

Case Report

Leptospirosis with Crescentic Glomerulonephritis

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Infection associated glomerulonephritis is well recognized. A 30-year-old man presented with fever, vomiting and oliguria for two weeks. He had a blood pressure of 150/105 mmHg and mild pedal oedema. Initial investigations revealed serum creatinine 921 $\mu\text{mol/l}$, with microscopic haematuria and proteinuria. Serum C3 levels were reduced. Renal histopathology revealed diffuse mesangial proliferation and neutrophilic exudation, as well as cellular crescents. IgG and C3 were seen on immunofluorescence. Leptospira IgM antibody titres were elevated. Myocarditis also developed during hospital admission. He was managed with cefoperazone/ sulbactam, azithromycin and intermittent haemodialysis. Intravenous methylprednisolone was started on seventh day for three doses. The patient responded to antibiotics, with complete recovery of renal/ cardiac functions and resolution of proteinuria. He has remained well over the last seven months. Leptospirosis is usually associated with tubulo-interstitial disease. This case is unique because crescentic glomerulonephritis has not been described in association with leptospirosis before.

Key-words: Acute kidney injury, complement C3, glomerulonephritis, rapidly progressive glomerulonephritis

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Introduction

Infections are an important cause of acute kidney injury (AKI). Underlying mechanisms could be multifactorial e.g. cellular injury from direct invasion by bacteria or hemodynamic disturbances and abnormal expression of cytokines in sepsis.¹ Damage from immune complex deposition is also relevant in this context. In fact, glomerulonephritis (GN) associated with infections is the most common cause of immune complex mediated AKI.² While some microorganisms are classically associated with GN, others typically inflict damage to the tubules and interstitium. This case report describes unusual occurrence of GN in an infection strongly associated with tubulo-interstitial nephritis. This is unique as this has not been reported before.

Case History

A 30-year-old man was admitted to our hospital in October 2019 with fever, anorexia, vomiting and reduced urine output for two weeks. He did not report any cough, dyspnoea, arthritis, rash, strenuous unaccustomed physical exertion or ingestion of NSAIDs/ herbal medicines. There was no history of sore throat or diarrhoea in the recent past. He had previously been well, apart from a gunshot injury to his legs couple of years ago. His blood pressure was elevated at 150/105mmHg and mild pedal edema was noted. There was no hyper-

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tensive retinopathy and the systemic physical examination was unremarkable. The patient was oliguric. Initial investigations revealed Hb 13.3 g/dl, TLC 11000/ μl , platelets 333000/ μl , serum urea 45.5 mmol/l, creatinine 921 $\mu\text{mol/l}$, sodium 134 mmol/l, potassium 5.1 mmol/l and normal liver functions. Arterial blood pH was 7.30, with bicarbonate 11 mmol/l. C-reactive protein was elevated at 138.7 mg/dl. Urine examination showed numerous red blood cells per high power field and albumin: creatinine ratio of 162.6 mg/mmol on spot sample. Ultrasound showed normal sized unobstructed kidneys. He was initially managed with haemodialysis and started on antibiotics including cefoperazone/ sulbactam and azithromycin. Three days later, the patient developed pulmonary edema in the evening, following a session of hemodialysis and ultrafiltration earlier during the day. Workup at this stage showed global hypokinesia with ejection fraction of 30% on echocardiogram. High sensitivity troponin I levels were normal (20.4 pg/ml), whereas pro-BNP levels were elevated at 35000 pg/ml. Renal replacement therapy was further intensified, with vigorous mechanical ultrafiltration.

Fever responded to antibiotics and C-reactive protein dropped down to 65.8 mg/dl after four days. The patient remained oliguric and dialysis dependent. He was

started on intravenous methylprednisolone (500mg once a day) on the seventh day of admission. Urine output started improving the next day, coupled with improvement in renal excretory function and cessation of haemodialysis (Figure 1). This response was too quick to be attributable to steroids. These were thus stopped after three doses.

