CEN Case Rep (2016) 5:1–4
DOI 10.1007/s13730-015-0179-9

CASE REPORT

BK virus-induced acute motor-axonal polyneuropathy in a renal transplant patient

Hulya Taskapan[1] · Uner Kayabas[2] · Baris Otlu[3] · Ozden Kamisli[4] · Cisel Yilmaz Yaprak[1] · Fatma Terzioglu Sahin[1]

Received: 17 November 2014 / Accepted: 1 April 2015 / Published online: 19 April 2015

Abstract Neurological complications are not uncommon in patients with renal transplantation, mostly affecting the central nervous system, and less frequently the peripheral nerves. BK virus infection is relatively common in transplant recipients and in some cases may lead to neurological complications. In this report, we present an interesting case of a patient who developed acute axonal motor polyneuropathy in the course of BK virus infection 3 months after kidney transplantation. After BK virus clearance in blood, a significant improvement was noted in her polyneuropathy. In patients with acute axonal motor polyneuropathy after transplantation BK virus-induced polyneuropathy should be excluded.

Keywords BK virus · Renal transplantation · Neuropathy

Introduction

Neurologic complications are not uncommon in renal transplant recipients, mostly affecting the central nervous system, and less frequently the peripheral nerves. Post-transplant neurological complications can be seen because of adverse events of immunosuppressive drugs, vascular complications (e.g., stroke), infections, and malignancies [1]. Neurotoxicity can be a serious complication due to the immunosuppressive regimen after renal transplantation. About 10–30 % of patients who are treated with calcineurin inhibitors (CNIs) develop some form of neurotoxicity such as tremors, paraesthesias, and acute polyneuropathy [2, 3]. Several viral infections such as cytomegalovirus (CMV), herpes zoster, herpes simplex, human T-lymphotropic virus-1 (HTLV-I), Poliovirus, Entrovirus, Echovirus, Cocksackie B, Cocksackie A can cause neurological complications in renal transplantation patients [1].

Here, we report a renal transplant recipient who presented with diminished strength in her lower limbs due to BK virus replication leading to acute axonal motor polyneuropathy, which resolved after BK virus clearance in blood. A special focus is given to alert clinicians to the possibility of this association during the differential diagnosis of neurological complications in patients with renal transplantation.

Case

A 52-year-old woman who received a renal transplant from non-related living donor in Egypt 3 months ago for renal failure due to unknown etiology was admitted to Nephrology outpatient clinic because she was unable to stand up and walk. She had been on peritoneal dialysis for 12 years prior to her transplantation.

It was learned that she was hospitalized in-patient clinic of Neurology Department with diminished strength in her lower limbs and difficulty in walking independently

✉ Hulya Taskapan
hulyataskapan@yahoo.com

[1] Department of Nephrology, Turgut Ozal Medical Center, Medical Faculty, Inonu University, Malatya, Turkey

[2] Department of Infectious Diseases and Clinical Microbiology, Turgut Ozal Medical Center, Medical Faculty, Inonu University, Malatya, Turkey

[3] Department of Clinical Microbiology, Turgut Ozal Medical Center, Medical Faculty, Inonu University, Malatya, Turkey

[4] Department of Neurology, Turgut Ozal Medical Center, Medical Faculty, Inonu University, Malatya, Turkey

15 days ago and she was discharged on day ago. In her history the patient noticed pain and numb finger tips and toes for 1 week prior to hospitalization in in-patient clinic of Neurology Department. Pain and numbness slowly progressed towards entire lower legs. She noticed diminished strength in her legs. She could not walk independently when she was admitted to Neurology Clinic. There were no disturbances in defaecation or micturition. On admission to the Neurology clinic the patient was on tacrolimus 1 mg twice/day, mycophenolate mofetil 1000 mg twice/day and prednisone 5 mg once/day.

At the Neurology Clinic neurologic examinations revealed hypoactive deep tendon reflexes. Her cranial nerves were intact. The power in proximal and distal muscles in upper limps was normal. The power in proximal and distal muscles in lower limbs was grade 3/5 and 4/5, on the right and left limps, respectively. Deep tendon jerks were absent and the plantar response was flexor. A paresis of legs (more prominent on the distal than proximal) was found.

On admission to the Neurology Clinic laboratory tests revealed hemoglobin, 10.5 g/dL; platelet count, $228 \times 10^3/mm^3$; creatinine, 1.19 mg/dL; urea, 24 mg/dL; sodium, 134 mmol/L; potassium, 4.8 mmol/L; calcium, 11 mg/dL; phosphorus, 2.4 mg/dL, her blood glucose level was 144 mg/d. Tacrolimus level was 3 ng/mL. Vitamin B12 225 pg/mL, HBA_1C 5.2 %.

Electromyography with a nerve conduction study revealed axonal dominant motor and sensory polyneuropathy. The patient was diagnosed as acute motor-axonal polyneuropathy.

