Acute interstitial nephritis, a rare complication of Giardiasis

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Abstract

Acute interstitial nephritis is a relevant cause of acute renal failure. Drugs are the predominant cause, followed by infections and idiopathic lesions. Acute interstitial nephritis as a form of hypersensitivity reaction is an uncommon manifestation in the setting of human parasitic infections. We present a case of acute interstitial nephritis in association with *Giardia* infection in a 54-year-old woman who developed an impairment of renal function after a prolonged period of slight fever and diarrhea. After an attempt to recover renal impairment by vigorous rehydratation, because of the unclear origin of the persisting renal failure, a percutaneous renal biopsy was performed and a diagnosis of severe acute interstitial nephritis was made. Steroid therapy was started and after six weeks, renal function had completely recovered. In cases of unexplained renal failure in patients affected by parasitic infections, interstitial nephritis should be considered and it is our opinion that a renal biopsy should be always performed.

Introduction

Acute interstitial nephritis is the cause of acute renal failure in about 15-20% of cases. Many factors lead to interstitial nephritis, which can be categorized into different forms: drug related hypersensitivity reaction, infection, immune-mediated diseases, hereditary, metabolic and idiopathic. Within these broad categories, nowadays drugs are the predominant cause of interstitial nephritis, followed by infections and idiopathic lesions.[1] Acute pyelonephritis caused by renal invasion of virulent microorganisms has to be distinguished from acute interstitial nephritis, which can occasionally be seen in the setting of systemic bacterial and viral infection as a hypersensitivity reaction,[2,3] whereas it is uncommon in human parasitic infections. Giardiasis is an infection of the small intestine caused by *Giardia lamblia* (also known as *G. intestinalis*), a flagellate protozoan. Giardiasis is the most commonly reported pathogenic protozoan disease in the USA and in Europe. Travelers are the largest risk group for Giardiasis infection, especially those who travel to the developing world. Giardiasis is spread via the fecal-oral route and its prevalence rates range from 2-7% in developed countries and 20-30% in most developing countries. The Center for Disease Control estimates there are up to 2.5 million cases of giardiasis annually.[4] The most common symptoms of *Giardia* infection include diarrhea for a duration of more than ten days, abdominal pain, flatulence, bloating, vomiting, and weight loss, but approximately 50% of infections are characterized as asymptomatic. Giardiasis is diagnosed by the detection of cysts or trophozoites in the feces, trophozoites in the small intestine, or by the detection of *Giardia* antigens in the feces.

Case Report

We report the case of a woman who developed an impairment of renal function, after a prolonged period of slight fever and diarrhea. A 54-year-old female had fever (maximum 38°C) and diarrhea for approximately ten days. Because of an elevated serum creatinine (3.0 mg/dL), she was admitted to our unit. Physical examination revealed no abnormalities. The patient had never been ill nor taken any regular medications. X-ray of the chest did not show any pathological findings. Ultrasound investigation showed normal sized kidneys with a slight increase in cortical echogenicity. No signs of renal artery stenosis could be found. Laboratory investigation revealed elevated C-reactive protein of 80 mg/dL (normal range 0-10 mg/dL) and elevated erythrocyte sedimentation rate of 120 mm/s. Complete blood cell count revealed leukocytosis of $11,400\times10^3$/mL (normal range 4-10) with eosinophilia of 0.45×10^3/mL (3.9% of white blood cells). Urinanalysis revealed a proteinuria of 0.4 g/day, hematuria and leukocyturia. Renal function was reduced (measured creatinine clearance 20 mL/min). Other blood parameters, *e.g.* electrolytes, were in the normal range. Testing for autoimmune antibodies, such as antinuclear antibodies, antiphospholipid antibodies, antineutrophil cytoplasmatic antibodies, antiglomerular basement membrane antibodies, as well as hepatitis B surface antigen and light chain proteinuria were negative. Complement C3 and C4 were in the normal range. Blood, urine, sputum and stool culture were negative. Because of the prolonged period of diarrhea, a screening for parasitic infections was performed and *Giardia lamblia* was found. Therefore, a therapy with metronidazole (500 mg/tid per 7 days) was administered. After an attempt to recover renal impairment by vigorous rehydratation, because of the unclear origin of the persisting renal failure, a percutaneous renal biopsy was performed. Histological examination showed cortically accentuated interstitial nephritis with a dense peritubular infiltrate of lymphocytes, monocytes and granulocytes (Figure 1). Light microscopy showed no glomerular lesions. Immunofluorescence staining was negative. About 15% of the cortical tubulointerstitium showed chronic alterations. After successful treatment of the underlying *Giardia* infection, clinical symptoms persisted and renal insufficiency had progressed further (serum creatinine 5.7 mg/dL, creatinine clearance 8 mL/min). This suggested ongoing interstitial nephritis, even after elimination of the pathological agent. Methylprednisolone 250 mg/die per three days was administered and followed by prednisone per os (0.5 mg/kg/die), maintained for two weeks. Within three days, renal function started to improve and after six weeks, renal function had completely recovered.

