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Case Report

Renal Allograft Tuberculosis with Infected Lymphocele Transmitted from the Donor

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ABSTRACT. Transmission of tuberculosis (TB) from a donor through renal transplantation is a rare incident. We are reporting a 53-year-old Qatari woman diagnosed with renal allograft TB infection. The disease was confirmed by isolation of *Mycobacterium tuberculosis* from fluid from the lymphocele and demonstration of caseating granuloma in graft biopsy with acid-fast bacilli seen on Ziehl–Neelsen staining. The diagnosis was made quite early post-transplantation. The presence of the granuloma, which is unusual with patients on intensive immunosuppressant medications, suggests that transmission of the infection occurred from the donor rather than from the activation of latent infection. In reviewing the literature, we found ten case reports of TB in transplanted kidney with transmission of TB infection from the donor. The presence of TB in lymphocele in association with the infected transplant by TB, to the best of our knowledge, was reported only once in the literature. Our case had unfavorable outcome and ended by renal allograft nephrectomy and hemodialysis. We are presenting this case of TB infection of renal allograft and lymphocele diagnosed early post-transplantation transmitted from the donor and pertinent review from the literature.

Introduction

Tuberculosis (TB) is one of the most common opportunistic infections developing following renal transplantation. The incidence of TB among organ recipients is as much as 74-times that of the general population.[1] The incidence differs in the literature from region to region, accounting for as high as 5.7–11.8 % in India and less than 1% in the United States.[1,2] It carries a high mortality and morbidity rate in addition to graft dysfunction and loss among renal transplant recipients.[2]

Mycobacterium tuberculosis can be transmitted by transplantation (Table 1). It was estimated previously to account for 4% of the reported post-transplant TB cases.[1] The presence of TB-infected lymphocele or para-nephric abscess along with the transplanted kidney is a rare occurrence, and, to the best of our knowledge, was reported only once before.[3]

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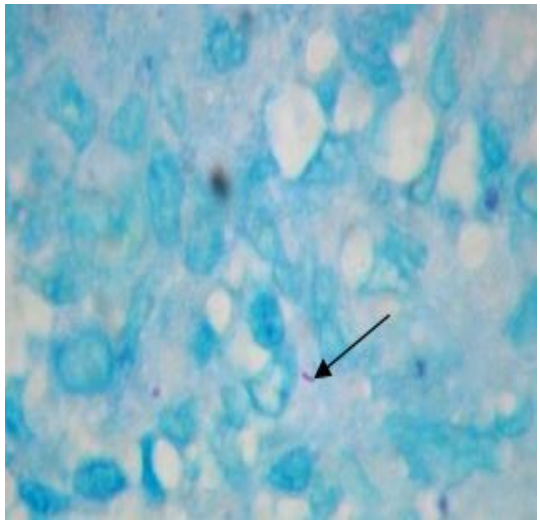

Figure 1. Renal allograft biopsy showing acid-fast bacilli was stained positive (modified Ziehl–Neelsen stain) seen in granuloma (arrow).

Case Report

A 53-year-old Qatari female patient with chronic kidney disease secondary to long-standing diabetes mellitus (DM) and hypertension, had two live unrelated renal allograft transplants. The first transplant was performed in 1993. She sustained chronic allograft rejection and ended up in transplant failure in early 2000. The second renal transplant was performed in November 2005. The transplantation was carried out in a different center (in Philippines) with a haplo-matched donor. Further detailed information about the donor was not available. It was followed by multiple complications, including dehiscence of the transplant wound with a sinus having persistent discharge from lymphocele. She developed allograft dysfunction; the initial one was secondary to cyclosporine toxicity proven by the allograft biopsy in December 2005.

She was re-admitted in January 2006 with rising urea and creatinine. She was complaining of abdominal pain and low-grade fever. *Escherichia coli* wound infection was found and was treated initially, but the patient continued to be febrile. There was no past history of TB in the patient or in her family. Purified protein derivative (PPD) skin test was negative prior to transplantation. No isoniazid (INH) prophylaxis was given. She was maintained on multiple immunosuppressant drugs including mycophenolate mofetil, cyclosporine and prednisolone.

Physical examination showed a febrile patient (38.2°C) with stable hemodynamic status. There was no lymphadenopathy or rash. Retina examination showed no evidence of choroidal TB. Abdominal examination revealed left side palpable allograft kidney. Other systemic examinations were unremarkable.