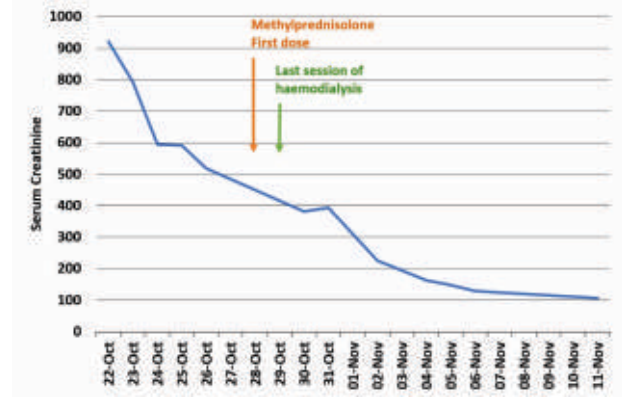


Figure 1. Trends in Serum Creatinine Levels

In the meantime, further evaluation showed reduced serum C3 levels (0.3 g/L) with normal C4. Serum anti-nuclear antibodies, extractable nuclear antibodies and antineutrophil cytoplasmic antibodies were negative. Antistreptolysin O titre was normal (<200 units/ml). Renal histopathology revealed thirteen glomeruli, all having diffuse mesangial proliferation and neutrophilic exudation. Cellular crescents were seen in seven glomeruli (Figure 2). The interstitium was edematous and infiltrated by moderate mixed inflammatory infiltrate comprising of neutrophils, lymphocytes and plasma cells. IgG (+) and C3 (+) were seen on immunofluorescence. Workup for underlying infectious etiology demonstrated serum *Leptospira* antibodies (IgM), detected by ELISA, elevated at 17 NTU (normal <9 NTU) on tenth day of admission. Dengue NS1 antigen and anti-dengue IgM antibodies were negative. No malarial parasites were seen on peripheral blood smear.

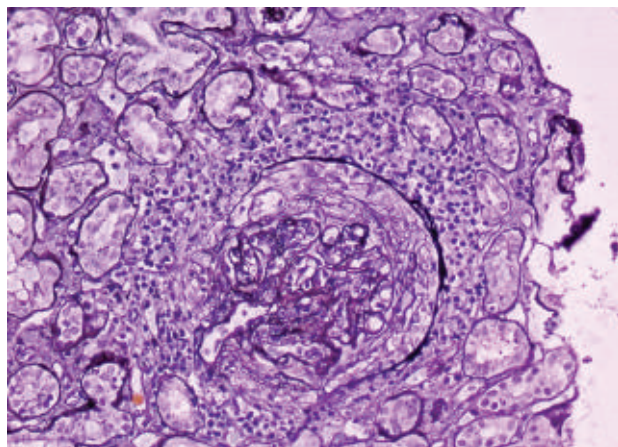


Figure 2. Renal Histopathology Showing Crescents,

Diffuse Mesangial Proliferation and Neutrophilic Exudation

Serum creatinine levels normalized by the end of third week in hospital. Repeat echocardiogram showed normal LV contractility and ejection fraction. Thallium scan did not show any significant adenosine induced reversible perfusion abnormalities. Cardiac MRI could not be done because of metallic splinters from a previous bullet injury.

The patient followed up in outdoor clinic after seven months. He was asymptomatic, had normal renal excretory functions and there was no proteinuria.

Discussion

Leptospirosis is a multisystemic disorder, endemic in tropical countries.³ The most severe form, Weil's disease, is characterized by jaundice and renal failure, and is associated with mortality rate of 22%.⁴ Renal involvement in leptospirosis is secondary to interstitial inflammation/ necrosis. Proximal tubular dysfunction with hypokalemia is also recognized. It is generally believed that leptospirosis spares the glomeruli, with only a few case reports describing different forms of GN. Silva et al reported mesangioproliferative GN in a young man with leptospirosis, AKI and nephrotic syndrome, who responded well to antibiotics alone.⁵ Similarly, focal necrotizing GN has also been mentioned in literature.⁶

Our case is unique because similar findings have not previously been reported in leptospirosis. This patient had normal liver function tests, not in keeping with severe leptospirosis. However, there is significant evidence to suggest that AKI requiring haemodialysis can occur with leptospirosis even in absence of jaundice/ liver function abnormalities.⁷ Myocarditis developed during the first few days of admission in our patient. This, despite being uncommon, is a well-documented complication, more frequently observed in autopsy specimens.⁸

Considering the non-specific clinical features and limitations of different diagnostic tests, a high index of suspicion is required to diagnose leptospirosis and reduce the associated morbidity/ mortality. Microscopic agglutination test is the gold standard for diagnosis of leptospirosis, but not widely available in Pakistan.⁹ Blood cultures take time and are frequently negative. We therefore rely on IgM antibody testing in our practice. A repeat test to document rising titres at four weeks interval was planned for this patient, but unfortunately, he did not report to us at that time. Nevertheless, the clinical course of illness, including the response to antibiotics, and the significantly elevated IgM titres on first testing confidently point towards the diagnosis.

Crescentic GN is an important and potentially treatable

cause of AKI. Steroids and other immunosuppressants (e.g. cyclophosphamide and mycophenolate mofetil) are the corner stones of pharmacological therapy. This patient was started on intravenous steroids to treat possible acute interstitial nephritis. However, these were stopped because of a quicker than expected recovery. Decision against further use was made possible by the positive serology. Evidence for use of immunosuppressants in infection-related GN is largely anecdotal and is not recommended on the basis of risk to benefit ratio.¹⁰

Conflict of interest

None

Funding Source

None

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