Archived at the Flinders Academic Commons:
http://dspace.flinders.edu.au/dspace/

‘This is the peer reviewed version of the following article:
Nayar, S., Pawar, B., Einsiedel, L., Fernandes, D., George, P.,
Associated With Human T-Lymphotropic Virus Type 1
Infection in a Renal Transplant Patient From Central
Australia: A Case Report. Transplantation Proceedings,
50(10), 3940–3942. https://doi.org/10.1016/
j.transproceed.2018.08.031

which has been published in final form at
https://doi.org/10.1016/j.transproceed.2018.08.031

© 2018 Elsevier Inc. This manuscript version is made
available under the CC-BY-NC-ND 4.0 license:
http://creativecommons.org/licenses/by-nc-nd/4.0/
A case report: Isolated neurogenic bladder associated with human t-lymphotropic virus type 1 infection in a renal transplant patient from central Australia.

Sajith Nayar, Basant Pawar, Lloyd Einsiedel, David Fernandes, Pratish George, Sajan Thomas, Cherian Sajiv

PII: S0041-1345(18)30751-6
DOI: 10.1016/j.transproceed.2018.08.031
Reference: TPS 28745
To appear in: Transplantation Proceedings
Received Date: 8 June 2018
Revised Date: 23 July 2018
Accepted Date: 29 August 2018


This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
A CASE REPORT: ISOLATED NEUROGENIC BLADDER ASSOCIATED WITH HUMAN T-LYMPHOTROPIC VIRUS TYPE 1 INFECTION IN A RENAL TRANSPLANT PATIENT FROM CENTRAL AUSTRALIA.

1. Sajith Nayar (Corresponding Author): Central Australian Renal Services, Alice Springs Hospital, 6 Gap Road, The Gap, Northern Territory, Australia 0870. Email: sajith.nayar@nt.gov.au Phone no: +61423400501.

2. Basant Pawar: Central Australian Renal Services, Alice Springs Hospital, 6 Gap Road, The Gap, Northern Territory, Australia 0870. Email: Basant.pawar@nt.gov.au

3. Lloyd Einsiedel: Flinders University/Northern Territory Rural Clinical School, Alice Springs Hospital, 0870 Northern Territory, Australia. Email: Lloyd.Einsiedel@nt.gov.au

4. David Fernandes: Central Australian Renal Services, Alice Springs Hospital, 6 Gap Road, The Gap, Northern Territory, Australia 0870. Email: David.fernandes@nt.gov.au

5. Pratish George: Central Australian Renal Services, Alice Springs Hospital, 6 Gap Road, The Gap, Northern Territory, Australia 0870. Email: Pratish.George@nt.gov.au

6. Sajan Thomas: Central Australian Renal Services, Alice Springs Hospital, 6 Gap Road, The Gap, Northern Territory, Australia 0870. Email: sajan.thomas@nt.gov.au

7. Cherian Sajiv: Central Australian Renal Services, Alice Springs Hospital, 6 Gap Road, The Gap, Northern Territory, Australia 0870. Email: Cherian.sajiv@nt.gov.au
ISOLATED NEUROGENIC BLADDER ASSOCIATED WITH HUMAN T-LYMPHOTROPIC VIRUS TYPE 1 INFECTION IN A RENAL TRANSPLANT PATIENT FROM CENTRAL AUSTRALIA.

Introduction

Human T cell Lymphotropic virus type 1(HTLV-1) is a retrovirus affecting 15–20 million people worldwide (1). The virus is endemic to South Western Japan(2), the Caribbean islands(3), sub-Saharan Africa(4), parts of South America, Middle East and Oceania. HTLV-1 is predominately transmitted during breast-feeding, sexual intercourse and blood transfusions. Central Australia has the highest reported adult prevalence of HTLV-1 infection in the world; exceeding 40% in remote communities where surveys have been performed (5). Common disease associations of HTLV-1 infection in Central Australia are bronchiectasis, blood stream infections, lower respiratory tract infections and strongyloidiasis (6). Three cases of adult T cell leukaemia/lymphoma (ATL) and 4 cases of HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) have been reported (7). In solid organ transplantation only 13 cases of HAM/TSP have been reported worldwide (8). A HTLV-1 proviral load greater than 1000 per 10^5 peripheral blood leukocytes is strongly associated with an increased risk and progression of HAM/TSP (9, 10).

This is probably the first case report of isolated neurogenic bladder without features of HAM/TSP, attributable to HTLV-1 infection in an Aborigine renal allograft recipient.

Case report

A 50-year-old Indigenous woman from Alice Springs was treated with haemodialysis for five years, for chronic kidney disease secondary to diabetic nephropathy following which she received a cadaveric renal transplantation in 2014. There were 5 out of 6 antigens mismatches. There were no pre-existing Class 1 or II antibodies detected. She did not have features of autonomic dysfunction and did not have lower urinary tract symptoms prior to transplantation. Immunosuppression was induced with basiliximab and maintained with mycophenolate mofetil, tacrolimus and prednisolone along with
standard CMV and Pneumocystis jiroveci pneumonia (PJP) prophylaxis. She had serological evidence of HTLV-1, Cytomegalovirus (CMV) and Epstein Barr Virus (EBV) infection prior to transplantation. She had chronic hepatitis B with Core antibodies present, HBV DNA by PCR was not detected and strongyloides serology was negative. The donor was not tested for HTLV-1. She had delayed allograft function. A day 13 renal allograft biopsy showed acute tubular necrosis with no evidence of acute rejection.

