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A 29-Year-Old Woman with Kidney Allograft Dysfunction and Dysuria

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Abstract: A case study of a 29-year-old woman who was hospitalized because of kidney allograft dysfunction due to BK virus nephropathy.

Key words: Kidney · Allograft Failure · BK Nephropathy

INTRODUCTION

BK polyomavirus (BKV) has been accepted as being an important human pathogen in immunocompromised populations. BKV particles are small, non enveloped virionswith capsids 40-44 nm in diameter [1]. The infection does not cause illness in healthy individuals despite is highly prevalent (>80% of the world's population is thought to be seropositive for BKV) [2]. The diseases caused by BK virus are tubulo interstitial nephritis(BK -induced nephropathy) and ureteral stenosis in kidney transplant recipients and hemorrhagic cystitis in bone marrow transplant recipients. The prevalence of BK virus induced nephritis in kidney transplant recipients is estimated to be 5% to 8%.When BKVN is advanced (Stages B2-3 and C), outcome is still suboptimal. Early treatment (Stages A and B1) yields better results in terms of graft outcome. Preemptive treatment on the basis of BK viremia seems at present the best option, but screening protocol has to be defined.

Case Report: A 29 years-old woman was admitted to hospital becauseof kidney allograft dysfunction, increasing dysuria and cough. She had received a living kidney donation 8 months earlier, after 3 years of hemodialysis and the early post-transplant course was excellent. The cause of her kidney failure was severe preeclampsia and underlying CKD. Three weeks before admission,she was admitted because of rise of serum creatinine from 1 to 2.24 mg/dl and dysuria at this hospital and because of decrease of serum creatinine from 2.24 to 1.56 mg/dl with methylprednisolone pulse and decreasing cyclosporine dose, the patient was discharged without graft Biopsy. In this admission the patient had a rising of serum creatinine from 1.56 mg/dl to 2.58 mg/dl and increasing of dysuria and nonproductive cough. There were no complaints of febrile episodes, dyspnea, diarrhea, or localized pain and any other symptom. On physical examination, the vital signs were stable and there was not any other finding.

Her drug history wasciclosporine, 250 mg/d, mycophenolatemofetil, 2 g/d and prednisolone, 5 mg/d. Laboratory data were as follows (Table).

The chest x ray was normal (Figure1). On ultrasonographic and Doppler examinations of the allograft, there was no evidence of hydronephrosis. The renal vein was normal and the resistive index was 0.7. Urin Culture was negative.The peripheral blood smear had not schistocyte. Urin BK virus detection by polymerase chain reactive assay was positive. Urine cytology was positive for presence of decoy cells (Figure 1).

An allograft biopsy was taken with the impression of BK virus nephropathy and for ruling out a rejection episode. Examination of biopsy specimens of the patient

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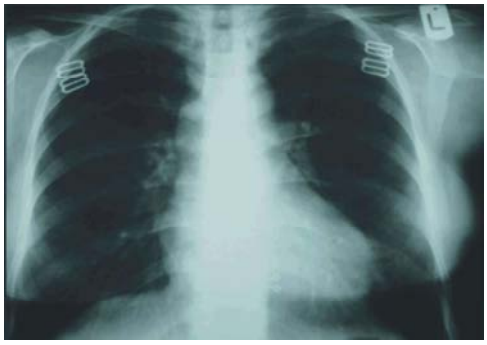
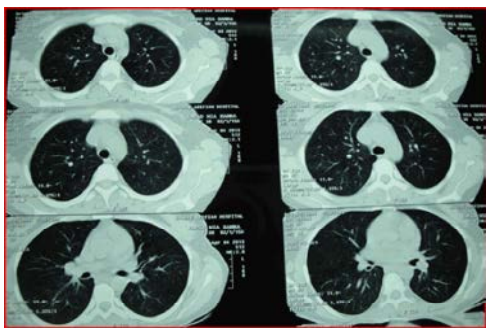
Table:

Laboratory data	3 weeks before admission	At admission
Hematocrite (%)	32.1	32.4
Hemoglubin (gr/dl)	10.4	10.6
WBC	3100	1950
Mean corpuscular volume(µm)	86	84
PLT	166000	116000
Na (mmol/l)	143	141
K	4.3	3.6
Urea (mg/dl)	49	67
Creatinine (mg/dl)	2.21	2.58
Glucose (mg/dl)	148	140
Magnesium (mg/dl)	–	2.55
ALT	13	13
AST	18	19
ALP	–	136
Albumine (mg/dl)	–	3
Uric Acid	–	5
TG	–	142
Cholestrol	–	135
LDH	–	725
CPK	–	46
P	2	1.79
Urinalysis	Pr=+1/ RBC=7-8/ WBC=3-4 Bac=Few	Pr=Trace/ RBC=20-25 WBC=2-3/ Bac= Neg

revealed patchy infiltration and flattening of the epithelial cells and denudation of the basement membrane along with flattening of the lining epithelium, bulging of epithelium tubular cells inside the tubules and cytopathic changes and nuclear enlargement. (Figures 2, 3).





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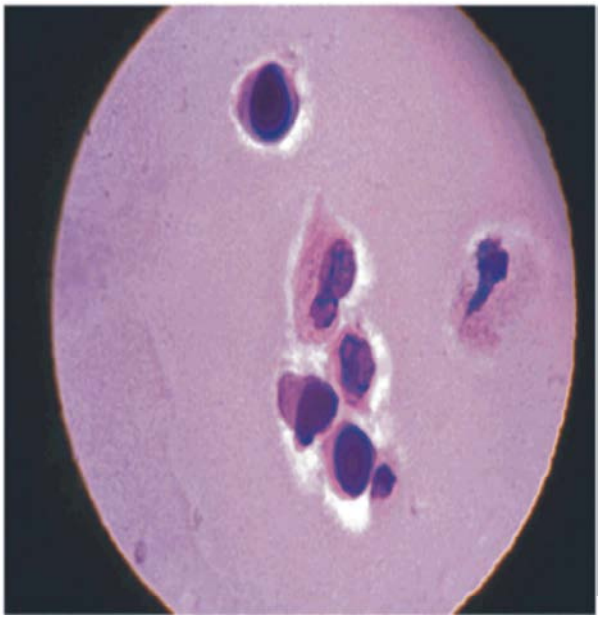

Fig 1: Detection of Decoy Cells Has a Sensitivity Close to 100 % but the Positive Peredictive Value Is 20%. The Predictive Value Increases If More than 10 Decoy Cells per High-power Field and Decoy Cell Cast Is Detected. Decoy Cell Can Be Seen in JC. BK Cytomegalovirus and Adenovirus Infections and Sometimes Resemble Shedding Cells in Renal Cell Carcinoma.

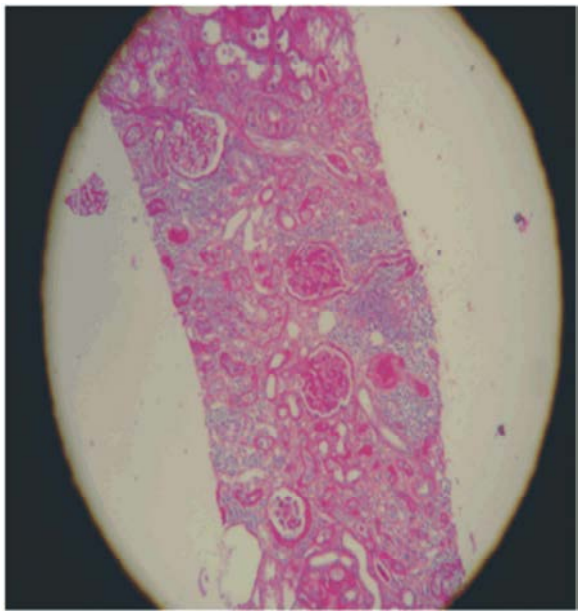

Fig 2: Patchy in Filtration and Flattening of Tubular Epithelial Cells.

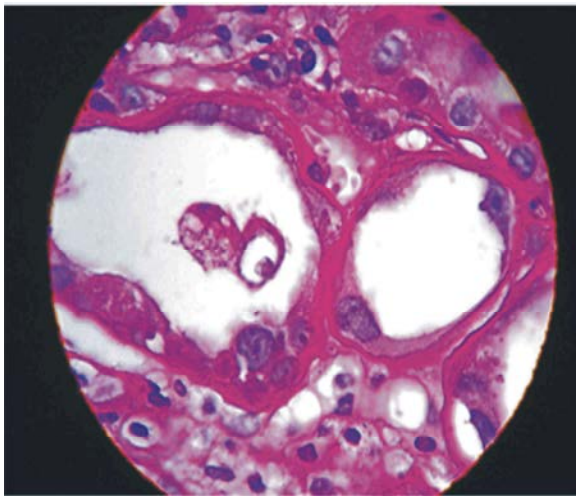

Fig 3: Viral Cytopathic Changes and Flattening and Denudation of Tubular Basement Membrane.