The initial investigations showed hemoglobin 6.9 g/dL, total leukocyte count 2100/mm^3, polymorphs 38.6%, lymphocytes 48% and platelets 125,000/µL. The erythrocyte sedimentation rate was 102 mm in the first hour. Urine examination was negative and no acid-fast bacilli (AFB) was seen in Ziehl–Neelsen (Z-N) staining. Serum urea was 15.5 mmol/L, creatinine was 128 µmol/L and calcium was 2.17 mmol/L. Blood and urine cultures done this time were sterile. Chest X-ray and computed tomography (CT) scan of the chest were normal. Ultrasound, CT scan and magnetic resonance imaging of the abdomen showed a large lymphocele surrounding the transplant, with normal angiographic appearance of pelvic veins and arteries, atrophic native and normal-appearing renal graft. There was no evidence of TB at any site. Transplant renogram showed normal perfusion with normal parenchymal appearance.

Repeated gram staining and cultures of lymphocele fluid were negative. However, lymphocele fluid was reported positive for AFB staining and the culture grew *Mycobacterium tuberculosis*. The second transplant kidney biopsy showed tubulo-interstitial inflammation with non-caseating granulomas with AFB seen on Z-N staining. There was no evidence of concomitant fungal infections (Figure 1).

The patient was started on full-dose quadruple anti-tubercular therapy (rifampicin, isoniazide, ethambutol and pyrazinamide). Despite the early diagnosis and treatment, the patient continued to have deterioration of the kidney function associated with symptomatic volume overload requiring hemodialysis. Because of

persistent fever despite anti-tubercular and empirical antifungal therapy, although with no apparent focus of fungal infection, transplant nephrectomy was performed. Histopathology of the removed graft was positive for fungal hyphae and spores; however, no culture was performed. After nephrectomy, the patient responded well to treatment. She was continued on anti-tubercular therapy for a total of one year. She is currently maintained on regular hemodialysis without evidence of tuberculosis reactivation.

Discussion

TB is more frequent in renal transplant recipients than in the general population in tropics.[2,4] In developed countries, the disease represents a significant health problem in patients following renal transplantation.[1] It causes serious damage to the graft and may lead to graft loss either because of delayed diagnosis or due to renal allograft rejection that can be attributed to the reduction in efficiency of the immunosuppressant drugs.[4,5]

The risk factors of TB post-renal transplantation are highly influenced by disease endemicity and the immunosuppressant regimen used following transplantation.[6]

Early tuberculosis infection (within the first year) post-transplantation was associated with the use of cyclosporine therapy.[6,7] Other risk factors for post-transplantation TB were DM and chronic liver diseases (CLDs). The combination of both DM and CLD and pre- or post-transplantation TB, along with other co-existing infections, are important risk factors for death.[7] The risk of post-transplant TB is increased in relation to prolonged duration of pre-transplant hemodialysis and the number of post-transplant rejection episodes.[6,8] The frequency of TB has been also correlated with a maintenance steroid dose of more than 10 mg/day or the use of pulse steroid therapy.[6]

The routine use of INH prophylaxis is controversial in endemic areas. While earlier it was not recommended by some, because of the high degree of PPD skin test positivity in the general population and the high frequency of false-negative tests among chronic renal failure patients,[4] it is being advised now by others.[6,7] INH hepatotoxicity may not be as high as previously thought, especially in non-hepatic transplant recipients.[1]

The diagnosis of TB is often made retrospectively after observing a complete response to anti-TB therapy. The most common site for TB is pleuro-pulmonary in renal transplant patients, accounting for 28–50%, followed by disseminated TB**.** Patients presenting with pyrexia of undetermined etiology account for 20–40%.[4] Examination of the retina is important to differentiate disseminated TB from isolated graft infection.[9] The other method is by bone marrow examination, which is not routinely done.

