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Case Report

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Rapidly progressive renal failure—a rare presentation of granulomatous interstitial nephritis due to tuberculosis—case report and review of literature

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Abstract
Granulomatous interstitial nephritis (GIN) is a rare manifestation of renal tuberculosis (TB). We report a case of rapidly progressive renal failure (RPRF), granulomatous inflammation of cervical lymph node and GIN as presenting manifestations of TB. Aspiration cytology of cervical lymph node showed granulomatous necrotizing inflammation with acid-fast bacilli (AFB). The renal biopsy and urine specimen did not show AFB. Urine polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* was positive. We observe that GIN due to TB can present as RPRF and emphasize the value of PCR-based techniques in making a correct diagnosis.

Keywords: granulomatous interstitial nephritis; rapidly progressive renal failure; renal tuberculosis

Introduction

Genitourinary tuberculosis (TB) is the second most common extrapulmonary form of TB after lymphadenopathy. Genitourinary TB accounts for 27% (range 14–41%) of nonpulmonary cases and is usually a late complication of pulmonary TB [1]. Renal damage due to caseous destruction of renal parenchyma or obstructive uropathy is well known. Mallinson *et al.* [2] in 1981 made the first clinical description of granulomatous interstitial nephritis (GIN) as the only manifestation of renal TB. Overall, data on GIN as the only manifestation of renal TB is limited to case reports and the most common clinical presentation is chronic renal insufficiency. Interestingly, most patients of GIN express active extrarenal foci, often pulmonary or peritoneal. We report a case of tuberculous GIN associated with active cervical lymphadenitis and review the pertinent literature on GIN due to TB in immunocompetent individuals.

Case history

A 24-year-old previously healthy man developed fever and left cervical lymphadenopathy for which he was prescribed antibiotics (erythromycin) and antipyretics (paracetamol) for 2 weeks. He was also prescribed two antihypertensive drugs and advised further evaluation for proteinuria, which he deferred. Two weeks later, he was referred to our center for fever, lymphadenopathy and recently detected renal failure. There was no history of treatment or contact with TB, loss of weight, red urine, skin rash, joint pains or use of native medicines.

Physical examination revealed pallor, bilateral pedal edema, pulse rate 92/min, blood pressure of 160/100 mmHg, temperature 38°C and respiratory rate 15/min. A solitary mobile painless left cervical lymph node 1 × 1.5 cm was present. Systemic examination was unremarkable.

His hemoglobin (1.16 g/L) was decreased and erythrocyte sedimentation rate was elevated to 94 mm/h. White blood cell count of 10.9×10^9/L ($4–10 \times 10^9$/L) with neutrophils 72%, lymphocytes 23%, eosinophils 3% and monocytes 2%, platelet count 205×10^9/L ($150–400 \times 10^9$/L) and reticulocyte count 1.2% were normal.

Serum creatinine was increased to 660 μmol/L (44–140 μmol/L) and the estimated four-variable Modification of Diet in Renal Disease- Glomerular Filtration Rate was 9.59 mL/min/1.73m^2. Serum uric acid, calcium, inorganic phosphorus, liver function tests and lipid profile were within normal limits. Urine analysis showed hematuria with 3+ proteinuria. Twenty-four-hour proteinuria was 3.2 g in 1500 mL of urine. There were 0–1 white blood cells per high power field, 8–10 red blood cells per high power field and no evidence of casts on microscopic examination of the urine sediment. Ultrasound revealed normal size kidneys with normal corticomedullary differentiation. Doppler ultrasound of renal vessels was normal. Further evaluation was done with a provisional diagnosis of rapidly progressive glomerulonephritis. Antinuclear antibody (negative), anti-dsDNA (12.25, 0–30 IU/mL) and anti-GBM titers (<3 KU/L) were within normal limits. Complement levels C3 0.78 g/L (0.60–1.2 g/L) and C4 0.26 g/L (0.15–0.30 g/L) were in normal range. HBsAg and anti-HCV antibody enzyme-linked immunosorbent assay were negative. Urine and blood cultures showed no growth. Chest X-ray did not reveal any abnormality.

Cervical lymph node aspiration cytology showed granulomatous necrotizing inflammation with acid-fast bacilli (AFB) suggestive of TB. He was initiated on antitubercular treatment (ATT), maintenance hemodialysis and ultrasound-guided percutaneous renal biopsy were done to identify the cause of rapidly progressive renal failure (RPRF). On light microscopy, 19 of the 22 glomeruli were normal and 3 showed global sclerosis. Interstitium showed lymphoid aggregates with well-formed epitheloid granulomas along with intense mononuclear infiltrate comprising of lymphocytes, histiocytes and plasma cells (Figures 1 and 2). The tubules showed marked atrophic changes and occasional tubules showed granular cast. Blood vessels were unremarkable. Immunofluorescent micrography revealed absence of specific immunoglobulin or complement (C3, C1q) deposits. Findings were consistent with a diagnosis of GIN. AFB were not seen on Ziehl–Nielsen staining and cultures for tubercle bacilli in renal biopsy were negative. On further evaluation, three samples of urine microscopy and culture for *Mycobacterium* were negative and bone marrow examination was unremarkable. Mantoux test was negative. However, urine DNA-polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* was positive. Serum angiotensin-converting enzyme levels were normal. He was started on steroid (oral prednisolone 1 mg/kg/day) together with ATT. Six months since the onset of illness, his lymphadenopathy resolved but renal failure did not recover. Steroids were tapered and withdrawn after 3 months and the patient is now on ATT and maintenance hemodialysis through radial arteriovenous fistula.