Discussion and Conclusions

Renal involvement in parasitic infections is polymorphic, ranging from direct invasion to various types of glomerulonephritis. Acute interstitial nephritis as a form of hypersensitivity reaction is an uncommon manifestation in the setting of human parasitic infections.[3] We present a case of acute interstitial nephritis in association with *Giardia* infection of a 54-year old patient. A combination of antibiotic and steroid therapy led to eradication of the helminths and to full recovery of renal function. To date only a few cases of acute interstitial nephritis in parasitic infections (*i.e. Ascaris lumbricoides* infection) have been

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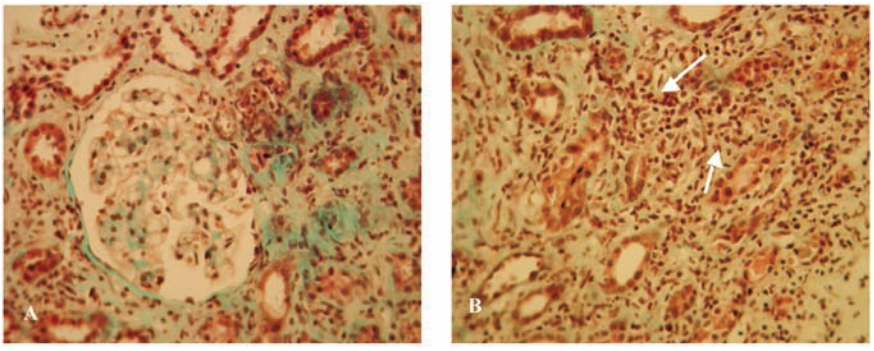

Figure 1. A) Glomerulus with regular basement membranes, typical mesangium and normal cell number. B) Focally dense inflammatory interstitial infiltrate, consisting of monocytes and lymphocytes. Tubules show focal acute damage (Trichrome staining).

described in the literature[5-7] and this is, in our knowledge, the first case of giardiasis reported. *Giardia intestinalis* affects about 30% of the world population, but acute interstitial nephritis is rarely seen and seems to be a quite uncommon complication in the course of infection, even when we consider that most infections occur in developing countries. In fact, in these countries medical standards are low and intermittent impairment of renal function might be underdiagnosed, as patients only have limited access to medical care. It is known that host genetics is an important determinant of the intensity and time course of most parasitic infections.[8] A special genetic or allergic predisposition could, therefore, have been the reason for the renal involvement in this patient. It is also possible that *Giardia*-derived antigens themselves did not lead to acute interstitial nephritis but had a permissive effect on other inflammatory stimuli in susceptible patients. In conclusion, in cases of unexplained renal failure in patients affected by parasitic infections, interstitial nephritis should be considered and a renal biopsy should be performed.

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