HIV-associated nephropathy — an initial presentation in an HIV-positive patient

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Abstract **The lesions of HIV-associated nephropathy occur in patients with AIDS, AIDS-related complex and in individuals clinically asymptomatic for HIV infection. We report on a 35-year-old black South African woman who presented with nephrotic syndrome and renal failure. The renal biopsy appearance suggested HIV infection and this was subsequently verified. This finding emphasises the possibility that otherwise asymptomatic patients presenting with renal disease may be HIV-positive.**

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A 35-year-old woman, previously well, presented with a short history of fever, vomiting, diarrhoea and oedema.

On examination her blood pressure was normal (120/80 mmHg); oedema was confirmed, but no other special features were noted. Urine examination showed haematuria 4+, proteinuria 4+ with dipstick, white blood cells+++, red blood cells+ and some white cell and hyaline casts.

Special investigations showed a haemoglobin value of 8,3 g/dl, a white blood cell count of 10 000 × 10^6/ml, a urea level of 9,4 mmol/l and a creatinine level of 172 μmol/l. The urinary protein level was 4,5 g/24 hours. Tests for VDRL, hepatitis B surface antigen (HBsAg) and antistreptolysin O titre were all negative. Her renal function declined rapidly within 10 days, and her serum creatinine level rose to 819 μmol/l.

Given the rapidly progressing renal failure, a biopsy was performed. A clinical differential diagnosis at the time included crescentic nephritis, vasculitis, systemic lupus erythematosus (SLE) and interstitial nephritis.

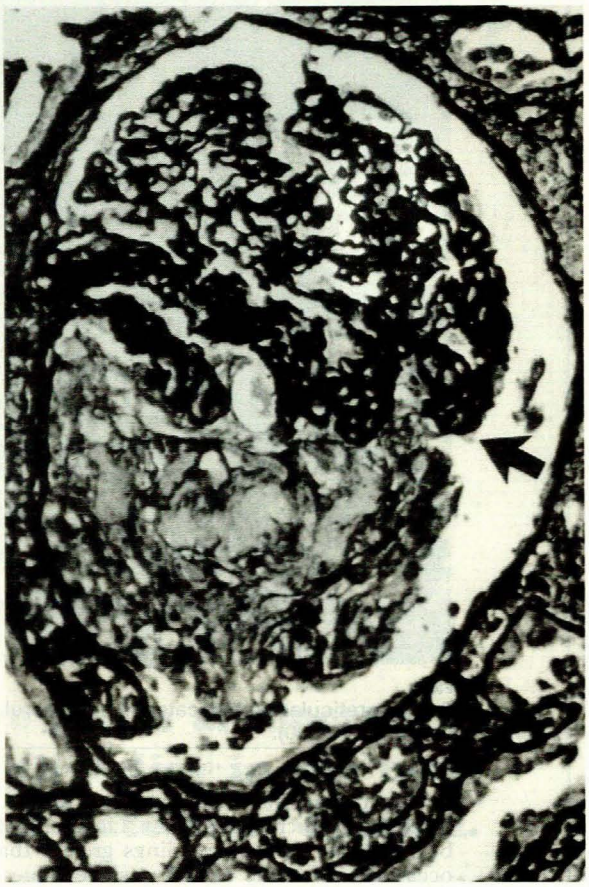

FIG. 1.
A glomerulus demonstrating an area of capillary collapse constituting segmental sclerosis (arrow). **Material of uncertain nature is present in Bowman's space (× 40 original magnification; silver stain).**

Pathological findings

The renal biopsy was performed according to our standard protocol[1] except that the initial fixation of the paraffin block tissue in glutaraldehyde was eliminated.

Light microscopy showed 18 glomeruli, 9 of which demonstrated areas of segmental sclerosis with 3 showing dilatation of Bowman's space. In another 3, cellular proliferation associated with eosinophilic material, possibly fibrin, was present in Bowman's space. In 1 area of sclerosis a foam cell was present. The non-sclerotic areas of glomeruli showed mesangial proliferation (Fig. 1).

The tubules showed areas of degeneration, necrosis and regeneration that were confirmed by the presence of mitoses. Some tubules were dilated and many contained red cells. Red cells were also present in the interstitium, where a moderate mixed inflammatory infiltrate was also seen. The infiltrate was prominent around a vein, but the blood vessels did not show any further specific abnormalities.

Immunofluorescence showed immunoglobulin (Ig)M strongly positive in the glomerular mesangial areas with IgA, IgG and C3 also positive, but less so. It was not clear whether fibrin was present.

Electron microscopy showed prominent tubuloreticular bodies in endothelial cells in the glomeruli and interstitium. A semiquantitative evaluation showed 18 tubuloreticular bodies in glomerular endothelial cytoplasm in a representative grid space of 100 μm² (Fig. 2). A small quantity of electron-dense material was seen in mesangial areas with isolated small subepithelial deposits. Areas of sclerosis and possible capillary collapse were seen.

