Immune complex glomerulonephritis and chronic anaerobic urinary infection—complications of filariasis

A. D. ORMEROD
M.B., M.R.C.P.

J. K. HUSSEY
M.B., F.R.C.R.

N. EDWARD
M.B., F.R.C.P.E.

J. PETERSEN
M.B., M.R.C.P.

J. WEIR
M.B., M.R.C.P., F.R.C.R.

Departments of Medicine and Radiology, Aberdeen Royal Infirmary, Foresterhill, Aberdeen

Summary

We describe a patient with chyluria due to abdominal Bancroftian filariasis. The patient showed two unusual complications, an immune complex glomerulonephritis and a chronic urinary infection. We also discuss the use of the CT whole body scanner in the diagnosis and delineation of the extent of the disease.

KEY WORDS: filariasis, glomerulonephritis, urinary tract infection.

Introduction

Chyluria is a frequent and well established complication of filariasis and is caused by fistulous connections between diseased lymphatic vessels and the urinary tract. More recently, there have been several reports of immune complex glomerulonephritis in patients with filariasis (Date, Shastry, and Johny, 1979b; Waugh, Alexander and Ibels, 1980). The immune complexes are thought to be formed in response to the parasitic antigen. Similar glomerular changes have been induced in animal models (Klei, Crowell and Thompson, 1974). Ascending lymphangiography forms an essential part of the investigation of chyluria but may also be aided by concurrent computerized tomographic (CT) whole body scanning; we report our findings using these techniques. We also discuss the factors that may have given rise to the unusual complication of chronic anaerobic urinary infection.

Case report

The patient, a Caucasian, aged 17 years, was born in the Persian Gulf. Educated in the United Kingdom he had spent about 3 months each year on

vacation in the Persian Gulf. At 13 years, whilst in Abu Dhabi, he suffered an undiagnosed pyrexial illness with delirium, which resolved spontaneously after 3 days. From the age of 14 years, he had recurrent episodes of milky urine and occasional loin pain. He passed debris in the urine which resembled tissue and which sometimes interrupted the stream, but had no frequency, dysuria, urticaria, orchitis or oedema.

Physical examination was normal. There was no fever, rash, lymphadenopathy, splenomegaly, pleural effusion, ascites or oedema. The patient's urine was yellow and milky.

Analysis of the urine revealed the presence of protein, blood and chylomicrons. The amount of proteinuria was 3 g/day with a glomerular electrophoretic pattern. The deposit contained lymphocytes, red cells and organisms but no polymorphonuclear leucocytes. Urine was sterile on routine culture, but culture for anaerobes revealed a mixed growth of anaerobes including *Bacteroides melaninogenicus*, *Bacteroides fragilis*, *Peptococcus prevotii* and *Propionibacterium granulosum*. There were no filariae in the urine nor were filariae found on thick and thin blood films or by micropore concentration techniques carried out on diurnal specimens of blood. Filarial immunofluorescent antibody test and schistosomal enzyme-linked immunosorbent assay were negative.

Haemoglobin was 15.6 g/dl, white cell count 2.4×10^9 /litre with 4% eosinophils. Blood urea, electrolytes, creatinine, liver function tests, plasma lipids, immunoglobulins and serum complement were normal. Autoantibodies were not present, ASO titre was less than 160, blood cultures and Mantoux test were negative. Intravenous pyelography was normal. Cys-

FIG. 1. Electron micrograph of part of a glomerulus showing a hypercellular mesangial lesion in which there are dense deposits (circled) of immune complex type ($\times 6175$).

toscopy showed heaping up of one area of mucosa, histology of which showed cystitis cystica.

In view of the degree of proteinuria, the presence of red cells in the urine and a depressed creatinine clearance (69 ml/min), a renal biopsy was carried out. It showed focal, mild hypercellularity of some capillary loops with the presence of red cells in the tubules. Electron microscopy showed minor mesangial hypercellularity with an increase in the mesangial matrix. In the mesangial regions of all glomeruli examined, immune complexes were present (Fig. 1). There was focal fusion of foot processes. Tubular changes were present with cell damage and individual cell death. Debris and fibrin were present in the tubules.

