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## CASE REPORT

### A CASE OF BK VIRUS NEPHROPATHY POST RENAL TRANSPLANTATION: A CASE REPORT

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## ABSTRACT

BK Nephropathy (BKVN) is a viral nephropathy that can lead to allograft failure. We report a 25 years old kidney transplant recipient who presented with asymptomatic progressive renal allograft dysfunction nine months after renal transplantation. He was worked up as inpatient and allograft biopsy came with a conclusion of viral nephropathy. Further work up for the etiology revealed the viral agent was BK Virus. As renal transplantation is still relatively new to developing countries, this case will highlight clinical feature, diagnosis and treatment options of the condition.

**Keywords:** BK Virus, Kidney Transplantation, Allograft, Nephropathy, Ethiopia

## INTRODUCTION

BK Nephropathy (BKVN) was first described in 1971 in a renal transplant recipient with ureteric stenosis. [1,2,3] It is caused by a DNA virus of the genus polyomavirus and was named after the initials of the first patient in whom the virus was isolated (19). It was not until 20 years later that BK was recognized as a cause of interstitial nephritis and allograft failure in renal transplant recipients (1-3).

BK Virus is a 25 – 45 nm, non-enveloped, double stranded DNA virus from the genus polyomavirus. Seroprevalence ranges 60 – 90 % among adults worldwide. BK Virus is also known for its latency in the genitourinary tract, reactivation during immunosuppression and tropism for the genitourinary tract. It causes a range of clinical syndromes in kidney transplant recipients with higher degree of immunosuppression. The major ones are asymptomatic viruria (with or without viremia), ureteral stenosis and obstruction, interstitial nephritis and allograft BKVN (1-4). The prevalence of BKVN can reach to 10% in transplant recipients.

It can occur as early as the first week and even as late as six years post transplantation (4,6).

BKVN is a cause of allograft dysfunction, not allograft rejection. Identifying one from the other is important as their management is basically opposite. A causal relationship between the two were not identified but their coexistence is well described in the literatures (8,9,12,13). We report a case of BKVN, which was successfully treated with decreasing immunosuppression and Leflunomide.

## CASE SUMMARY

A 25 years old man with end stage renal disease of unknown etiology received a live donor kidney transplant after staying two years on regular hemodialysis. His donor was his haplomatch brother. He had a smooth intra and post-operative courses. He underwent his induction immunosuppressive therapy with Basilixmab based regimen and was discharged with prednisolone, mycophenolate mofetil and tacrolimus.

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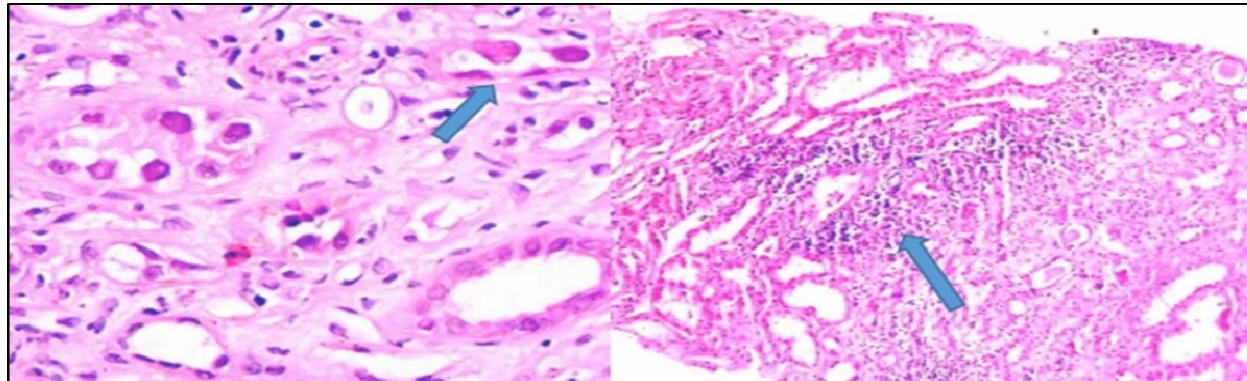
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He was also given miconazole oral gel for fungal prophylaxis, valganciclovir for Cytomegalo Virus (CMV) prophylaxis, trimethoprim-sulfamethoxazole for Pneumocystis pneumonia prophylaxis and isoniazide for tuberculosis prophylaxis dosed as per our transplant center’s protocol.

The first eight months post renal transplant were uneventful. He came with his first abnormal renal function test (serum creatinine – 1.58 mg/dl, Urea – 57 mg/dl) on

December, 2016. He had no symptoms, no abnormal physical findings and no major laboratory additional abnormalities except records of leukopenia ranging from 1500-2900/mm<sup>3</sup>. His tacrolimus level stayed in target range with in the whole course of follow up.

Further deterioration of renal function required further work up as inpatient. Allograft biopsy revealed viral intra nuclear inclusions in the renal tubular cells with interstitial inflammation. (Figure 1).



