HIV-associated nephropathy with massive polyclonal hypergammaglobulinaemia

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Abstract

A particular form of renal disease in patients infected with the human immunodeficiency virus (HIV) is the HIV-associated nephropathy. It is important to consider this entity in the differential diagnosis of renal disease in these patients. This condition is usually characterized by a severe proteinuria rapid progression to end stage renal disease, with the most typical pathologic alteration being focal segmental glomerulosclerosis. We describe here a colored patient with HIV1 infection presenting nephrotic syndrome. The patient also had a massive form of polyclonal hypergammaglobulinaemia (IgG 71 g/l) and the renal biopsy showed a focal and segmental glomerulosclerosis. The possible etiopathogenesis of this condition is discusses.

Key words: HIV infection, HIV nephropathy, AIDS, hypergammaglobulinaemia, nephrotic syndrome.

Introduction

In recent years, renal parenchymal lesions predominantly involving the glomeruli have been described, under the usual designation of "HIV-associated nephropathy", in patients in various phases of HIV infection. The clinical expression is varied, and includes proteinuria, nephrotic syndrome and kidney failure, sometimes evolving rapidly.[1] Segmental glomerulosclerosis is the most commonly described anatomopathological substrate,[2,3] although it is now recognized that the histopathological spectrum is much more diverse, including "minimal lesions", crescentic or non-crescentic IgA nephropathy, and diffuse proliferative glomerulopathy.[4]

The clinical case is presented of a patient with HIV1 infection, who developed nephrotic symptoms associated with a solid form of IgG polyclonal hypergammaglobulinaemia. This latter aspect was recently described in the literature, and will be discussed in the context of various pathogenic hypotheses for nephropathy associated with HIV.

Clinical case

A male patient, aged 29 years, Black, originally from Zaire and living in Portugal since July 1992, was admitted for investigation of a febrile syndrome evolving for 2 months, with profuse night sweating along with anorexia and weight loss of 5 kg (± 5% of body weight). In the two days preceding admission, he reported right side thorax pain, which worsened on inhalation and was accompanied by non-productive cough and difficulty breathing, which grew progressively worse. There was nothing noteworthy in the personal history, and a diagnosis of mild arterial hypertension since the age of 20 years is noted, which was not medicated and bronchial asthma since childhood. On objective examination, it was observed that the patient had: fever (39ºC), blood pressure of 130-100 mm Hg and cervical (± 2 cm) and inguinal adenopathies (< 1 cm) on both sides, which were painless and mobile, with elastic consistency. The pulmonary observation was compatible with the existence of a pleural effusion on the right, and there was also an enlarged liver (4 cm below the right costal margin) and enlarged spleen of 4 cm. Of the laboratory exams, a Hb 8.4 g/dl, ESR 135 mm, kidney function with urea of 5.8 mmol/l (N:1,7-8,3), creatinine of 106 µmol/l (N:44-100) and sediment with proteinuria (+) and haematuria (+) were highlighted. AP Chest radiography confirmed the clinical suspicion of pleural effusion, as well as showing condensation of the upper right lung lobe. Thoracocentesis showed as serofibrinous liquid, with proteins of 8.7 g/L, 1410 cells/mm^3 (lymphocytes 81%) and deaminase adenosine (ADA) of 73. Direct,

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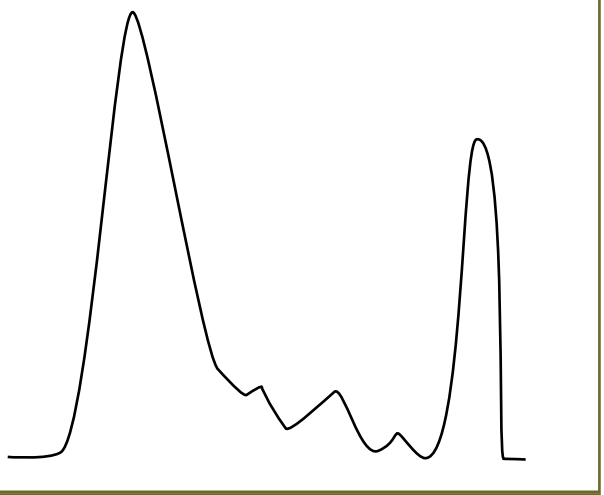
Received for publication on 22nd January 1997



Electrophoresis of proteins revealing polyclonal hypergammaglobulinaemia of 80 g/L.

FIG. 1

cultural bacterial and BK culture were negative. Lung biopsy showed tuberculosis with signs of activity.

Because the patient is Black, from an African country, antibody HIV1 and HIV2 antibody tests were carried out, with positivity for HIV1 by the ELISA method, confirmed by Western-Blot. The immunological evaluation at the time showed CD4+ lymphocytes of 479 cells/mm^3 (20%) and CD8+ lymphocytes of 1532 cells/mm^3 (64%). A good response was obtained with tuberculostatic therapy (isoniazid, rifampicin, pyrazinamide and ethambutol).

