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CASE REPORT

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Renal dysfunction in Leishmaniasis and Chagas disease coinfection: a case report

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ABSTRACT

Visceral leishmaniasis (VL) is an endemic parasitic disease frequently found in Northeast Brazil and may cause acute kidney injury (AKI) and glomerulonephritis. After appropriate treatment, renal function recovery may occur. We describe the rare case of a patient with VL, who developed severe AKI requiring dialysis and was subsequently diagnosed with Chagas disease coinfection. After specific treatment for VL, there was partial recovery of the renal function, followed by the onset of Chagas disease cardiomyopathy.

KEYWORDS: Leishmaniasis. Acute kidney injury. Glomerulonephritis. Chagas disease. Parasitic diseases. Cardiomyopathy.

INTRODUCTION

Visceral leishmaniasis (VL), also known as Kala-Azar, is a zoonosis caused by a flagellate protozoan called *Leishmania donovani*, a parasite that lives and multiplies in monocytes[1]. Kidney involvement in VL may result in acute kidney injury (AKI) and glomerulonephritis. VL-associated nephropathy is still not completely understood[2], but it may be caused by immune-complex deposition in renal tissues, activation of T-cells and of adhesion molecules[3]. Complete recovery may occur after treatment[4,5].

We describe the case of a patient with VL, who developed severe AKI requiring dialysis and was subsequently diagnosed with Chagas disease coinfection. After specific treatment for VL and glomerulonephritis, there was partial recovery of the renal function, followed by the onset of Chagas disease cardiomyopathy 5 months later.

CASE REPORT

A 48-year-old male farmer, born in Jaguaribe and living in Pereiro, in the State of Ceara, Northeast Brazil, had hematuria, enlarged abdomen and skin pallor. After 5 months, he evolved with disorientation and dyspnea on exertion and was taken to the hospital. Physical examination showed skin and mucous membrane pallor, hepatosplenomegaly and lower-limb edema.

The patient had a history of cigarettes and alcohol consumption. The first laboratory tests showed creatinine 4.3 mg/dL, urea 246 mg/dL (Table 1), hypergammaglobulinemia in plasma protein electrophoresis, in urinalysis 369 red cells per high-power field and proteinuria (1+/4+). Due to evident signs of AKI,

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Table 1 - Laboratory tests performed during first hospitalization

		Start of Dialysis		Start of Amphotericin					End of Dialysis	Discharge
Hosp Stays	D1	D2	D3	D5	D6	D8	D16	D18	D20	D39
HB (g/dL)	6.6	7.3	6.2	8	7.8	7.4	6.6	8.3	8.2	9.9
Leukocytes (mm³)	5,400	5,803	3,625	4,878	5,659	5,106	3143	3662	5481	5812
Platelets (mm³)	135,000	154,300	139,700	136,100	133,300	104,900	127,800	101,200	98,690	
Creatinine (mg/dL)	4.3	4.2	3.9	3.1	3	2.8	2.5	2.2	2.2	2.2
Urea (mg/dL)	246		183	129	131	103	107	116	86	68
PT		1.4	1.45	1.39	1.38	1.32	1.38	1.37	1.39	1.37
APTT		1.83	1.61	1.63	1.7	1.48	1.58	1.67	2.89	1.49
Prot 24 h (mg/day)						2.35 g/24 h				51.9 mg/24 h