The time to TB diagnosis from transplantation date in renal allograft recipients varies. On an average, it usually occurs more than two years following transplantation. It was estimated to occur 11 months following transplantation by some studies.[1,10]

A search of the literature by us revealed that transmission of TB from the donor along with the transplanted kidney was reported only in ten patients in previous case reports and case series. Characteristics of those patients in comparison with our case are summarized in Table 1. Previously, it was estimated to account for 4% of the reported post-transplant TB cases.[1]

Occurrence of TB in renal allograft with infected lymphocele or para-nephric abscess is reported in only one previous case report.[3] In this case report, transmission from donor was not suggested and it was diagnosed five months post-transplantation by both ultrasound-guided aspirate from peri-nephric collection and urine being tested positive for AFB. Our patient did not have any of the recognized risk factors for TB, including previous exposure, malnutrition or living in an endemic area. The incidence of all forms of TB in Qatar was 55/100,000 population in 2008.[11]

Our case report is unique in providing diagnosis of the TB from the lymphocele discharge as usually the infection is checked in the urine sample and in the allograft biopsy where granulomas with AFB-positive bacilli are found.[12-18]

Table 1. Tuberculosis isolated to renal allograft transmitted from donor with or without dissemination of tuberculosis by case reports and case series.

No. of patients	Time from transplantation to TB diagnosis (months)	Type of transplant	Tuberculosis dissemination	Diagnosis methods	Outcome	Case report no.
1	29	Deceased donor renal transplant	No	Graft biopsy showing caseating granuloma and urine culture grows AFB.	Recovery	15
1	3	Deceased donor renal transplant	No	Graft showing caseating granuloma, with AFB seen on Z-N staining. Positive early morning urine cultures for MTB.	Failure with allograft nephrectomy	8
2	2, 6	Deceased donor renal transplant (same donor)	Yes, both	Both urine grows AFB, both disseminated TB.		13
2	1.5, 1.5	Deceased donor renal transplant (same donor)	Yes, both	First: Bone marrow aspirate positive for AFB. Second: Blood and urine AFB, bone marrow granuloma and PCR positive.	Former expired, second patient recovery	12
1	No available information	-	Yes	-	-	9
2	1, 1	Deceased donor renal transplant (same donor)	First: Yes, Second: No	First: Bone marrow, urine and pleural fluid positive for AFB. Second: Urine positive for AFB.	Failure with allograft nephrectomy (both)	10
1	14	Deceased donor renal transplant	No	Graft biopsy showing caseating granuloma, with AFB seen on Z-N staining + positive early morning urine cultures for MTB.	Failure with allograft nephrectomy	14
1	2	Living unrelated renal transplant	No	Graft biopsy showing caseating granuloma, with AFB seen on Z-N staining. Lymphocele.	Failure with allograft nephrectomy	Our case

Z-N stain: Ziehl–Neelsen stain, MTB: Mycobacterium tuberculosis, AFB: Acid-fast bacilli

Moreover, our case was unusual compared with previously reported cases as the transmission occurred from a live unrelated transplant rather than a deceased donor transplant (Table 1).

Finding a granuloma formation in the early course post-transplantation supports the high possibility of transmission of the infection from the donor kidney rather than activation of latent infection in the host. It was assumed earlier that a high dose of corticosteroids plays an important role in the presentation of an exudative form of TB, preventing the formation of granulomas, and granulomatous forms occur mainly after the first year of transplantation.[5]

The initial renal graft biopsy was negative for presence of granulomatosis disease. We believe that the reason for that is related to the nature of granulomatosis that was scattered throughout and not involving the whole organ. Possibly, the first biopsy missed an area with granulomas. Also, it is important to mention that superinfection with *E. coli* masked the presentation. Moreover, the fungal infection that involved the transplanted kidney was not present at the beginning and it was not shown in either biopsy taken earlier. The immunosuppression was stopped with nephrectomy performed in order to gain control of the infection. These are common problems with this type of patient.

Transmission of TB from the donor should be suspected when there is absence of clear risk factors or other evidence from recipient pretransplantation screening.[16] Other recipients from a common donor might be at risk and should be evaluated for TB as well.[9,14,16,17]

TB of the renal allograft should be seriously considered in any transplant patient with pyrexia of unknown origin. Renal allograft biopsy should be performed as early as possible for every transplant case where a cause for fever is not reached.

Because it often goes unsuspected, a high index of suspicion is needed to diagnose it timely in order to avoid graft loss. TB transmitted with the organ donor should be thought of if the donor status is unknown or if the donor is from endemic areas. Other recipients from the same donor should be checked as well.

Conflict of Interest

The authors of this manuscript have no conflicts of interest to disclose as described by the *Saudi Journal of Kidney Diseases and Transplantation*. Also, this manuscript was not prepared or funded by any commercial organization.

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