The combination of prominent tubuloreticular bodies, glomerular and interstitial involvement as well as the absence of clinical and serological features of SLE and hepatitis B carrier state (two other known causes of tubuloreticular bodies in renal biopsies) indicated possible HIV nephropathy.[2,3]

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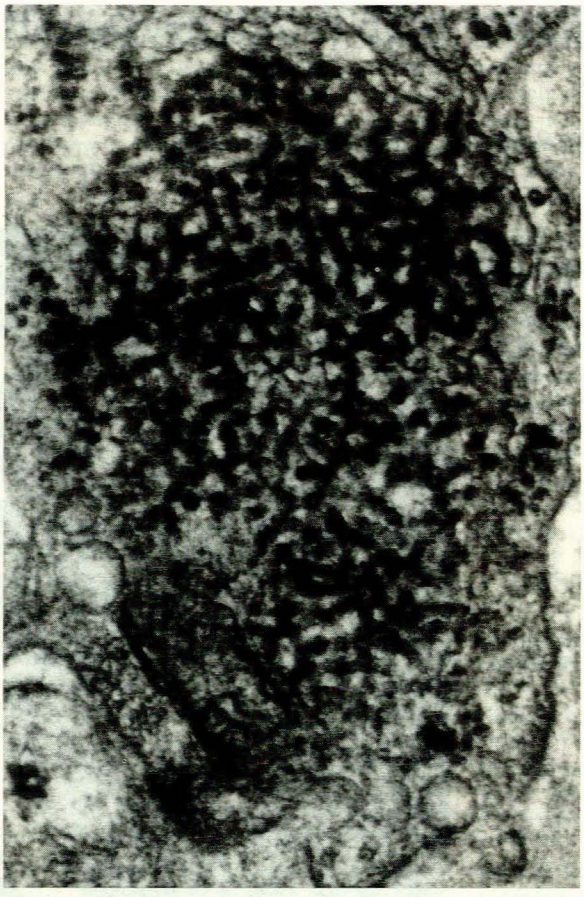

FIG. 2.
A tubuloreticular body located in a glomerular endothelial cell (× 70 000).

The patient was tested by means of the HIV MIXT Vironostika Microelisa system (Organon), and shown to be HIV-positive with readings greater than 3 on two occasions when the cut-off positive values were 0,059 and 0,062. The Western blot IgG assay for HIV-1 (Diagnostic Biotechnology) was positive, demonstrating the following bands: gp160, gp120, gp41, p68, p55, p52, p31, p24 and p18.

The patient was counselled before HIV testing as well as afterwards, but has unfortunately been lost to follow-up.

Discussion

Although a variety of renal lesions may occur in AIDS, an aggressive form of focal and segmental glomerulosclerosis with capillary collapse has emerged as HIV-associated nephropathy. It is characterised by a combination of lesions: focal and segmental sclerosis often at an early stage of evolution, tubular necrosis without an identifiable nephrotoxic or haemodynamic aetiology, interstitial oedema, large plasma protein-containing tubular casts in all segments of the nephron associated with marked tubular dilatation and widespread tubuloreticular structures in vascular endothelium.[2]

In contrast, neither the sclerosing glomerular changes nor the tubulo-interstitial abnormalities are present in HIV-infected patients with other forms of immune complex glomerulonephritis. Biopsies do, however, show the tubuloreticular bodies. The tubular and interstitial changes as well as the tubuloreticular bodies are absent in heroin-abuse nephropathy. At present, this is probably of more practical use in the differential diagnosis in the USA than in South Africa.

The lesions of HIV-associated nephropathy occur in patients with AIDS, AIDS-related complex as well as in individuals clinically asymptomatic for HIV infection.[2]

In Cohen and Nast's[2] series of 9 patients with HIV-associated nephropathy, 3 were asymptomatic and because of the biopsy findings, a test for the presence of HIV antibody was performed. They found that the morphological features on renal biopsy in asymptomatic patients were sufficiently specific to allow for an accurate diagnosis of HIV. This, together with our ongoing interest in tubuloreticular bodies and the fact that these are specifically looked for in all our renal biopsies, prompted the suggestion of HIV nephropathy in our patient.

A recent review of the clinical features of HIV-associated nephropathy indicated that it was initially described in clusters of predominantly black patients from New York and Miami, but that subsequent reports have come from many centres around the USA. Since then, other cases have been reported from, *inter alia*, Brazil, Canada, France, Great Britain, Haiti, Mexico, Spain and Trinidad. The incidence of HIV-associated nephropathy in Africa is still unknown.[4]

The American experience has shown that while the incidence of HIV disease in whites is three times that in blacks, there is a 10:1 ratio of blacks to whites in the prevalence of HIV-associated nephropathy, a finding still unexplained. It has been stated that if race *per se* were the determining factor, one would expect to find more cases of HIV-associated nephropathy in Africa.[4]

A Medline database search in February 1992 could not find any published cases of HIV-associated nephropathy from southern Africa, although at least two cases from other parts of Africa had been documented — a case of focal segmental glomerulosclerosis in a black man from Senegal[5] who was both HIV- and HBsAg-positive, and a glomerulonephritis in a boy from Zaire viewed as a variant of HIV-associated nephropathy.[6] Our patient may therefore be the first documented case of HIV-associated nephropathy in southern Africa, particularly in a patient without other HIV-infection manifestations. Renal involvement in HIV disease may well become of growing importance and concern in the future.

Addendum

A French study[7] suggests that there are three main patterns of HIV-associated renal disease. The one we have described, namely focal and segmental glomerulosclerosis, predominantly in black patients, an immune-complex-type glomerulonephritis and an interstitial nephritis. The latter two have been found in both black and white patients.

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