classified as KDIGO 3, hemodialysis was started. On the same day, rK39 antigen test was positiveand a bone marrow aspirate evidenced amastigote-like forms of *Leishmania donovani*, confirming VL diagnosis. Leishmania antigen dosage was not performed. Serologies for hepatitis virus B, C and HIV were negative. Complement test levels were C3-55 mg/dL and C4- 15 mg/dL. VDRL, p-ANCA, c-ANCA, FAN and anti-ds-DNA tests showed negative results. Renal biopsy showed rapidly progressive, post-infectious glomerulonephritis with mesangial hypercellularity and endocapillary proliferation (Figure 1). Immunofluorescence was positive for IgM, C3 and C1q. The Polymerase Chain Reaction (PCR) assay for *Leishmania* on the renal biopsy was not performed. Treatment consisted of liposomal amphotericin B 200 mg a day for 7 days and 1 g of methylprednisolone a day for three days. Renal function improved and dialysis was discontinued (Table 1). The transthoracic echocardiography showed ejection fraction (EF) of 51%, significant tricuspid regurgitation and moderate mitral regurgitation, mild pericardial effusion in the left ventricle (LV) and significant pericardial effusion in the left atrium, with eccentric LV hypertrophy. The patient was discharged with the following prescriptions: enalapril, amlodipine and prednisone 60 mg/day. Five months later, the man sought medical care at the emergency room due to symptoms of cardiac decompensation, wheezing, irregular heart rhythm with a fourth heart sound. The electrocardiography showed atrial fibrillation and the transthoracic echocardiography showed EF of 25%, moderate mitral regurgitation, atrial fibrillation (AF) and dilated cardiomyopathy showing systolic function worsening. He also had positive IgG antibodies for Chagas disease by two methods (ELISA – titer > 1.8 and IFA – titer > 1:160), but there was no need for dialysis during this second hospitalization and the heart condition was defined as a complication of chronic Chagas disease. After compensating for his medical condition, the patient was discharged, is currently receiving outpatient care, and is no longer taking prednisone (the patient has already weaned it). He is currently receiving enalapril, 5 mg a day, carvedilol 12.5 mg twice a day, digoxin 0.25 mg a day, spironolactone 25 mg, furosemide 40 mg/day and warfarin 7.5 mg/day.

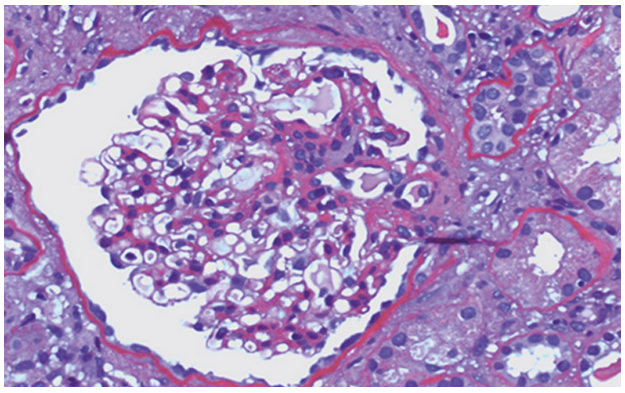

Figure 1 - Mesangial cell proliferation (PAS, 400 x).

Clinical and laboratory findings, after the patient was discharged from the hospital, confirmed the patient's renal function improvement throughout the months (Table 2).

DISCUSSION

We have described an unusual case of kidney disease associated with VL: rapidly progressive glomerulonephritis and AKI. Most commonly, kidney disease associated with VL shows a mild presentation, manifesting as mild to moderate creatinine increase and proteinuria. Mesangial and membranoproliferative glomerulonephritis are the most frequent types of glomerular diseases caused by VL[5,6].

VL is an endemic disease in our region, caused by a flagellate protozoan called *Leishmania donovani*. The parasite lives and multiplies in monocytes. Most patients do not show any symptoms and may heal spontaneously[1].

Table 2 - Exams performed during outpatient care

Post-treatment after discharge	3mo	6mo - Second hospitalization	7mo	8mo	3y	1 y and 3 mo
HB (g/dL)	13.9	13	14.2	12.6	14	12.4
Leukocytes (mm^3)	10,190	8,212	11,150	9,900	6,870	5,940
Platelets (mm^3)	167,100	110,900	161,900	152,000	162,000	148,000
Creatinine (mg/dL)	1.5	1.8	1.3	1.33	1.6	1.52
Urea (mg/dL)	70	155	94	59	60	66
C3	117 (80-180)					
C4	26.8 (10-40)					
Albumin(g/dL)				4.0	3.7	3.8
Proteinuria 24h	2.4g v=1.6 L				945 mg/24 h	702 mg/24 h
Urine	+++ protein 20 Red blood cells			++ protein 8 Red blood cells	+ protein 0 Red blood cells	