**Figure 1A:** Basophilic intra nuclear viral inclusions in the renal tubular cells (Arrow).

**Figure 1B:** Focal Interstitial inflammatory cells (Arrow).

Whole blood CMV PCR was negative. Plasma BK virus -DNA-PCR was 7,930,000 copies per ml. With the diagnosis of BK nephropathy(BKVN),patient underwent a month trial of immunologic Containment by discontinuing mycophenolate moefetil and decreasing the dose of tacrolimus to the minimum effective dosage.

After a month BK viral load decreased from 8 million copies to 2 million Copies but seum creatinine level remained in the range of 2.58 – 2.67 mg/dl. Leflunomide tablet at a dose of 20 mg once per day was added. After eight weeks of treatment with Leflunomide, our patient’s renal function started to recover and viral load declined to 40,000 copies per ml (Table 1).

**Table 1:** Patient’s progress as outpatient and in-patient

Date	5/9/16	19/9	20/10	19/11	19/12	27/12	2/1/17	26/1	30/1	2/2	9/2	14/2	16/2	21/4	2/6
WBC			5110	5400	3690	2900	BK DNA PCR 7,930,000	00		1500			6860		6330
Hgb			15.5	10.3		12.4	↓	11.7		13.2					
Pit			286	302	306	274	MMF – D/C Tac – ↓	41		241		BK DNA PCR 2,000,000			BK DNA PCR 40,300
Urea	23	22	34			57		0.3	60	47	82	68	58.4	43	44
Cr	1.16	0.97	1.16			1.59	1.81	2.58	2.13	2.59	2.76	2.6	2.67	2.49	2.02
LFT			N			N	Admitted	1qaz						N	N
Tac level								5.72							6.83
Alb									6.0	5.6	5.6				6.0
FBS								104		97	99				96

## DISCUSSION

Our case is a twenty-five years old man who underwent live kidney donor renal transplantation. He was doing well for the first eight months after transplantation. On the ninth month, allograft dysfunction which required investigations including biopsy revealed BK Viral Allograft Nephropathy. He was successfully treated with immunologic containment and Leflunomide.

Kidney transplantation is still relatively new to developing countries. Here in Ethiopia, we began to give the service almost three years back. As the service continues to expand, post renal transplantation complications will be much more common. We report this case as its one of the typical complications which can be seen after renal transplantation.

As described in the introduction section of this report, BK Virus can cause a range of clinical syndromes in kidney transplant recipients. The major ones are asymptomatic viruria (with or without viremia), ureteral stenosis and obstruction, interstitial nephritis and BKVN (1,2,4). The prevalence of BKVN reaches 10 % in patients with viruria and graft loss can occur in up to 5% of the cases (2,6). The risk factors identified are degree of immunosuppression, extremes of age, male gender, delayed graft function, treatment for acute rejection, HLA or ABO mismatches, and high BK antibody titer in donor with a negative or low BK virus antibody titer in the recipients (4,6).

The commonest presentation is asymptomatic rise in serum creatinine during the first post-transplant year (2,8). The onset may be as early as a week and as late as six years (5,6). Definitive diagnosis requires allograft biopsy which may show characteristic cytopathic changes and positive immunohistochemistry staining using antibodies directed specifically against BK or the cross-reacting SV40 Large-T antigen. Non-invasive tests like BK virus DNA PCR from plasma and decoy cells from urine cytology serve as supportive evidences (1,9,12).

The main pathologic features of BKVN include BK viral intranuclear basophilic inclusions in the tubular cell nuclei and occasionally in the glomeruli parietal epithelium. Focal and demarcated areas of tubulointerstitial inflammations are also features (1,9). The degree of tubular atrophy and interstitial inflammation correlate with outcome (9).

Although histological findings in BKVN could resemble those of rejection, making the correct diagnosis is critically important as treatments for the two conditions is diametrically opposite. In BKVN, reduction rather than augmentation of the immunosuppressive regimen is warranted (1,2,7,11).

A trial of immunologic containment of BK viral replication is the accepted main stay of initial management to be followed by agents that have anti viral activity such as Leflunomide, cidofovir, Intravenous immunoglobulin (IVIg) or flouroquinolones. [8,13,18] Although head-to-head comparative studies between the management options are lacking, Leflunomide has good treatment outcomes in number of studies (2,9,14).

Preemptive treatment which means treating BK viremic patient with stable allograft function, is also another strategy which has shown clear benefit in number of Studies which were done in centers who do plasma screening for the virus after transplantation (15,16).

In this particular case, high index of suspicion, histopathology and serum viral load have played an important role in the diagnosis. Trial of immunologic containment with reduction of immunosuppressive agents has led to significant reduction in the viral load but rather initiation of leflunomide seems to be one responsible for halting allograft function deterioration.

In general, despite treatment, 30-60% of patients with established BKVN show progressive decline in renal function with graft loss (2,5,7,9). But early diagnosis and intervention was shown to result in better prognosis (15,16). Our case is a good example of this.

### Conclusion

This report highlights one of the causes of allograft dysfunction after renal transplantation, which is relatively new modality of treatment in most third world countries. Differentiating BKVN from cellular rejection could be done on that basis of renal biopsy result. Early diagnosis and treatment is essential for better outcome. Preemptive screening with treatment and other cost effective ways of screening are points for further studies.

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### Competing Interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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