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Complete remission of loiasis-associated nephrotic syndrome with collapsing glomerulopathy after diethilcarbamazine treatment

Summary

Case report: A 42-year-old male from Equatorial Guinea with nephrotic syndrome (NS) and renal dysfunction. Loa loa microfilariae were detected on a peripheral blood smear and renal biopsy showed collapsing glomerulopathy. In absence of other causes of NS, the treatment with diethylcarbamazine brought a complete remission
Key words: Loa loa. Nephrotic syndrome. Collapsing glomerulopathy. Diethilcarbamazine.

Resumen

Caso Clínico: Hombre de 42 años de Guinea Ecuatorial con un síndrome nefrótico e insuficiencia renal. Se encontraron microfilarias de Loa loa en sangre periférica y la biopsia renal mostró una glomerulonefritis colapsante. No se objetivó otra causa de síndrome nefrótico y el tratamiento con el filaricida dietilcarbamacina consiguió una remisión completa de su patología.
Palabras clave: Loa loa. Síndrome nefrótico. Glomerulonefritis colapsante. Dietilcarbamacina.

Introduction

In recent years, an increasing number of patients with imported tropical diseases are treated in Europe. The increase is attributed to higher immigration rates and more frequent tourist travels. These relatively infrequent diseases constitute a diagnostic challenge and should be considered in the appropriate circumstances. Active infection with the filarial nematode Loa loa is reported to be present in up to 20% of the population in West and Central Africa. In particular, inhabitants of South-Eastern Nigeria, Central Cameroon, South Central African Republic, Continental Equatorial Guinea, Gabon, and the North and the West of the Democratic Republic of Congo[1] are affected. Differences in clinical presentation between endemic and non-endemic populations are thought to be related to differences in the host immune response[2]. Nephropathy is a known complication of loiasis, which may lead to hematuria and proteinuria[3].

Case report

A recently immigrated 42-year-old male from Equatorial Guinea was admitted to our hospital with anasarca and hypertension. He reported to have had edema for the last 4 months. Urinalysis detected a proteinuria of 10,3 g/24h and serum biochemistry showed albumin 0,7 g/l, cholesterol 609 mg/dl, creatinine 2.6 mg/dl, and urea 188 mg/dl. Creatinine clearance was 25 ml/min. Hemoglobin was 7,4 mg/dl and eosinophil count was 1.700 per mm^3. A peripheral blood smear showed microfilariae Loa loa with 220 microfilariae/ml (Figure 1) and Mansonella perstans. Thick smear and antigens for Plasmodium were negative. Toxoplasma, Brucella, Epstein-Barr virus, Cytomegalovirus, syphilis, hepatitis C virus and Human Immunodeficiency Virus (HIV) serologies were negative and serology for hepatitis B indicated cured infection. Investigation of intestinal parasites was negative. Serum and urine proteinograms showed a minimal Immunoglobulin G condensation in the gamma region. Antinuclear antibodies and rheumatoid factor were negative.

