Recurrence urinary tract infection by Burkholderia cepacia in a live related renal transplant recipient
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Abstract
Burkholderia cepacia is a high virulent organism usually causing lower respiratory tract infections especially in Cystic fibrosis (CF) patients and post lung transplant. Urinary tract infections with Burkholderia cepacia have been associated after bladder irrigation or use of contaminated hospital objects.

Post renal transplant urinary tract infection (UTI) is the most common infectious complications. Recurrent urinary tract infection with Burkholderia cepacia is a rare finding. Complete anatomical evaluation is essential in case recurrent urinary tract infections (UTI) after renal transplant. Vesico-ureteric reflux (VUR) and neurogenic urinary bladder was found to be important risk factors.

Keywords: Urinary tract infection, Burkholderia cepacia, Renal transplant.

Introduction
In renal transplant recipients, UTI is the most common infectious complication which contributes significantly to mortality and morbidity. Structural abnormalities, urological procedures, placement of stents, colonization of indwelling urinary catheters or bladder irrigation with contaminated fluids are the established risk factors. These risk factors may provide nidus for bacterial growth leading to infections and also contribute to recurrence. Members of Enterobacteracea family are the main causative pathogens causing UTI in this patient population. However, rare opportunistic organisms which are usually considered as contaminants could cause infections. Burkholderia cepacia is not a common genito-urinary tract infection causing pathogen and is usually introduced after some urological procedures or catheterization.

We report a case of recurrent urinary tract infections with B. cepacia in a renal transplant recipient which did not respond on repeated prolonged courses of antibiotics.

Case Report
A 25-years-old male had allogenic live related renal transplant. His pre-operative urinary tract evaluation was normal. Renal graft placement with ureteroneocystostomy was done followed by placement of double-J stent, which was removed 2 weeks post-transplant.

He was started on triple regimen immunosuppression (Prednisolone, Azathioprin and Cyclosporine). After four days of uneventful postoperative period his creatinine increased to 2.84mg/dl without any clinical signs and symptoms. Acute cellular rejection (ACR) was found on graft biopsy. Injection Solumedrol was given for 5 days; and immunosuppression was changed to Cellcept (mycophenolate mofetil). Urine detailed report (DR) and urine culture were unremarkable. He was discharged home on baseline creatinine of 2.09mg/dl with histological evidence of resolved rejection.

Within a week, he presented with high grade fever and graft dysfunction with serum creatinine level of 2.2mg/dl. All other laboratory parameters and cultures were normal except urine culture which showed growth of $10^5$ cfu/ml of non lactose fermenter, oxidase positive gram negative rods. Burkholderia cepacia was identified on Analytical profile index (API-Biomerieux) 20NE. Disc diffusion method was used for susceptibility testing according to Clinical...
Laboratory Standard Index (CLSI) recommendations. It was found sensitive only to Ceftazidime and Ciprofloxacin. After initial intravenous antibiotics, his creatinine decreased to the baseline and he was asymptomatic. He was discharged on oral Ciprofloxacin for 4 weeks. He was closely monitored on monthly follow up visits.

Three months after resolution of his last infection, he again presented with renal dysfunction and significant weight loss of approximately 6 kilograms. There were no other clinical signs and symptoms. Urine culture was positive for Burkholderia cepacia without pyuria with similar susceptibility pattern. This time he was started on injection Ceftazidime which was continued for 4 weeks. He was discharged with weight gain of 4 kilograms and 1.35 mg/dl creatinine.

A month later, he presented with complaint of high grade fever and chills, tenderness over graft site and graft dysfunction with creatinine level of 1.88mg/dl. Significant viable count of B. cepacia with pyuria was detected in urine. Injection ciprofloxacin was started initially and once patient became afebrile and graft function improved, he was discharged on oral antibiotics for 4 weeks.

On his next follow up visits he was asymptomatic with normal base line renal function and negative urine culture.

One and half month after the last admission he presented with high grade fever, vomiting, graft site tenderness and graft dysfunction with four times rise in creatinin (5.44 mg/dl). He was found to have urosepsis again with same B. cepacia and started on injection Ceftazidime for four weeks. His renal function gradually improved and at the time of discharge his serum creatinine level was 1.40 mg/dl.