Ascending lymphangiography showed a remarkable degree of abnormality of the lymphatics proximal to the inguinal nodes, with tortuosity and dilatation notably around the bladder and left kidney (Fig. 2). The abdominal lymph nodes were not demonstrated and the lipiodol contrast did not pass into the calyces of the kidney.

A CT scan performed 48 hr after the lymphangiogram showed multiple dilated lymphatic channels up to 5 mm in diameter, extending into the mesentery,

porta hepatis and splenic hilum. The spleen was enlarged to 2–3 times the normal size. Lymph nodes were not enlarged (Fig. 3).

The patient was treated with penicillin, 500 mg four times daily, and metronidazole, 400 mg three times daily, for 2 weeks, with considerable improvement in the appearance of the urine which was rendered sterile and protein free. He was then given diethylcarbamazine in a dose of 2 mg/kg body weight for 3 weeks. On treatment, there was no evidence of an allergic reaction, no eosinophilia or fever. At review, he continues in his longest remission of 6 months free from urinary abnormality.

Discussion

The diagnosis of Bancroftian filariasis was made from the history of residence in an endemic area, exclusion of other causes of chyluria and the classical appearances of the lymphangiogram (Ko Ko, Aye and Aung, 1975). The absence of antibodies to filariae and of demonstrable parasites indicate only that the infection is inactive and is not inconsistent with the diagnosis. Chyluria is a late complication of this disease which usually develops after the worms

FIG. 2. (a) Ascending lymphangiogram showing grossly abnormal dilated, tortuous lymphatics in the region of the bladder; (b) dilated lymphatics in the region of the left kidney.

FIG. 3. Abdominal computerized axial tomography scan showing contrast within dilated lymphatics (arrowed) extending into the root of the mesentery.

have been eliminated by treatment or by the immune response (Koo and Van Langenberg, 1969).

Lymphangiography is valuable in the diagnosis of the disease and may have a therapeutic effect. Akisada and Tani (1968) reported improvement in 8 of 25 patients following lymphangiography. The whole body CT scanner was particularly useful in excluding malignant enlargement of the abdominal lymph nodes. In severe persistent chyluria, losses of fat and protein can lead to severe wasting of the body and weight loss. In such cases, treatment by surgical disconnection of the lymphatics from the renal tract is often successful (Koo and Van Langenberg, 1969; Waugh *et al.*, 1980). The CT whole body scanner may prove useful in determining the extent of the disease prior to surgery.

The patient's renal biopsy showed a minor mesangioproliferative glomerulonephritis with evidence of mesangial immune complex deposition, mild mesangial cell proliferation and focal podocyte fusion. After the exclusion of other potential causes, this is

thought to have arisen as a consequence of the antigenic stimulation of the filarial infection. Similar changes occurring in filariasis have been reported elsewhere (Date *et al.*, 1979a, 1979b; Waugh *et al.*, 1980). Waugh *et al.*, also reported IgG, IgM and C₃ deposition in the capillary wall and mesangium. Electron dense deposits representing immune complex deposition were also present. Similar findings have been produced experimentally in animal models of filariasis (Klei *et al.*, 1974). The exact mechanism of immune complex deposition remains speculative (Wilson and Dixon, 1981).

In addition, the patient we describe was unusual in having a chronic anaerobic urinary infection. We suggest that these organisms passed from the colon, through the abnormal lymphatics to the urinary tract. As there is retrograde flow in the lymphatics organisms may bypass the lymph nodes. Experimental occlusion of the renal lymphatics renders the kidney more prone to infection (Murphy *et al.*, 1959). This tendency to infection may have been increased by the depletion of lymphocytes in the chyluria and the neutropenia resulting from splenomegaly. The infection has not recurred since therapy with metronidazole. We suggest that anaerobes are specifically sought in patients with chyluria as they may not be discovered on routine aerobic culture.

Acknowledgments

We are indebted to Dr H. G. Smylie for his help in the bacteriological assessment of the patient.

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