Discussion

The interesting features in our patient were (i) coexistence of active renal and cervical lymph node TB in a 24-year-old male, (ii) GIN presenting as RPRF and nephrotic range

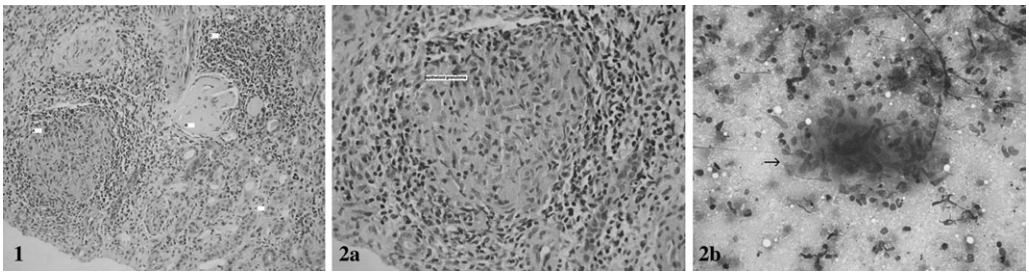

Fig. 1. Renal biopsy showing epithelioid cell granuloma (**A**), sclerosed glomerulus (**B**), atrophic tubules (**C**) and interstitial inflammation (**D**); (hematoxylin and eosin stain; ×20 magnification).

Fig. 2. (**a**, **b**) Epithelioid cell granuloma surrounded by mantle of lymphocytes (hematoxylin and eosin stain; ×40 magnification) (epithelioid cell marked with arrow in figure 2b).

Table 1. Summary of case reports with GIN due to renal TB[a]

Author (year)	Country	Extra renal manifestations	Urine AFB/culture/ others	Treatment	Renal outcome
Mallinson *et al.* [2] (1981), three cases	Immigrants to UK	Pulmonary TB-2	Neg/neg	ATT	ESRD
			Neg/neg	ATT	ESRD
		TB peritonitis-1	Neg/neg	ATT + steroids	PR
Mignon *et al.* [6] (1984), three cases	France	Nil-2, yes-1	NA	ATT + steroids	PR-2
			NA	ATT	ESRD-1
Benn *et al.* [7] (1988)	Ugandan immigrant to UK	Nil	Neg/neg	ATT + steroids	PR
El-reshaid *et al.* [8] (2001)	Kuwait	Pulmonary fibrosis	Neg/neg	ATT	CR
Larsen *et al.* [9] (2008)	African-American	Pulmonary infiltrates, bone marrow granulomas	NA	ATT	NA
Sampathkumar *et al.* [4] (2009)	India	No	NA/NA/, [b]renal tissue DNA PCR for *M. tuberculosis* positive	ATT + steroids	CR
This report (2011)	India	Cervical lymphadenopathy	Neg/neg, [b]urine PCR positive	ATT + steroids	ESRD

[a]ESRD—end-stage renal disease; NA—not available; Neg—negative; CR—complete recovery; PR—partial recovery.
[b]Other diagnostic techniques.

proteinuria and (iii) diagnosis was made by positive urine PCR for *M. tuberculosis*, when AFB could not be demonstrated in urine or renal biopsy.

Renal TB is rarely present in patients <25 years of age and can occur during primary infection or pulmonary reactivation. If there is a history of pulmonary infection, the latency period from the time of the initial infection to diagnosis with renal disease ranges from 5 to 40 years [3]. Coexistence of active renal and cervical lymph node TB is a deviation from the normal time frame for development of renal TB. Similar case reports of GIN with pulmonary and peritoneal foci are described, but to the best of our knowledge, this is the first report of cervical adenitis in a patient with GIN due to TB. It is possible that our patient had a primary infection involving the lymph node and the kidneys.

Another remarkable feature is the clinical presentation of hypertension, RPRF and nephrotic range proteinuria, mimicking a glomerular disease. Similar presentation of GIN has so far been reported in only one other patient [4] and there is no possible explanation for the nephrotic proteinuria seen in these patients. Such presentations may be seen with Non-Steroidal Anti-Inflammatory Drug-induced acute interstitial nephritis but in our case, detailed evaluation for other causes of GIN like drugs, infections and systemic conditions like sarcoidosis, Wegener's granulomatosis revealed negative results [5].

