Renal involvement in a patient with visceral leishmaniasis

Sir,

Human visceral leishmaniasis, a parasitic infection caused by the protozoan Leishmania and responsible for approximately 5000 deaths annually, is more frequently reported in immunocompromised individuals, such as HIV patients [1] and renal transplant recipients [2], and can rarely involve the kidneys, in the form of haematuria, proteinuria or renal function impairment. Herein, we report the case of a patient of good immunological status suffering from visceral leishmaniasis with severe, histologically confirmed renal involvement, where successful treatment of the disease resulted in improvement of renal function.

A 65-year-old Caucasian man, with an 8-year-long history of type 2 diabetes mellitus (under insulin treatment), was referred to our department because of pancytopenia (WBC 2300/mm³, haematocrit 25.5%, and platelets 80 000/mm³) and renal failure (urea 114 mg/dl, serum creatinine 5 mg/dl, 2 g protein/24 h urine collection). Clinically, hepatosplenomegaly was noted. Extensive viral serology was only positive for hepatitis B surface antigen, and immunological investigation was unremarkable. Ultrasonography revealed that the kidneys were normal in appearance and length (10.5 cm). Bone marrow aspiration and biopsy indicated the presence of phagocytes and monocyte fragments filled with leishmaniasis, as well as PAS-stain positive granules in the protoplasm of histiocytes. Serum antibodies against Leishmania infantum were found positive, confirming the diagnosis of chronic visceral leishmaniasis.

The subsequent renal biopsy revealed chronic tubulointerstitial nephritis, arteriosclerosis, mild diabetic glomerulosclerosis and absence of the parasite. Immunohistochemical stains showed sparse IgM and C3d mesangial and IgG basement membrane depositions. The patient received treatment with liposomal amphotericin B (AmBisome®) and corticoids, gradually resulting in a significant improvement of renal function (creatinine: 2.5 mg/dl, urea: 110 mg/dl, proteinuria: 300 mg/24 h) within the first 10 days of therapy, and a later decrease in titre of the antibodies against Leishmania.

There have been reports of visceral leishmaniasis with involvement of almost all systems, however renal involvement is scarce and appears as glomerulonephritis or interstitial nephritis (or both) [3,4]. There are also significant indications, mainly derived from observations in animals [5,6], that involvement of both glomeruli and tubules results from immune complex deposition, the antigens of which belong to the parasites [6]. In addition to that, we attributed our patient’s interstitial nephritis to the systemic parasitic disease, because renal function improved while treating the infection and no other possible causes (e.g. drugs) could be found in the patient’s history. However, based on present serum immunology and immunohistochemical findings, we cannot be certain of the immune-mediated nature of the renal involvement, although it seems likely.

In conclusion, visceral leishmaniasis must be in the mind of the clinician treating a patient with constitutional symptoms, pancytopenia and renal involvement. Confirmation of a likely immune pathogenetic mechanism would facilitate treatment, but is still pending.

Conflict of interest statement. None declared.


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Sir,
Fungal peritonitis is a rare but serious complication of peritoneal dialysis (PD) and is associated with significant mortality. Observational studies suggest that it accounts for approximately 2–7% of PD related peritonitis, but it can be difficult to clear, can result in catheter loss and can frequently lead to conversion to haemodialysis [1–3].

Case. A 65 year-old male patient on automated peritoneal dialysis (APD) for almost two years was admitted with a 24h history of dysuria and fever. He had a history of recurrent urinary tract infections during the last 3 months. He had received multiple antibiotic regimens for different pathogens and was carrying an indwelling urinary catheter. He had no prior episodes of PD-related peritonitis.

On admission, his temperature was 38.5°C, pulse 100 bpm and blood pressure 120/70 mmHg. His abdomen was slightly distended and he had pain on the pubic area with no rebound or guarding and normal bowel sounds. The PD catheter exit site did not show any evidence of infection. Laboratory investigation was remarkable for leucocytosis. Urine examination revealed severe pyuria. A urine culture was taken and he was empirically started on i.v. ciprofloxacin, as pyelonephritis was suspected. However, during the first 24h after admission, he started complaining for abdominal pain and distension, a cloudy peritoneal fluid was noticed and the diagnosis of peritonitis was made. He was transferred to continuous ambulatory peritoneal dialysis and was put on intraperitoneal administration of cefuroxime and tobramycin, according to our PD-related peritonitis treatment protocol.

However, on the third hospital day, fungi were isolated from his urine, blood and peritoneal fluid cultures. The previous regimen was stopped and he was started on fluconazole i.p. and i.v. and liposomal amphotericin B i.v. The patient remained febrile, complained of severe abdominal pain and became hypotensive. As the patient was becoming septic, the PD catheter was surgically removed and a right internal jugular venous catheter for haemodialysis was placed. The isolated pathogen was Candida albicans resistant to all azoles and sensitive only to amphotericin B. The patient remained febrile (39°C) and hypotensive for the next six days despite treatment with amphotericin B, without any signs of improvement. Caspofungin (Cancidas®) 50 mg daily was added to his regimen and he became afebrile after three days of caspofungin plus amphotericin B therapy. The combined therapy was administered for a total of fifteen days without any adverse effects.

Comments. Fungal peritonitis is uncommon, but by no means rare (2–7%). It is associated with significant mortality (20–30%). Prior use of antibiotics, the immunosuppressed state, diabetes mellitus and malnutrition (low serum albumin levels) are risk factors for fungal peritonitis [2–4].

Our patient had received multiple antibiotic regimens in the past three months for recurrent urinary tract infections without any antifungal prophylaxis and he was carrying an indwelling urinary catheter. He also had evidence of candidaemia and systemic candidiasis, as Candida albicans was isolated from the urine specimens, blood cultures and peritoneal fluid. A possible explanation for the peritonitis episode might be the urinary tract colonization with fungus, as the patient had received many antibiotics without antifungal prophylaxis, resulting in candidaemia and peritonitis through the haematogenous route. Early removal of the PD catheter might have contributed to our patient’s favourable outcome in a way, but the patient did not improve and remained febrile, even after six days of amphotericin B administration. The addition of caspofungin to the initial regimen seems to have contributed to the favourable outcome, as the patient became afebrile only after three days of combination therapy.

There is no established therapy for fungal peritonitis and most centres use combination therapies with variable success. Most authorities suggest early PD catheter removal, because the catheter is usually contaminated with fungi [4]. Echinocandins is a new class of antifungal agents and caspofungin was the first of the class been licensed. There is only one report in the literature regarding caspofungin use in peritoneal dialysis, but no report of combination of caspofungin with amphotericin B. Madariaga et al. have described a patient intolerant to amphotericin B who presented peritonitis due to Trichosporon inkin and had a favourable outcome by caspofungin administration [5].

In conclusion, we report a case of fungal peritonitis due to Candida albicans resistant to azoles, with signs of systemic candidiasis (candidaemia) that responded to a combination therapy with caspofungin and amphotericin B without adverse effects. We do not suggest the routine empirical use of caspofungin for fungal peritonitis in PD as the available data are very limited, but our favourable outcome might indicate the addition of a new antifungal agent in our armamentarium against severe and life-threatening fungal infections in patients undergoing peritoneal dialysis.

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1 Department of Internal Medicine-Nephrology and Infectious Diseases University Hospital of Patras Patras-Greece
Email: johnvl@med.upatras.gr