With difintive diagnosis of BKV nepropathy, her drugs was changed to Rapamun 1 mg daily, MMF 500 mg daily, Ciprofloxacin 500 mg daily and prednisolon 10 mg daily. After 12 months of follow up the patint's Cr was 1.7 to 1.8 mg/dl.

DISCUSSION

BKV particles, similarly to other human polyomaviruses, are small, non enveloped virions with icosahedral capsids 40-44 nm in diameter [1]. Although the virus is highly prevalent, the infection does not cause illness in healthy individuals [2]. The major diseases caused by BK virus are tubulointerstitial nephritis (The prevalence is estimated to be 5% to 8%) and ureteral stenosis in kidney transplant recipients and hemorrhagic cystitis in bone marrow transplant recipients. The patients should undergo screening for BKV every time an unexplained rise in serum creatinine occurs and after treatment for acute rejection [3]. There are multiple screening tests for detection of BK virus. Examination of urine sediment for decoy cells is an inexpensive test, but decoy cells are neither sensitive nor specific for BK virus infection, because they can be confused with other viruses such as cytomegalovirus and adenovirus (Positive predictive value, 20%). The positive predictive value increased by: decoy cells with allograft dysfunction, extended and persistent shedding (>6weeks) [4]. Thus, the absence of decoy cells does not rule out the disease [5]. The presence of BK virus DNA in plasma (More than 10 000 copies per milliliter) and urine (More than 10^7 copies per milliliter) as examined with polymerase chain reaction assay was associated with a sensitivity and specificity of 100% and 88%, respectively, for diagnosis of BK virus nephropathy [6]. If one of the above tests is positive, kidney allograft biopsy should be obtained to diagnose BK-induced nephropathy definitely [7]. A plasma viral titer greater than 10 000 copies per milliliter is presumptive of BK virus nephropathy, even in the absence of histologic evidence on biopsy [8]. Since specific antiviral therapy does not currently exist, the cornerstone of therapy is to decrease immunosuppressive medication [9]. In a study on 24 patients [10], reduced doses of mycophenolatemofetil and tacrolimus resulted in a successful elimination of viremia in a mean period of 6 months and improved allograft survival in 23 patients at a mean follow-up period of 31 months. Reduction in immunosuppressive therapy resulted in development of acute rejection in 3 patients. After a mean follow-up period of 43.5 months, all of the 24 patients were alive and 23 had a functioning graft. Seventeen patients had stable or improved graft function [11]. Replacingacalcineurin inhibitor with rapamycin with or without discontinuation of the antimetabolite has the advantage of avoiding the long-term calcineurin inhibitor-related nephrotoxic effect [12]. Lowering the dose of the calcineurin inhibitor may slow down the loss of kidney function [13]. There are several drugs that may have efficacy against BK-induced nephropathy [14]. Ciprofloxacin (A quinolone antibiotic) may have anti-BK virus effects. In one study on patients with hematopoietic

stem cell transplantation, administration of standard-doseciprofloxacin was associated with decreased urinary BK viral load [15]. In a single-center study of 8 affected patients, a reduction of immunosuppressiondose plusintravenous immunoglobulin saved allograft in 7 patients after a 15-month follow-up [16]. There is suggestive evidence of efficacy of leflunomide in BK-induced nephropathy (Unclear mechanism) [17]. Cidofovir is another drug that may have efficacy against BK-induced nephropathy. Cidofovir should only be used when all other interventions have failed after a period of 3 month. Recently, a lipid-bound cidofovir is being developed that may make cidofovir safer and more effective [19]. Overall, the initial management of BK-induced nephropathy is immunosuppressive dose reduction and in those with no response, antiviral therapy may be indicated [20]. Preemptive treatment on the basis of BK viremia seems at present the best option, but screening protocol has to be defined. Early treatment (Stages A and B1) yields better results in terms of graft outcome. When BKVN is advanced (Stages B2-3 and C), outcome is still suboptimal. The urine/plasma viral load should be monitoring per 2-4 weeks and therapeutic intervention should be guided by plasma DNA levels. In case of failure to reduce viral load or, when immunosuppression reduction is contraindicated, the administration of cidofovir and/or the surgical removal of the alloureter and kidney could be considered.