Usual symptoms are fever, chills, sweating, asthenia, skin and mucous membranes pallor, generalized microadenopathy, weight loss and hepatosplenomegaly[1,3,5]. Laboratory tests show pancytopenia, hyperglobulinemia and hypoalbuminemia[4]. Tubular and glomerular renal functions might be affected and the patient may develop proteinuria and hematuria[6,7]. The urinary alterations found in a previous report describing 11 patients were proteinuria in 10 (90.9%), leukocyturia in 6 (54.5%) and hematuria in 7 patients (63.6%)[6].

AKI may be attributed to dehydration, hypotension (pre-renal AKI) and immune-mediated glomerular disease (intrinsic renal AKI)[8]. Kidney biopsies might show glomerular mesangial cell proliferation or focal endocapillary proliferation. IgG, IgM and C3 can be observed in proliferation areas through immunofluorescence.[5] Renal function can recover after specific treatment[4,5].

Although the patient improved the renal function after receiving specific treatment for kala-azar associated with pulse therapy, it is possible that he was already infected with *Trypanosoma cruzi* in the first hospitalization (period in which the diagnosis of VL was made and hemodialysis was required). According to Martinez-Perez *et al*.[9] reactivation of preexisting chronic Chagas disease can occur due to immunosuppressive drugs. This manuscript reported worsening of renal and cardiac function, but the conservative treatment of prior renal disease was maintained. The diagnosis of Chagas disease was made through serological tests in the second hospitalization, and was defined as chronic Chagas cardiomyopathy due to the presence of severe heart failure associated with atrial fibrillation in the presence of specific IgG antibodies[10]. Parasitological tests are not routinely performed in the chronic phase of Chagas disease due to low parasitemia thus, serological tests that detect antibodies against the etiological agent are used[11]. Antitrypanosomal therapy is not warranted for patients with advanced Chagas heart disease, as the available drugs are not effective for eradication of preexisting pathological injuries. In these patients, management is focused on supportive care for heart failure, arrhythmia and thromboembolism[12]. There is evidence of functional and structural renal alterations after *T. cruzi* infection, whether associated with decreased renal blood flow or damage to the proximal tubule cells, in addition to significant renal interstitial inflammatory infiltrate[11]. Oliveira *et al*.[13], in 2009, demonstrated the presence of severe renal lesions characterized by early glomerular deposition of IgM, with intense inflammatory renal response promoting the formation of immune complexes resulting in glomerulopathy with impaired renal function. There may be decreased renal function, especially when infection with high parasite load is present. The occurrence of glomerulonephritis in the chronic phase of the disease has been reported in infections by *T. cruzi*, as well as other trypanosome species, such as the African type.

Despite the occurrence of glomerulopathy associated with Chagas disease, the cardiac component was more relevant because, after heart function compensation, plasma creatinine and urea levels returned to the levels seen before the worsening of renal function during the second hospitalization.

CONCLUSION

This case shows the importance of including post-infectious glomerulopathies in the differential diagnosis

of rapidly progressive glomerulonephritis, since recovery associated with renal function improvement may make renal replacement therapy unnecessary, with consequent reduction of morbidity and hospital stay. The side effects of immunosuppressive therapy should be better evaluated during the treatment of glomerulopathies in patients at high risk of infectious endemic diseases. Endemic diseases in our country, such as visceral leishmaniasis and Chagas disease should be investigated in cases of AKI and glomerulonephritis.

AUTHORS' CONTRIBUTIONS

Cid Carlos Soares Alcântara: contributed to the article design and participated in all stages until the final writing of the article; Laís Regina Lacerda Santana: collection, organization of clinical data and contributed to the writing of the article; Priscila Dourado Evangelista: collection, organization of clinical data and contributed to the writing of the article; André Costa Teixeira: interpretation and histopathological analysis of renal biopsies; Geraldo Bezerra da Silva Junior: contributed to the guidance and writing of the manuscript; Elizabeth De Francesco Daher: contributed to the guidance and writing of the manuscript.

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