficiency of cell-mediated immune response in patients with lepromatous leprosy results in a prolongation of survival of allogenic skin grafts (Heart and Rees, 1967; Turk, 1970; Han *et al.*, 1971). This may be of importance in clinical organ transplantation.

Case Report

A 27-year-old Anglo-Indian with end-stage chronic renal failure and hypertension and with a history of fevers, backache, and haematuria at the age of 17 years suggestive of chronic pyelonephritis was referred for dialysis and transplantation in June 1966. After preliminary haemodialysis he received a cadaveric renal transplant in July with immediate diuresis. No HL-A typing was available at the time. Immunosuppression was started with hydrocortisone and azathioprine and he was subsequently maintained on prednisolone and azathioprine. He was discharged home two months after operation with a creatinine clearance of 60 ml/min and he remained well for the next two years maintaining a creatinine clearance of 70 ml/min.

Twenty-three months after his transplant he developed a pyrexial illness with a left epididymo-orchitis, thickening of some peripheral nerves, and erythema nodosum on his limbs, trunk, and face. These developments were clinically suggestive of lepromatous leprosy complicated by a lepra reaction. Skin biopsy and smears showed the presence of large numbers of acid-fast bacilli. Coincidentally his renal function deteriorated, his creatinine clearance falling to 35 ml/min. At this stage the patient admitted to having developed leprosy in India in 1952. He had received regular treatment for four years and after this had treated himself intermittently until the time of his renal transplant.

He was now treated initially with dapsone at a dose of 1 mg daily and the prednisolone was increased to cover the lepra reaction. After initial improvement he developed a further reaction and his therapy was changed to clofazimine. On a dose of 300 mg daily his skin lesions regressed rapidly although he developed a bright red pigmentation of his skin.

He remained well until December 1970, when he was readmitted with deterioration of renal function coincident with a further lepra reaction. His creatinine clearance was 5.2 ml/min and

a renal biopsy showed the appearances of a chronic rejection process. He was re-established on outpatient haemodialysis. Three months later he developed pneumonia with a cavity in the apex of the lower lobe of the left lung. This was assumed to be tuberculous and he was treated with antituberculosis therapy. He had a severe lepra reaction with rifampicin, but this improved by changing to isoniazid and PAS. However, he then developed a cholestatic jaundice and died a week later, four years nine months after renal transplantation.

At necropsy changes affecting many tissues and organs were found. There was a papular rash mainly on the trunk and upper limbs. Some papules contained large clusters of vacuolated cells (lepra cells) in the dermis around vessels and nerves but in none of these cells were any acid-fast bacilli found. Macroscopically many organs were a lilac pink colour which was more noticeable after fixation in a formalin-saline solution. This discoloration, although affecting the stomach, duodenum, and particularly the entire ileum, was conspicuously absent in the greater part of the jejunum. *Klebsiella aerogenes* was cultured from the lower lobe of the left lung which was uniformly consolidated. No organisms were isolated from a cavity at the apex of this lobe in which there was caseation. Cytomegalovirus was grown from lung tissue and inclusion bodies typical of this virus were seen both in the lungs and submandibular salivary gland. The heart was enlarged (435 g) due mainly to left ventricular hypertrophy and was partly covered by a fibrinous pericarditis. The liver was engorged and many lobules included centrilobular cholestasis. The biliary tract was patent and normal. An abscess from which no micro-organisms were identified replaced the distal third of the body of the pancreas. Both testes had lost their septate pattern and included ill-defined areas of firm grey fibrous tissue. Their tubules were necrotic and the epididymes thickened.

Both the patient's own kidneys were equally small with finely and evenly granular surfaces. Microscopically in both kidneys there was widespread atrophy of nephrons with an interstitial infiltrate of mononuclear cells and fibroelastic intimal thickening of arteries. No distinctive glomerular lesions were recognized and no amyloid deposits seen.

The grafted kidney was in the retroperitoneal tissues of the right iliac fossa. The renal artery was patent and anastomosed end-to-end to the right internal iliac artery. The renal vein was occluded by thrombus and sutured to the side of the right external iliac vein. The allograft ureter was patent and drained into the bladder. The kidney was slightly enlarged (12.0 by 6.0 by 3.0 cm) with a smooth surface, tough consistency, and evenly thinned cortex. Thrombus filled many intrarenal veins. The calyces and pelvis were unremarkable.

Moderate-to-substantial fibroelastic intimal thickening affected many arteries, often associated with breaks in the internal elastic lamina, with patchy medial atrophy and with focal medial fibrosis. Partly calcified thrombus and moderate fibrous intimal thickening were seen in some veins. Moderate numbers of mononuclear cells surrounded most vessels and a substantial increase in fibrous interstitial tissue was present. The principal glomerular and tubular appearances included atrophy and fibrous replacement.

No deposits of IgG, IgM, or C3 component of complement were found by immunofluorescent studies.

Comment

A high incidence of renal disease and chronic renal failure is found in lepromatous leprosy (Brusco and Masanti, 1963). The renal disorder of leprosy shows pronounced regional variation. Particularly under the age of 50 uraemia was the most important cause of death. In America renal amyloid predominates contributing to as many as 38% of deaths in one series (Powell and Swan, 1955). Elsewhere a high incidence of pyelonephritis, interstitial nephritis, and urinary tract infections has been found (Thomas *et al.*, 1970; Tin Shwe and Jopling, 1973).

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This patient was transplanted before the diagnosis of leprosy was made. Recrudescence of leprosy two years after transplantation was presumably associated with suspension of anti-leprosy treatment on the patient's part, and a lepra reaction became manifest as a result of reducing the dosage of immunosuppressive drugs. He was treated with clofazimine, a riminophenazine dye which combines an anti-leprosy action as effective as that of dapsone with an anti-inflammatory effect which is valuable in suppressing lepra reactions. Control of his leprosy assessed clinically and by the fall in morphological index was good.