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REFERENCES

1. Imperiale, M.J. and E. O. Major, 2007. In Fields Virology (Edsknipe, D.M. andHowley, P.M.) 2263-2298 (Lippincott Williams and Wilkins, Philadelphia).
2. Goudsmit, J., 1982. The role of BK virus in acute respiratory tract disease and the presence of BKV DNA in tonsils. J. Med. Virol., 10: 91-99.
3. KDIGO, 2009. Clinical practice guideline for the care of kidney transplant recipients. Am. J. Transplant., 9(Suppl. 3): S44-S58.
4. Nickeleit, V., 2002. BK virus infection after kidney transplantation. Graft, 5(DecemberSuppl): S46-S57.
5. Hirsch, H.H., W. Knowles and M. Dickenmann, 2002. Prospective study of polyomavirus type BK replication and nephropathy in renal-transplant recipients. N Engl J Med, 347: 488-96.
6. Costa, C., M. Bergallo and S. Astegiano, 2008. Monitoring of BK virus replication in the first year following renal transplantation. Nephrol Dial Transplant, 23: 3333-6.
7. Hirsch, H.H., D.C. Brennan and C.B. Drachenberg, 2005. Polyomavirus-associated nephropathy in renal transplantation: interdisciplinary analyses and recommendations. Transplantation, 79: 1277-86.
8. Hirsch, H.H., D.C. Brennan and C.B. Drachenberg, 2005. Polyomavirus-associated nephropathy in renal transplantation: interdisciplinary analyses and recommendations. Transplantation, 79: 1277-86.
9. Celik, B., R. Shapiro, A. Vats and P.S. Randhawa, 2003. Polyomavirusallograft nephropathy: sequential assessment of histologic viral load, tubulitis and graft function following changes in immunosuppression. Am J Transplant, 3: 1378-82.
10. Saad, E.R., B.A. Bresnahan and E.P. Cohen, 2008. Successful treatment of BK viremia using reduction in immunosuppression without antiviral therapy. Transplantation., 85: 850-4.
11. Mantyjarvi, R.A., P.P. Arstila and O.H. Meurman, 1972. Hemagglutination by BK virus, a tentative new member of the papovavirus group. Infect Immun., 6: 824-8.
12. Wali, R.K., C. Drachenberg and H.H. Hirsch, 2004. BK virusassociated nephropathy in renal allograft recipients: rescue therapy by sirolimus-based immunosuppression. Transplantation, 78: 1069-73.
13. Vasudev, B., S. Hariharan, S.A. Hussain, Y.R. Zhu, B.A. Bresnahan and E.P. Cohen, 2005. BK virus nephritis: risk factors, timing and outcome in renal transplant recipients. Kidney Int., 68: 1834-9.
14. Josephson, M.A., J.W. Williams, A. Chandraker and P.S. Randhawa, 2006. Polyomavirus-associated nephropathy: update on antiviral strategies. Transpl Infect Dis, 8: 95-101.
15. Leung, A.Y., M.T. Chan and K.Y. Yuen, 2005. Ciprofloxacin decreased polyoma BK virus load in patients who underwent allogeneic hematopoietic stem cell transplantation. Clin Infect Dis, 40: 528-37.
16. Sener, A., A.A. House and A.M. Jevnikar, 2006. Intravenous immunoglobulin as a treatment for BK virus associated nephropathy: one-year follow-up of renal allograft recipients. Transplantation., 81: 117-20.

17. Chong, A.S., H. Zeng and D.A. Knight, 2006. Concurrent antiviral and immunosuppressive activities of leflunomide in vivo. Am J Transplant, 6: 69-75.
18. Josephson, M.A., D. Gillen and B. Javaid, 2006. Treatment of renal allograft polyoma BK virus infection with leflunomide. Transplantation, 81: 704-10.
19. Kuypers, D.R., A.K. Vandooren and E. Lerut, 2005. Adjuvant low-dose cidofovir therapy for BK polyomavirus interstitial nephritis in 2005 renal transplant recipients. Am J Transplant., 5: 1997-2004.
20. Vandercam, B., M. Moreau, E. Goffin, J.C. Marot, J.P. Cosyns and M. Jadoul, 1999. Cidofovir-induced end-stage renal failure. Clin Infect Dis, 29: 948-9.