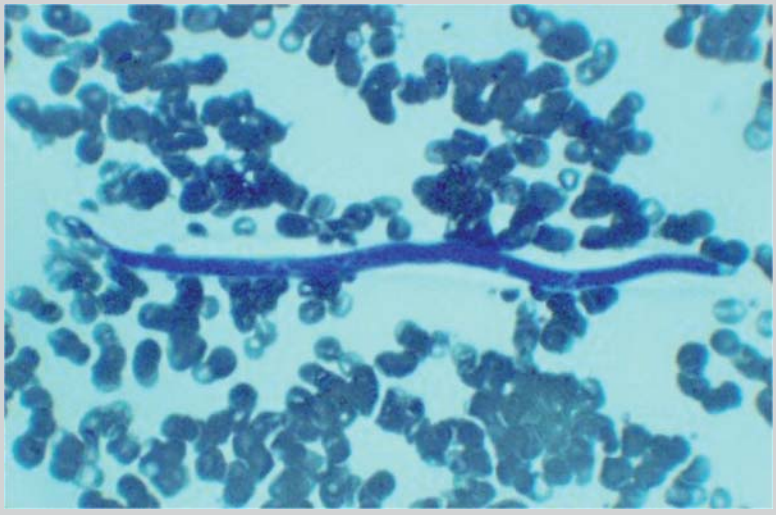

Figure 1. Microfilaria of *Loa loa* in peripheral blood smear

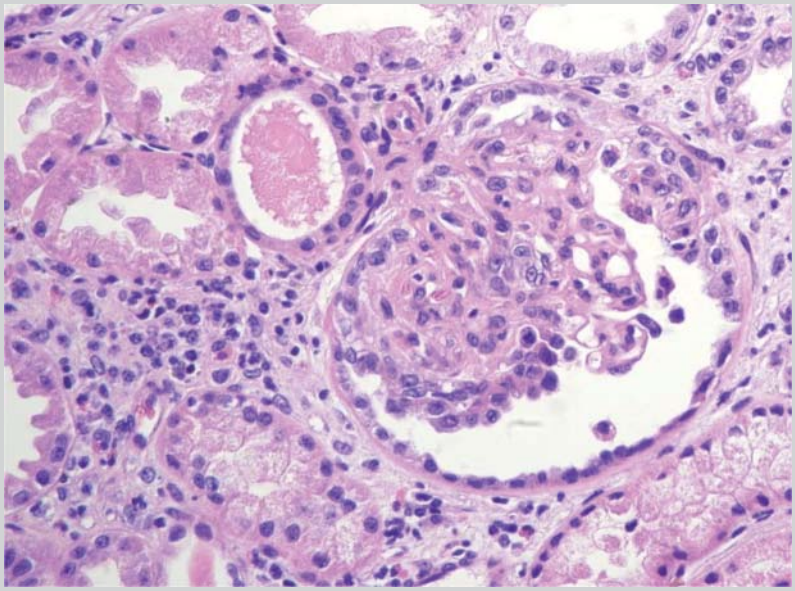

Figure 2. Glomerulus with segmental collapse of the capillary tuft. HE 400x

The patient received a continuous intravenous infusion of furosemide, oral spironolactone and chlorothiazide for 15 days and a negative fluid balance with a body weight reduction of 20 Kg was performed. Loiasis was treated with diethylcarbamazine (DEC), at an initial daily dose of 50 mg, which was progressively increased to 200 mg three times daily on day four. Prednisolone, 1 mg/Kg/day, was given during the first three days of anti-filarial therapy to prevent potential allergic reactions caused by antigen release from dying microfilariae. DEC therapy was maintained for 21 days. No additional steroids or other immunosuppressive drugs were given. Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor II antagonists (ARA II) were not employed to control blood pressure or proteinuria. Packed blood cell transfusions and nutritional support were given as needed.

On day 10 after admission a percutaneous renal biopsy was performed. Light microscopic showed segmentary hialinosis and collapse of the capillary tufts in 4 of 18 glomeruli (Figure 2). The remaining glomeruli were normal. The interstitium was widened with patch scars associated with inflammatory cell infiltrate comprising lymphocytes, plasma cells and conspicuous eosinophils (Figure 3) with abscess formation. In scarred areas the tubuli were atrophic and occupied by hyaline or granular casts. Foci of tubular necrosis and regeneration were also present. The vessels were preserved and only some arterioles

revealed moderate wall hyperplasia. No filarias were identified. Electron microscopic examination of the glomeruli showed segmentary effacement of the foot process of the podocytes, swollen endothelial cells, moderate widening of the mesangial matrix and occasional nonspecific granular deposits. Immunofluorescence study was negative for immunoglobulin and complement deposits.

Follow-up at two months showed that edema had completely resolved, blood pressure was normal, serum creatinine was 0.82 mg/dl, with a calculated creatinine clearance of 72.24 ml/min and urinary protein was 2 g/24h. Anemia had resolved and no microfilariae were detected in a blood smear. At a two-year follow-up the renal function remained normal (calculated creatinine clearance 94 ml/min), urine protein excretion was 242 mg/24h, serum cholesterol was 272 mg/dl and serum albumin 4.7 g/l.