For radiological evidence, he had regular Colour Doppler Imaging (CDI) of grafted kidney. It was well perfused graft with no evidence of hydronephrosis and perigraft collection on every admission. On his last admission he was thoroughly evaluated for anatomical abnormality. Cystoscopy was unremarkable.

No residual urine or vesico urethral reflux was detected in ultrasound KUB with prevoid and postvoid micturition. Transrectal ultrasound and prostatic secretion culture for prostatic abscess and chronic prostatitis respectively was also unremarkable. However, after performing voiding cysto-uretherogram (VCUG) it was found that Grade III vesico-ureteric reflux was present in both native kidneys. Urine flowmetry (UFM) showed minimal post void urine in urinary bladder.

Urodynamic studies revealed low flow pressure system consistent with type I neurogenic bladder. He was started on Tamsulosin, a selective alpha receptor blocker. Left native kidney nephrectomy was also done.

Histopathology of native kidney showed acute on chronic pyelonephritis with multiple micro tubular abscesses (Figure-1). Patient was on close follow up for next 8 months (240 days) with no signs and symptoms of urinary tract infection and average creatinine levels remained at 1.75 mg/ml. His immunosuppression was also modified on his last admission and changed from Cellcept to Azathioprin along with Prednisolone and cyclosporine.

**Discussion**

Urinary tract infection is an important infectious complication after renal transplant. Burkholderia cepacia complex (BCC) is ubiquitous in our environment and has been recognized as a group of highly virulent organisms in Cystic fibrosis (CF) and chronic granulomatous disease (CGD).

However, it has wide spectrum of infections ranging from superficial to deep-seated and disseminated infections in non-CF population. Exposure to contaminated hospital instruments and chemicals contributes to B.cepacia associated nosocomial infections.

Previously Li et al reported a case of Burkholderia urinary tract infection in renal transplant recipients which end up with graft nephrectomy. However, this is the first reported case of recurrent urinary tract infection with B. cepacia in renal transplant recipients. This organism was resistant to multiple groups of antibiotics and had repeated infections despite prolonged use of appropriate antibiotics.

The source of infections could not be elucidated and it may have been acquired during the transplant surgery or had post transplant colonization of urinary tract.
The ureteroneocystostomy have been reported to cause episodes of febrile urinary tract infection in patients operated for primary vesicoureteric reflux disease (VUR).\(^8\) There is no consensus guideline for diagnosis of VUR in adult immunocompromised population. Our patient was routinely assessed on each occasion by serial sonogram of native and transplanted Kidney and Urinary Bladder (KUB) which showed no post void urinary retention or reflux with any obvious urinary tract abnormality.

Ultrasound is considered a good method for screening or evaluating the kidney for structural abnormalities. However, if vesicoureteric reflux (VUR) is suspected ultrasonography is not a reliable modality.\(^9\)

Our observation also support the evidence that VCUG is the best test to perform and it should be performed along with sonograms incase of recurrent urinary tract infections. The cystoscopic examination is subjective to expertise and finding can be missed easily by an inexperienced examiner. Unfortunately proper water and other environmental culture were not considered which could rule out environmental factors.

High doses of immunosuppressants and poor HLA match could be contributory factors for recurrent infections after transplant.\(^10\) Our patient received injection Solumedrol for early rejection and then was converted to mycophenolate mofetil (potent antiproliferative agent) very early after transplant. Both are potent immunosuppressant and has high predilection for more infections.

Change in immunosuppressant regimen should be considered in case with potent immunosuppresion to less potent agent could help in limiting the rate of infections. We have modified to less potent regimens including prednisolone and cyclosporine.

Although this isolate was resistant to multiple groups of antibiotics but every episode were properly treated for nearly 4 weeks duration according to available susceptibility.

**Conclusion**

This nosocomial pathogen has been rarely reported to cause urinary tract infection in renal transplant recipients. For eradication appropriate antibiotics are required for adequate period of time, complete and proper anatomical evaluation and surgical intervention.

**Conflict of Interest:**

No conflict of interest to declare.

**Reference**