Her initial immunosuppressive regimen consisted of tacrolimus and corticosteroids, with mycophenolate mofetil. The patient was converted to rapamycin due to possibility of new-onset neurotoxicity. She was treated with five sessions of plasma exchange over the course of 10 days. Despite the conversion of oral tacrolimus to rapamycin, and plasma exchange her muscular weakness did not improve, the loss of strength was still progressive. She was discharged.

Next day the patient was admitted to Nephrology Clinic. She reported further decline in motor strength and inability to stand up.

On examination her cranial nerves were intact. The deep tendon reflexes were symmetrically diminished in her lower limps. The muscle force grading was 2/5 in her both lower limbs. A paresis of legs was found.

On the admission at the Nephrology Clinic Laboratory tests revealed hemoglobin, 9.9 g/dL; platelet count, $156 \times 10^3/mm^3$; creatinine, 1.2 mg/dL; urea, 13 mg/dL; sodium, 136 mmol/L; potassium, 3.6 mmol/L; calcium, 10.6 mg/dL; phosphorus, 2.5 mg/dL, her blood glucose level was 136 mg/dL. C reactive protein 1.06 mg/dL. Her serum rapamycin level was 7 ng/mL.

Cytomegalovirus (CMV) serum polymerase chain reaction (PCR) was negative. The patient's serum was tested for viruses Epstein–Barr virus (EBV), hepatitis B and C, herpes simplex virus, human herpes virus 1 and 2, parvo B19, human immunodeficiency virus (HIV). Serology against all these organisms was negative. Anti-nuclear antibodies were negative. BK virus polymerase chain reaction was positive (14.737 copies/mL). BK Virus DNA was extracted from blood with the EZ1 automated extraction system (EZ1 Virus mini kit v2.0, Qiagen, Hilden, Germany) and detection by real-time polymerase chain reaction (Artus BK PCR QS-RGQ, V1 Kit, Qiagen, Germany).

Cranial tomography was normal. A magnetic resonance imaging of the spine revealed mild degenerative cervical spine disease without evidence of spine compression. We could not perform spinal tap.

We reduced mycophenolate mofetil as 500 mg twice daily. The patient was treated with intravenous immunoglobulin (IVIG 1 g/kg) for 8 days and ciprofloxacin 500 mg twice a day. One week later, significant improvement was noted in her muscular weakness. Clinical improvement in strength was evident during the follow-up. Fifteen days later viral load for BKvirus DNA was reported positive as less than 100 copies/ml. There was no deterioration of graft function or urinary tract symptoms such as dysuria or any leucocytosis in urine during the follow-up.

At 15 days following IVIG, the patient had mild residual weakness in the lower extremities, and was able to walk with minimal assistance. One month later, BK virus was undetectable on blood PCR. Two months later she was completely normal.

Discussion

Our patient developed an acute progressive axonal paraparesis with electrodiagnostic evidence of polyneuropathy. Her strength improved after clearance of BK viremia. Since the symptoms significantly improved after BK virus elimination, BK virus-induced polyneuropathy or BK virus seems to be the most probable cause of muscle weakness in the present report.

It has been suggested that high levels of tacrolimus may contribute to an early onset of neurotoxicity, but can occur with normal levels [2, 3]. Unfortunate, our patient did not improve after tacrolimus was replaced by rapamycin. Switching to CIN-free immunosuppression, for example, sirolimus and mycophenolate mofetil, might have been equally or more effective alternative to manage tacrolimus-induced neurotoxicity [2–4].

Recently, an increasing body of evidence favors the possible neurotropism of BKV, since BKV DNA has been

detected in the brain tissue and cerebrospinal fluid (CSF) of both immunocompetent and immunocompromised individuals (mostly adults) with or without neurological symptoms in addition to the JC virus (the other member of the same family known to be strongly neurotropic and responsible for the progressive multifocal leukoencephalopathy) [5–8]. We could not test for JC virus in this patient. However, we regularly perform polymerase chain reaction test for BK virus as a routine follow-up during the first year of transplantation. We detected that BK virus polymerase chain reaction was positive (14.737 copies/mL), whereas previous BK virus polymerase chain reaction had been negative in this patient.

Primary asymptomatic BK virus infection usually occurs during childhood via the respiratory tract. The infection is usually asymptomatic. However, latent infection is established in renal epithelial cells and possibly other tissues (including brain, since BK virus DNA has been detected in the brain tissues from normal subjects) with most individuals having antibodies to BK virus. Reactivation may subsequently occur in immunocompromised and healthy individuals, but may be more likely if there is an impairment of the immune function (patients with T cell deficiencies). Subsequent viral reactivation, particularly in immunocompromised patients, may present as hemorrhagic cystitis, ureteric stenosis, tubulointerstitial nephritis, retinitis, encephalitis, and pneumonia [5–8].

BK virus is an emerging problem in renal transplantation with the advent of newer, more potent immunosuppressive regimens. It is observed mainly in patients receiving a combination of tacrolimus and MMF. Encephalitis due to BK virus is a rare and emerging condition with most cases being reported in patients with acquired immunodeficiency syndrome (AIDS) or after transplantation [5–8].