Around one year after the diagnoses of tuberculosis and seropositivity for HIV1, the patient experienced symptoms of intense, pulsing headaches in the frontal region. The blood pressure values, which until this time had remained the same without significant alterations, rose to values of systolic pressure of between 170-190 mm Hg and diastolic pressure of 120-130 mm Hg. Observation of the ocular fundi was normal, and in the heart auscultation there was an intensification of S2. The laboratory exams showed: Hb 10.4 g/dl, leukocytes of 7350 and platelets of 180000. ESR was 125 mm, urea 9.6 mmol/L, creatinine 178 µmol/L, uric acid 660 µmol/L (N: 200-420), with normal cholesterol and triglyceride values. The total proteins were 123g/l, with hypoalbuminaemia of 23 g/L and hypergammaglobulinaemia of 80 g/l (Fig. 1). The immunoglobulin count showed an IgG of 71.9 g/L (N: 7.23-16.85), an IgA of 1.85g/l (N: 0.69 – 3.82) and an IgM of 2.57 g/l (N: 0.63-2.77) and k light chains: 67.7 g/l (5.58-13.29), l 20.9 g/l (2.8-6.65), and k/l 3.24 g/l (1.47-2.9). Faced with the clinical suspicion of nephropathy associated with HIV, liver biopsy was carried out, which showed two glomeruli with focal sclerosis and the remainder with segmental sclerosis, as well as tubulointerstitial nephritis. Immunohistochemical studies showed IgG deposits. The patient received therapy with nifedipine (30 mg/day) and isoniazid (300 mg/day) and zidovudine (500 mg/day) were maintained. In the two subsequent months, the values for blood pressure remained controlled, and renal function did not worsen. In this period, the patient had returned to his country of origin.

Discussion

The present patient with a diagnosis of HIV infection and pleural-pulmonary tuberculosis, which was treated, and good response to therapy, appeared one year after the establishment of these diagnoses with symptoms of arterial hypertension, alteration in renal function and proteinuria of nephrotic levels. Liver biopsy showed the existence of segmental glomerulosclerosis. The term "HIV-associated Nephropathy" has been used to describe cases of glomerulopathy sometimes accompanied by tubulointerstitial lesions, the glomerulosclerosis being the most common type of anatomopathological lesion reported in these cases[1-3] despite the more recent description of a more diversified anatomopathological spectrum,[4,5] including lesions of the "minimal lesion" type, nephropathy IgA (crescentic or non-crescentic) and diffuse proliferative glomerulopathy.[4]

The etiopathogenesis of these lesions, which has been predominantly described among Black people,[6] has been much discussed[7-10] and the hypothesis has been proposed that there are factors directly related to the human immunodeficiency virus, suggested by the existence of viral DNA in the renal biopsies of these patients,[11] as well as the response to antiviral therapy, with regression of the nephrotic syndrome and improvement in renal function.[12] The possibility of involvement of the circulating immune complexes has also been proposed[13-14] and on this subject, it is interesting to highlight the existence of a solid IgG hypergammaglobulinaemia in our patient. Although the exceptionally high levels of serum gammaglobulin do not necessarily imply lesions by type III hypersen-

sitivity, it is possible to speculate on the possibility that these levels are associated with major immunoregulatory disturbances, with a possible role in the pathogenesis of the glomerulopathy.[15] The pathogenic role of immunoregulatory disturbances was recently emphasized by the recent observation that HIV infection of the renal cells was associated with increased synthesis of TGF-B, a cytokine with a confirmed role in various fibrotic lesion and in experimental models of glomerulosclerosis.[16] On the other hand, recent research suggests that apoptosis of the renal tubular cells may constitute a mechanism involved in the pathogenesis of the lesions.[17] Another important aspect is the higher prevalence of these renal complications in patients in whom the risk factor for HIV infection is drug-dependence, and on the other hand, in Black patients, as in the case of the patient described here. It is in fact possible that particular immunogenetic aspects are responsible for a greater vulnerability of renal lesions associated with HIV infection.[18,19]

Many patients with HIV infection develop, over the course of the disease, alterations in renal function with highly variable severity, with diverse etiological factors, such as dehydration, hypotension, adverse drug reactions, and post-renal lesions by tumoral obstruction or opportunistic infections. It is important, in this context, to identify this particular form of renal involvement, nephropathy associated with HIV, due to the severity of this condition, which often develops into nephrotic syndrome and terminal kidney failure. Although the treatment needs further investigation, some patients have responded to antiviral therapy[12] and others to immunomodulatory therapy with corticoids and cyclosporin, although in the majority of cases, recurrences are observed after suspension of the drug. This aspect has led to an attitude of reservation when prescribing these therapies in seropositive patients, due to the potential risks of pharmacological immunosuppression.[20] It is important to stress that nephropathy associated with HIV can occur in early phases of immunodeficiency with the number of CD4+ maintained or in advanced phases,[4] and there are reports in the literature of isolated cases of response to corticoid therapy in any stage of the immunodeficiency.[21]

In conclusion, this case of nephrotic syndrome by focal glomerulosclerosis associated with HIV infection clearly illustrates the possibility of renal complications of this infection, particularly among Black patients, and the presence is highlighted, of a solid IgG polyclonal hypergammaglobulinaemia, an aspect that was only recently described, and that suggests the association of immunoregulatory disturbances. ■

Acknowledgements

We are grateful to Prof. Carlos Silva Duarte, the cooperation in the renal pathological anatomy study as well as Dr. Antonio Gomes da Costa for the discussion of some nephrology aspects.

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