Tuberculous granulomatous interstitial nephritis of the solitary kidney in a renal donor

Arumugham Kanakaraj[*,1], **Balaji Kirushnan**[*], **Mohammed Shujauddin Akhil**[*] **and Rajan Ravichandran**[*]
[*]Department of nephrology, MIOT International, 4/112, Mount Poonamallee Road, Manapakkam, Chennai, 600089, India.

ABSTRACT Background: Unexplained azotemia in a renal donor needs urgent evaluation. Renal biopsy is required when the urine examination shows proteinuria and when there is an unexplained worsening of renal functions. Granulomatous interstitial nephritis of the solitary kidney in a renal donor has not been reported so far in the literature. **Case summary:** We would like to report on the benefits of performing a renal biopsy of a solitary kidney in establishing a diagnosis. A 51-year-old woman, who donated her kidney 15 years ago, developed azotemia with mild proteinuria in the setting of significant weight loss of 10 kilograms in 3 months. A kidney biopsy revealed granulomatous interstitial nephritis with areas of caseating necrosis, suggestive of tuberculosis. She received first-line anti-tuberculous treatment for nine months and her serum creatinine improved from baseline, which remained stable after one year. **Conclusion:** Unusual causes of renal impairment needs to be considered in a patient without any obvious precipitating conditions. A kidney biopsy would help in identifying the exact cause, in particular, a kidney donor, especially when a kidney biopsy is considered a relative contraindication.

KEYWORDS Tuberculosis, Renal donor, renal biopsy, solitary kidney

INTRODUCTION

Tuberculosis is a relatively common infection affecting people of all socio-economic strata, especially in India, where it is endemic. Both pulmonary and extra-pulmonary manifestations have been described. Early diagnosis and treatment are essential for a gratifying outcome. The extra-pulmonary disease can involve the nervous system, the skeletal system and the genito-urinary system. Renal manifestations of tuberculosis include scar manifestations resulting in ureteral stricture and hydronephrosis, chronic cystitis leading on to small capacity "thimble bladder" and secondary amyloidosis as well as granulomatous interstitial nephritis. Granulomatous interstitial nephritis has various causes including sarcoidosis, crystal deposits, medications and infections. Caseating granulomas are common in tuberculosis but also found in fungal infections.We report an unusual case of tuberculous granulomatous interstitial nephritis of the solitary kidney in a renal donor.

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[1]Arumugham Kanakaraj, Department of Nephrology, MIOT International, 4/112, Mount Poonamallee Road, Manapakkam, Chennai, 600089, India,
E-mail:rajikanak@yahoo.com

CASE REPORT

A 51-year-old woman, the native of Tamilnadu, a state of southern India, had undergone left open donor nephrectomy in 2000, for her sister. DTPA Renogram before nephrectomy showed a total GFR of 90ml/min with a split GFR of 44ml/min in left kidney and 46ml/min in right kidney. Right kidney had two renal arteries and a single vein. Left kidney had single renal artery and vein. The left kidney was selected for donor nephrectomy. There were no intra-operative complications noted during open nephrectomy. She was not on regular follow-up annually after 2008, when her serum creatinine was 1mg/dl. She had developed hypertension from 2012. She was on amlodipine 5mg/day and clonidine 100mcg three times a day for blood pressure control. In 2015 serum creatinine was 2.0mg/dl. The period from normal kidney function to the onset of azotemia was not known. Ultrasound showed normal size right kidney with no hydronephrosis. She had 500mg/day of proteinuria

(estimated by 24 hours urine protein) with no RBC casts or dysmorphic RBC's. Renal Doppler showed no evidence of renal artery stenosis. There was a history of loss of weight of more than 10 kg in 3 months. However, there was no fever or history of a cough. Chest X-ray did not show evidence of tuberculosis. CT chest showed bilateral mediastinal lymphadenopathy. C reactive protein was 6.5. ESR was 92mm/hr. Kidney biopsy was done from the lower pole of the right kidney given worsening azotemia with mild proteinuria. It showed 15 glomeruli. 2 glomeruli showed ischemic shrinkage of the glomerular tuft. Rest of the glomeruli were normal. Tubules showed extensive colloidisation and atrophy with numerous granuloma composed of histiocytes, macrophages and epithelioid cells. Few areas of caseation necrosis were seen. AFB stain was negative. Granulomatous interstitial nephritis with hypertensive nephrosclerosis was diagnosed. ANCA done by ELISA was negative. ACE levels were within normal limits. There was no history of intake of other drugs. Thus, the diagnosis of tuberculosis was made after diagnostic exclusion of other diseases. She was started on rifampicin 450mg/day, isoniazid 300mg/day, pyrazinamide 750mg/day and ethambutol 200mg every day. Repeat CRP after 2 weeks of therapy was 0.6. Creatinine improved to 1.5mg% and she is on regular follow up. One year after the event she has a creatinine of 1.6mg%, is doing well with a good appetite and has gained weight by 3 kg compared to her previous year. Blood pressure is controlled with two drugs.