The mainstay of treatment for BK virus replication is to decrease the immunosuppression, as there is currently no specific anti-viral for BK virus. Several agents have been putatively used in treatment, including ciprofloxacin, intravenous immune globulin, leflunomide and Cidofovir [9–12].

Reduction in immunosuppression results in a significant increase in BK virus-specific IgG antibody titers, emergence of BK virus-specific cellular immunity, clearance of viremia [9, 10]. In our patients we reduced the dosage of the immunosuppression. We started ciprofloxacin and IVIG. Quinolones are antibacterial drugs that are DNA gyrase inhibitors. The proposed mechanism of action in BK virus treatment is interference with large T antigen helicase activity for BK virus both in vivo and in vitro [11, 12]. IVIG has immunomodulatory properties and has been shown to contain polyomavirus-reactive antibodies [13]. It seems that clearance of BK viremia can be indicative of neuropathy resolution. The exact pathogenesis by which the virus causes the disease is not clear. The involvement of the central nervous system in the viral disease could be due to direct invasion of the central nervous system by the virus. Therefore, it seems most likely that transport of antibodies occurs across a disrupted blood–nerve barrier during inflammatory reaction of nerve roots. A cross-reaction between Schwann cells, myelin or other peripheral nerve antigens remains a possibility.

The main limitation in the present report is the lack of documentation of spinal nerve involvement with BK virus. However, the presence of high titre viral DNA in the blood, immunosuppression, and absence of other alternative diagnosis strongly favor the diagnosis of BK virus-induced polyneuropathy.

As far as we know, this is the first report of such an association in a renal transplant patient. Physicians should be aware of polyneuropathy due to BK virus and test for BK virus. Thus, an early diagnosis and a quick restoration of immunity, by limiting viral replication, is currently the most effective way to control the disease.

Conflict of interest There is no conflict interest.

References

1. Ponticelli C, Campise MR. Neurological complications in kidney transplant recipients. J Nephrol. 2005;18:521–8.
2. Patel MK, Rashed A, Mesraoua B, Khaddash S, Romeh SA. Cyclosporine neurotoxicity presenting as an unilateral foot drop in a renal transplant patient. Nephron. 1991;58:116.
3. Chegounchi M, Hanna MG, Neild GH. Progressive neurological disease induced by tacrolimus in a renal transplant recipient: case presentation. BMC Nephrol. 2006;7:7.
4. Kaczmarek I, Schmauss D, Sodian R, Beiras-Fernandez A, Oberhoffer M, Daebritz S. Late-onset tacrolimus-associated cerebellar atrophia in a heart transplant recipient. J Heart Lung Transplant. 2007;26:2–89.
5. Boothpur R, Brennan DC. Human polyoma viruses and disease with emphasis on clinical BK and JC. J Clin Virol. 2010;47:306–12.
6. Vallbracht A, Löhler J, Gossmann J, Glück T, Petersen D, Gerth HJ, Gencic M, Dörries K. Disseminated BK type polyomavirus infection in an AIDS patient associated with central nervous system disease. Am J Pathol. 1993;143:9–29.
7. Voltz R, Jäger G, Seelos K, Fuhry L, Hohlfeld R. BK virus encephalitis in an immunocompetent patient. Arch Neurol. 1996;53:101–3.
8. Bratt G, Hammarin AL, Grandien M, Hedquist BG, Nennesmo I, Sundelin B, Seregard S. BK virus as the cause of meningoencephalitis, retinitis and nephritis in a patient with AIDS. AIDS. 1996;13:1071–5.
9. Hirsch HH, Mohaupt M, Klimkait T. Prospective monitoring of BK virus load after discontinuing sirolimus treatment in a renal transplant patient with BK virus nephropathy. J Infect Dis. 2001;184:1494–5.
10. Ramos E, Drachenberg CB, Papadimitriou JC, Hamze O, Fink JC, Klassen DK, Drachenberg RC, Wiland A, Wali R, Cangro CB, Schweitzer E, Bartlett ST, Weir MR. Clinical course of

polyoma virus nephropathy in 67 renal transplant patients. J Am Soc Nephrol. 2002;13:2145–51.
11. Leung AY, Chan MT, Yuen KY, Cheng VC, Chan KH, Wong CL, Liang R, Lie AK, Kwong YL. Ciprofloxacin decreased polyoma BK virus load in patients who underwent allogeneic hematopoietic stem cell transplantation. Clin Infect Dis. 2005;40:528–33.
12. Randhawa PS. Anti-BK virus activity of ciprofloxacin and related antibiotics. Clin Infect Dis. 2005;41:1366–7.
13. Sener A, House AA, Jevnikar AM, Boudville N, McAlister VC, Muirhead N, Rehman F, Luke PP. Intravenous immunoglobulin as a treatment for BK virus associated nephropathy: one-year follow-up of renal allograft recipients. Transplantation. 2006;81:117–20.