A literature search revealed 10 similar case reports (Table 1). Urine cultures (three to five samples) of the first urine of the day are considered 'gold standard' in diagnosis of genitourinary TB but are often negative. In comparison to urine cultures, PCR primers and probe derived from *M. tuberculosis* species-specific DNA insertion sequence, IS6110 has an overall sensitivity of 95.59% and specificity of 98.12% in the diagnosis of genitourinary TB [10].

GIN is seen in only in 0.5–0.9% of renal biopsy and of this 5% is caused by infections [11–13]. Often, features on biopsy do not help to determine the cause of GIN [13]. AFB may be demonstrated in the renal biopsy tissue with Ziehl–Nielsen or auromine-O stain but is positive only in 32–43% of specimens [14]. We suspected TB as the cause of GIN due to the presence of AFB in the cervical lymph node and subsequently, a positive urine DNA PCR for *M. tuberculosis* helped to confirm the diagnosis.

ATT (two, three or four drugs of isoniazid, rifampicin, pyrazinamide and ethambutol) has been used to treat all these patients. Treatment duration varies from 6 to 12 months. It has been observed that concomitant use of steroids bring about favorable recovery in these patients. Since granulomatous inflammation heals by fibrosis; steroids may decrease the inflammation and thereby reduce the amount of interstitial fibrosis [2]. Sampathkumar *et al.* [4] reported a similar case presenting as RPRF with nephrotic proteinuria and obtained complete renal recovery with a combination of ATT and steroids.

Remarkably, the majority of these (rare) cases were observed in patients from India or Black Africans or African-Americans. This could be due to a genetic predisposition causing varied host immune response or due to variations in phage type of *M. tuberculosis* [2]. However, such correlations are yet to be proven.

In summary, TB must be considered as a cause of GIN particularly in patients with Asian or African origin. Urine PCR can have a significant role in the diagnosis of culture negative renal TB. Steroids in combination with ATT should be considered as the first-line treatment for GIN due to TB.

Conflict of interest statement. None declared.

References

1. Eastwood JB, Corbishley CM, Grange JM. Tuberculosis and the kidney. *J Am Soc Nephrol* 2001; 12: 1307–1314
2. Mallinson WJ, Fuller RW, Levinson DA *et al.* Diffuse interstitial tuberculosis an unusual cause of renal failure. *Q J Med* 1981; 57: 31–35
3. Gibson MS, Puckett ML, Shelly ME. Renal tuberculosis. *Radiographics* 2004; 24: 251–256
4. Sampathkumar K, Sooraj YS, Mahaldar AR *et al.* Granulomatous interstitial nephritis due to tuberculosis-a rare presentation. *Saudi J Kidney Dis Transpl* 2009; 20: 842–845
5. Chung S, Park CW, Chung HW *et al.* Acute renal failure presenting as a granulomatous interstitial nephritis due to cryptococcal infection. *Kidney Int* 2009; 76: 453–458
6. Mignon F, Mery JP, Mougenot B *et al.* Granulomatous interstitial nephritis. *Adv Nephrol Necker Hosp* 1984; 13: 219–245
7. Benn JJ, Scoble JE, Thomas AC *et al.* Cryptogenic tuberculosis as a preventable cause of end-stage renal failure. *Am J Nephrol* 1988; 8: 306–308
8. El-Reshaid KA, Madda JP, Al-Saleh MA. A case of progressive tubulo-interstitial nephritis due to culture-negative renal tuberculosis. *Saudi J Kidney Dis Transpl* 2001; 12: 534–537
9. Larsen CP, Moreira RK, Hennigar RA *et al.* Kidney biopsy findings in a patient with fever, bilateral pulmonary infiltrates, and acute renal failure. *Am J Kidney Dis* 2008; 51: 524–529
10. Moussa OM, Eraky I, El-Far MA *et al.* Rapid diagnosis of genitourinary tuberculosis by polymerase chain reaction and non-radioactive DNA hybridization. *J Urol* 2000; 164: 584–548
11. Bijol V, Mendez GP, Nosé V *et al.* Granulomatous interstitial nephritis: a clinicopathologic study of 46 cases from a single institution. *Int J Surg Pathol* 2006; 14: 57–63
12. Viero RM, Cavallo T. Granulomatous interstitial nephritis. *Hum Pathol* 1995; 26: 1347–1353
13. Joss N, Morris S, Young B *et al.* Granulomatous interstitial nephritis. *Clin J Am Soc Nephrol* 2007; 2: 222–230
14. Goel MM, Budhwar P. Immunohistochemical localization of Mycobacterium tuberculosis complex antigen with antibody to 38 kDa antigen versus Ziehl Nielsen staining in tissue granulomas of extrapulmonary tuberculosis. *Indian J Tuberc* 2007; 54: 24–29

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