Year	Events
2000	Donor nephrectomy
2008	Serum creatinine 1mg/dl
2012	Hypertension
2015	Serum creatinine 2mg/dl, kidney biopsy – tuberculous granulomatous interstitial nephritis, anti-tuberculous treatment
2016	Serum creatinine 1.6mg/dl

DISCUSSION

Renal donors are a group of the population who theoretically represent the healthy population, as they undergo thorough evaluation before donation. Thirty years ago, Barry Brenner developed an elegant theory of the pathophysiological consequences of nephron mass reduction [1]. After nephrectomy, the remaining kidney presents a functional adaptation by an increase in renal filtration in every single nephron due to the increase renal plasma flow (renal hyperfiltration) which is accompanied by an increase in intraglomerular pressure [2]. This renal hyperfiltration, and especially the increase in intraglomerular pressure, may eventually adversely impact the kidney function in the long-term [3]. High BMI is a significant risk factor observed by many studies which accelerate the loss of GFR in donors [4]. Advanced age per se has no effects on the decline in GFR according to many studies, but there has been a decline in GFR of donor kidney in African American subgroups [5]. Kidney donors who develop diabetes mellitus are usually hypertensive and have proteinuria [6]. Long-term studies have not shown a difference in the incidence of chronic kidney disease among renal donors as compared to the general population [7]. Studies, however, have shown a statistically significant decrease in GFR among kidney donors as compared to general population, but this did not translate into a clinical risk of end-stage renal disease [8]. Hypertension in a renal donor is of particular concern. A comparison all of the living donors in Ontario, Canada, from 1993 through 2005 to controls matched for age, sex, income, and use of non-physician health care reported a significant increase in the number of living donors with hypertension (16.3%) compared with the control group (11.9%)[9]. Another study which included 48 studies from 28 countries revealed that living kidney donors will see an average increase of 5-mm in blood pressure within five to ten years after donation over that anticipated by ageing alone[10]. Unexplained azotaemia or significant proteinuria in a donor needs an urgent evaluation to rule out reversible and treatable causes. Kidney biopsy in a donor (solitary kidney) has traditionally been considered a contraindication. But many studies have disproved the above, and renal biopsy in a solitary kidney is no longer an absolute contraindication [11, 12]. Ultrasound-guided percutaneous renal biopsy using an automated spring-loaded biopsy device has made renal biopsy safe and reliable. Real-time ultrasound guidance has reduced the rate of post-biopsy bleeding complications and has been shown to be superior to blind ultrasound technique. A retrospective study of 129 patients showed a higher mean number of glomeruli per biopsy in the sonographic-guided group compared to the blind biopsy group and fewer large hematomas requiring intervention (0% versus 11%) [13]. There is hardly any literature from India regarding solitary renal biopsy, although it is performed in many institutes with real-time ultrasound guidance. We report the benefit of performing a renal biopsy in a solitary kidney to identify treatable causes like tuberculosis. Tuberculosis is the most common endemic infection in India. There are about 2.5 million cases of active tuberculosis in India. It is estimated that about 40% of the Indian population is infected with Mycobacterium tuberculosis, the vast majority of who have latent rather than active tuberculosis [14]. Renal manifestations of tuberculosis include secondary amyloidosis, granulomatous interstitial nephritis, and calcification of the cortex, pelvicalyectasis, ureteral strictures, hydronephrosis, pyonephrosis and tuberculous cystitis ("Thimble bladder"). Granulomatous interstitial nephritis (GIN) is a rare histologic diagnosis that is present in between 0.5 and 0.9% of native renal biopsies and 0.6% of renal transplant biopsies [15, 16]. It has been associated with the medication, infections, sarcoidosis, crystal deposits, paraproteinemia, and Wegener's granulomatosis and also is seen in an idiopathic form. Medications implicated include anticonvulsants, antibiotics, nonsteroidal anti-inflammatory drugs, allopurinol, and diuretics. Mycobacteria and fungi are the main infective causes and seem to be the main causative factor in cases in renal transplants [16]. Most cases are reported in patients of Asian Indian or African descent, which may reflect the higher incidence of disease in these populations [17]. Renal involvement is insidious and can remain undetected for up to 20 years. Granulomatous interstitial nephritis due to tuberculosis in a renal donor has never been reported in the literature till now. Renal biopsy was done given azotaemia and proteinuria in the donor with systemic features of weight loss and dry cough. Unlike other studies, we were not able to demonstrate AFB in kidney biopsy specimen or had a TB PCR done in the renal biopsy [18].Caseation although most commonly encountered in tuberculosis can be seen in fungal,

rare parasitic infections and beryllium exposure. But our patient was not immunocompromised to have an invasive fungal infection. The clinical scenario led to tuberculosis as the diagnosis of exclusion and patient responded well to treatment.

CONCLUSION

Tuberculosis is endemic in many countries including India. Pulmonary and extra-pulmonary manifestations are well known to occur. Extra-pulmonary manifestations may be subtle, and a high degree of suspicion is required for early diagnosis and treatment. Tuberculous granulomatous interstitial nephritis is a rare manifestation, but the potentially treatable cause of renal failure if detected early. We would like to highlight the aspect of performing a renal biopsy in solitary kidney especially in a renal donor where normalising renal functions as early as possible is the goal.

COMPLIANCE WITH ETHICAL STANDARTS

Disclosure of potential conflicts of interest: All authors have declared no competing interests.

Research involving human participants and animals: Ethical approval: All procedures performed in studies involving human participants were by the ethical standards of the institutional and national research committee at which the studies were conducted and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all involved participants included in the study.

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