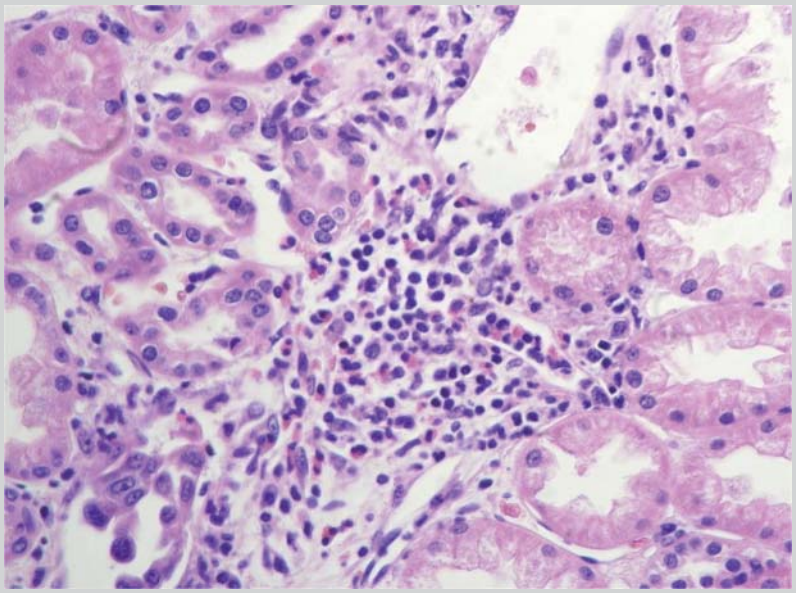

Figure 3. Focal interstitial inflammation with numerous eosinophilic leukocytes. HE 400x

Discussion

There are many known etiologic agents for nephropathy an NS in the tropics[4,5]. The co-existence of more than one in the same patient makes it difficult to incriminate any one in the etiology of the disease. Furthermore, it is likely that the number of antigens which can produce glomerulopathy is extremely large, but the number of identifiable antigens is reduced[3].

Several types of glomerulonephritis (GN) due to filariae have been observed including type I membranoproliferative GN, minimal-change, membranous GN, mesangial-proliferative GN[6] and focal segmental glomerulosclerosis (FSGS)[7]. This wide spectrum of renal histologic changes may be influenced by the other possible coexisting conditions, particularly filariae specie, the duration of the disease in some cases and the various treatments received before the biopsy[4]. The exact mechanism of renal involvement in loiasis is unclear. Immune complexes and microfilariae are frequently found in the renal biopsy, and further studies consider that the passage of microfilariae through the glomerular capillaries and, especially, the deposition of immune complexes may be the main mechanisms[2]. To date there is no description of nephropathy secondary to Mansonella perstans infection.

The renal biopsy of our patient was described as a collapsing glomerulopathy. This entity is considered similar to FSGS, with black racial predominance and a high incidence of NS[8]. Usually there is rapidly progressive renal failure with poor outcome. The cause of this disorder is unknown, although it has been associated with HIV and parvovirus B19 infection, lymphoproliferative disorders and autoimmune diseases. The optimal treatment is unknown, but it may include steroids, prolonged immunosupressive therapies in addition to ACEI and/or ARA II, lipid lowering agents, apart from the specific treatment for the causal disease[8]. At this moment only one case of collapsing glomerulopathy secondary to loiasis has been reported but with fatal outcome[7].

Other causes of NS were ruled out in this patient, including other infectious agents and immunologic diseases[9]. No treatment had previously been given in Equatorial Guinea. During his hospital stay no immunosupressive agents were given, except for three days of prednisolone, neither ACEI nor ARA II were required at any time. Specific therapy with the anti-filarial agent DEC was associated with a positive response and a complete remission of the NS and loiasis eradication[10].

Several cases of Loa *loa* infection-associated NS with favourable response to treatment[6] have been published. However, we are only aware of one other report describing collapsing glomerulopathy[7] in a patient who had a fatal course after receiving antifilarial and steroids therapy. The authors considered that this patient may have been exposed to a large number of immunogenic environmental agents influencing

the clinical course. Also the renal biopsy findings encountered were more severe and extensive than in our case.

In conclusion, we report on the first case of collapsing glomerulopathy associated with loiasis responding favourably to anti-filarial therapy. Our patient evolved towards complete and sustained remission at two-year follow-up.

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Conflicts of interest: none declared.

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