Patients with lepromatous leprosy have a specific loss of cell-mediated immune response against *Mycobacterium leprae* and also a diminution in the ability to show other aspects of cell-mediated immune response—for example, contact sensitivity and skin homograft rejection (Hart and Rees, 1967; Bullock, 1968; Turk, 1970; Han *et al.*, 1971).

As the lepra reaction is an antigen-antibody reaction, immunosuppressive agents such as steroids and azathioprine which suppress antibody-mediated cellular immunity as well as antibody production would be expected to benefit the lepra reaction of lepromatous leprosy as well as the renal allograft.

At necropsy all the changes on histology of the renal graft could be readily explained on the basis of immune rejection and its consequences. There was no evidence to suggest involvement of the graft by the renal complications of leprosy.

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References

- Brusco, C. M., and Masanti, J. G. (1963). *International Journal of Leprosy*, 31, 14.
 Bullock, W. E. (1968). *New England Journal of Medicine*, 278, 298.
 Desikan, K. V., and Job, C. K. (1968). *International Journal of Leprosy*, 36, 32.
 Han, S. H., Weiser, R. S., and Kac, S. T. (1971). *International Journal of Leprosy*, 39, 1.
 Hart, P. D., and Rees, R. J. W. (1967). *British Medical Bulletin*, 23, 80.
 Powell, C. S., and Swan, L. L. (1955). *American Journal of Pathology*, 31, 1131.
 Thomas, G., Karat, A. B. A., Rao, P. S. S., and Prathapkuma, C. (1970). *International Journal of Leprosy*, 38, 170.
 Tin Shwe, and Jopling, W. H. (1973). *International Journal of Leprosy*. In press.
 Turk, J. L. (1970). *Leprosy Review*, 41, 207.

Mononeuritis Multiplex Occurring in a Diabetic Patient with Hb C Disease

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Mononeuritis multiplex is a well recognized complication of diabetes mellitus. It is seen in elderly patients but is not a feature in young diabetics (Raff and Asbury, 1968).

We report the case of a youth with homozygous Hb C disease who developed mononeuritis multiplex after hyperosmolar diabetic coma complicated by acute renal failure.

Case History

A previously healthy 14-year-old Negro from Barbados was admitted to hospital comatose on 4 January 1972 with a two-week history of increasing thirst, polydipsia, and polyuria. He was dehydrated and hypotensive (B.P. 70/0 mm Hg). The urine contained sugar and a trace of acetone. The blood sugar was 1,000 mg/100 ml, plasma bicarbonate 26.5 mEq/l., and the blood urea 186 mg/100 ml. He was treated with intravenous fluids and soluble insulin. Over the next three days plasma sodium concentration rose from 144 to 174 mEq/l., he became oliguric, and the blood urea level rose to 330 mg/100 ml. Plasma osmolality was not measured but the calculated osmolality ranged from 360 to 380 mOsm/l. On 7 January he was transferred to St. Leonard's Hospital hypotensive (B.P. 90/0 mm Hg), oliguric, and uraemic. Haemoglobin was 8.0 g/100 ml, packed cell volume 20%, mean corpuscular haemoglobin concentration 40%, reticulocytes 3%, white blood count 24,900/mm³ (polymorphs 93%), platelets 120,000/mm³. A single band with the mobility of Hb C was noted on haemoglobin electro-

phoresis. The presence of the disease was confirmed by observing the characteristic crystals of Hb C in 3% sodium chloride. There was no evidence of intravascular coagulation apart from the moderate thrombocytopenia.

Acute tubular necrosis secondary to hypovolaemia and hypotension was suspected. High dose excretion urography, however, did not show the typical findings associated with acute tubular necrosis but those observed with severe glomerular disease (Fry and Cattell, 1972). Peritoneal dialysis was begun, and after two weeks a diuresis occurred. Creatinine clearance returned to normal after eight weeks. The diabetes was treated by carbohydrate restriction (180 g/day) and soluble insulin (24-36 units/day). After recovering consciousness the patient remained apathetic for 10 days and his limbs were noticed to adopt unusual postures. The cerebrospinal fluid was normal. As his mental state improved, it became clear that he had bilateral wrist and foot drop. On the right there was a radial palsy distal to the branch to brachioradialis, and a median palsy distal to the origin of the branch to flexor digitorum. On the left there was a patchy and incomplete radial palsy. In the right leg there was a complete lateral popliteal and a posterior tibial palsy, accompanied by sensory loss in the distribution of these nerves. In the left leg there was a complete lateral popliteal palsy. The tendon reflexes were normal. Five weeks later the right posterior tibial palsy had recovered and there was some return of power to the forearm radial muscles on each side. The other neurological signs were unchanged. Electromyography of the right tibialis anterior at this time showed profuse fibrillation without units under voluntary control. Evidence of partial denervation was found in the right abductor pollicis brevis, and areas of extensor carpi radialis were completely denervated. The right median and ulnar sensory action potentials were normal.

Comment

The development of mononeuritis multiplex in a young, acute onset, diabetic is extremely unusual. This prompts consideration of the possible role of the associated haemoglobinopathy in the pathogenesis of the neuropathy.

Isolated lesions of peripheral nerves have been observed in sickle cell disease (Konotey-Ahulu, 1972), but we are not aware of any published report of such lesions in homozygous Hb C disease. The finding that the pathological change in mononeuritis multiplex complicating polyarteritis nodosa (Lovshin and Kernohan, 1948) and diabetes mellitus (Raff *et al.*, 1968) is localized infarction of the affected nerves suggested that the neuropathy in this case might be due to occlusion of vasa nervorum. Red cells from patients with homo-

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