Abstract: Renal transplant recipients are at increased risk of viral infections. There are few case reports of adenovirus infection following renal transplantation in literature. Here we report a case of adenovirus in a second renal transplant recipient who presented with graft dysfunction and hematuria. This case has been reported to highlight the presentation of adenovirus infection in a renal transplant recipient.

Keyword: adenovirus, renal transplantation

Introduction

Adenovirus is a common pathogen that has the potential to cause opportunistic infections with significant morbidity and mortality in immunocompromised hosts. The typical manifestations are haemorrhagic cystitis and tubulointerstitial nephritis. There are no guidelines on monitoring and treatment of adenovirus following renal transplantation. This case highlights the need to consider adenovirus as a cause for hematuria and graft dysfunction.

Case report

We report Miss M a 32 year old woman who had undergone a living related renal transplantation in 2009 with paternal aunt as the donor. Her native kidney disease was biopsy proven Focal segmental sclerosis since 2002. She had lost her graft in first month itself. The transplant was done elsewhere. Exact details of post-transplant status and cause of graft loss was not known. She had been on maintenance hemodialysis since June 2009. She underwent deceased donor renal transplantation in September 2014. She received standard immunosuppression with tacrolimus, mycophenolate, and prednisone. Induction therapy was given with two doses of basiliximab. She had delayed graft function and required a brief dialysis support. She was on valganciclovir prophylaxis. She had hematuria from day 11 and then developed diarrhoea. She had loss of appetite and weight. Upper GI endoscopy was done and a biopsy was taken from a tiny ulcer in distal oesophagus. In view of her second transplant and ulcer in oesophagus CMV PCR and PP65 were done and were negative. The biopsy was stained for CMV and was negative. Plasma BKV DNA was negative. Her output gradually improved and her creatinine got stabilised at 2mg/dl. Her ultrasound abdomen was normal. The DJ stent was removed at day 33 and CT scan abdomen done in view of persistent hematuria was normal. Renal biopsy was not done. Her symptoms of dyspepsia, intermittent diarrhoea and hematuria persisted. She was treated with broad spectrum antibiotics and symptomatic measures. All work-up for diarrhoea was negative. In view of persistent hematuria adenovirus infection was thought of and urine PCR for adenovirus was sent. Urine adenovirus PCR was positive. MMF was stopped, steroid dose tapered to 20 mg OD and tacrolimus was continued as 4mg/day (C0-2ng/ml). Two months post-transplant her creatinine was 0.9mg/dl and after three months post-transplant her tacrolimus dose was increased and MMF was added. She is on regular follow-up with normal graft function.

Discussion

Our case report highlights a case of adenovirus infection post renal transplantation. She is a second renal transplant recipient who presented in the immediate post-transplant period with diarrhoea, hematuria and graft dysfunction. The classical time table of post-transplant infections does not apply to her as she was already immunosuppressed. The presentations of adenovirus includes fever, graft dysfunction, hematuria, diarrhoea, acute renal failure including interstitial nephritis and obstructive uropathy. The renal manifestations of adenovirus are shown in table. Renal biopsy was not done in our case since the diagnosis was strongly corroborated the diagnosis in our case. A renal biopsy is essential to demonstrate adenovirus nephritis and rule out other causes for graft dysfunction. Pathological findings in the renal allograft associated with adenovirus infection consist of tubular cell necrosis with viral cytopathic effects: nuclear enlargement, peripheral condensed chromatin and basophilic nuclear inclusions representing viral particles. The tubular cell abnormalities are associated with severe interstitial inflammation with lymphocytes, plasma cells and neutrophils. The main differential diagnosis of adenovirus interstitial nephritis is acute rejection which is differentiated by viral cytopathic effects, intimal arteritis and presence of c4d. Electron microscopy shows the typical 70–80 nm diameter adenoviral particles within the nuclei and cytoplasm of tubular epithelial cells. PCR techniques are reproducible and sensitive diagnostic tools providing reliable results and high detection rates. Adenovirus-PCR appears to be superior to direct adenovirus isolation from organs or body fluids in early diagnosis of adenovirus infection after transplantation. Adenovirus was detected in urine PCR in our case.
patient. Positive Adenovirus-PCR might also represent latent infection or subclinical reactivation. Therefore, interpretation of results always requires careful assessment of the patient's clinical state and the likelihood of adenovirus as a causative agent. 

There are no guidelines for management and monitoring of adenovirus post renal transplantation. Immunosuppression reduction is the mainstay of treatment as T-cell mediated immunity plays a major role in adenovirus infections. The optimal immunosuppressive strategy or regimen is unknown due to paucity of data. The immunosuppression reduction strategy consists of reduction in MMF to discontinuation of all medications. In our case we discontinued MMF and continued tacrolimus without increasing dose even when C0 level was only 2ng/ml and low dose steroids. Any reduction needs to be balanced against rejection as she was in her early post-transplant period.

The role of antiviral therapy in adenovirus infection is unknown. Cidofovir is used as the standard treatment for adenovirus infection in many centres in spite of its nephrotoxicity and and neutropenia. Ribavirin despite having activity against adenovirus is not used now. Hypogammaglobulinemia is a risk factor for adenovirus infection and IV immunoglobulin had been used in some centres. Previous data have shown that MMF-containing immunosuppressive regimens are more prone to induce hypogammaglobulinemia than regimens employing azathioprine-containing regimens. Hence we stopped MMF in our patient.

**Conclusion**

This case report highlights the importance of adenovirus in renal transplant recipients. Adenovirus infection should be considered in the differential diagnosis of patients presenting with graft dysfunction and hematuria. A high index of suspicion for adenovirus is warranted in these patients and re-establishing immunocompetence is the mainstay of therapy.

**References**