A week after transplantation, an ultrasound examination showed post void residual urine volume of 220 mls, with mild graft hydronephrosis. This was complicated by recurrent urinary tract infections (UTI) with extended spectrum beta lactamase (ESBL) producing Escherichia coli and graft dysfunction. Urodynamic studies were performed a month after transplantation revealing features of stress incontinence and detrusor overactivity, with no intrinsic urethral sphincter deficiency. These abnormalities persisted over the next six months. Her diabetes was adequately controlled. Four months after transplantation CMV DNA levels were 9390 copies/ml during, which improved with valgancyclovir. Pre-transplantation the HTLV-1 proviral load was 947.2 copies per 10^5 peripheral blood leucocytes. This increased to 6152.04 copies per 10^5 peripheral blood leucocytes 7 months after transplantation. There was CSF lymphocytic pleocytosis with mainly small lymphocytes with mildly elevated CSF protein (0.57 g/L; normal range, 0.15-0.45g/L) and normal CSF glucose levels (3.1 mmol/L; normal range, 2.7-4.2 mmol/L). The cerebrospinal fluid (CSF) proviral load was 46,400 copies per 10^5 peripheral blood leucocytes. The MRI myelogram did not show evidence of myelitis. High HTLV-1 proviral loads in peripheral blood and CSF, lead to the diagnosis of HTLV-1 related bladder dysfunction. She was managed with continuous bladder drainage and intermittent clean bladder catheterisation. A renal graft biopsy performed for deterioration in renal allograft function showed features of acute pyelonephritis. A suprapubic catheter was inserted for continuous drainage. This resulted in stabilisation of graft function, but she had chronic colonisation of the bladder with ESBL Escherichia coli.
Discussion

The lifetime risk of developing HTLV-1 associated myelopathy and tropical spastic paraparesis (HAM/TSP) is variable (between 0.25-4%) and is perhaps dependent on the route of infection, ethnicity and human leukocyte antigen (HLA) subtypes(11). The risk of subsequently developing adult T cell leukaemia/lymphoma (ATL) is 1-5% and appears to be dependent on the region the patient belongs(11). Neurogenic bladder is known to occur in patients with HTLV-1 HAM/TSP and may be its first manifestation. Isolated neurogenic bladder dysfunction in HTLV-1 infected individuals without HAM/TSP has been reported in general population and the risk is estimated to be 4.3% and HTLV-1 proviral loads were found to be higher in these patients compared with asymptomatic carriers (12).

This report describes a patient with isolated bladder dysfunction without features of HAM/TSP in a renal allograft recipient with HTLV-1 infection. The symptoms of bladder dysfunction became apparent after renal transplantation, probably because she had minimal urine output while she was on dialysis. During early and later stages of chronic kidney disease, she did not suffer from urinary tract infections and ultrasound demonstrated normal bladder wall with normal post void volume of less than 50 mls. She did not have classical features of diabetic cystopathy, as the urodynamic study did not show reduced detrusor contractility and areflexia. The study showed detrusor overactivity with no intrinsic urethral sphincter deficiency. Detrusor overactivity has been reported as the most frequent urodynamic finding with HTLV-1 infection. In our patient, post void residual volume of 220 ml is elevated possibly due to detrusor-external sphincter dyssynergia. Both disorders could possibly coexist as part of the neurogenic bladder (20).

Majority of the renal transplant recipients who developed HAM/TSP were HTLV-1 seronegative prior to transplantation and acquired the infection from the donor (8). The donor was not tested for HTLV-1 infection, but was residing in a region of low endemicity. The development of HAM/TSP in an HTLV-1 seropositive graft recipient is uncommon. In this case, the HTLV-1 proviral load in the blood and CSF exceeded 1000 per 10^5 PBL associated with CSF lymphocytic pleiocytosis,
consistent with HTLV-1 associated neurological disease. The high proviral load in the pathogenesis of HTLV-1–associated disease is supported by the observation that when the proviral load exceeds a threshold level HTLV-I-specific cytotoxic T lymphocytes could contribute to inflammation and damage to the nervous system (21).

The effect of immunosuppression on the natural history of HTLV-1 infection is unknown. Paradoxically, cyclosporine and prednisolone have been used to treat patients with HAM/TSP (13), yet the acquisition of HTLV-1 infection in the setting of solid organ transplantation appears to be associated with an increased risk of developing HAM/TSP. Nevertheless, overall graft survival does not differ between HTLV-1 positive and negative recipients (14-17). Most people living with HTLV-I infection are asymptomatic and neurological disease may develop in some patients after solid organ transplantation who are serologically either HTLV-1 donor positive/recipient negative or donor negative/recipient negative. According to Clinical Guidelines for Organ Transplantation from Deceased Donors published by Transplantation Society of Australia and New Zealand (April 2016), epidemiologic exposure to HTLV-I must be determined during pre-transplantation evaluation and selective screening of donors and recipients with HTLV-I risk factors should be considered in regions of high endemicity. Routine screening of donors for HTLV-infection in populations with low prevalence is not recommended (14, 18). HTLV-I positive potential solid organ transplant recipients should be informed about the higher risk of diseases such as ATL, with development rates of 20% over 5 years (19) and HAM/TSP as part of the informed consent process, as there is no available treatment for this infection. Detection of HTLV-I infection early in the post-transplant course should also include monitoring of infected recipients for evidence of clinical disease, and timely implementation of various management strategies.

Conclusion

Isolated bladder dysfunction is a rare manifestation of HTLV-1 infection associated with high proviral load, which may adversely affect graft and patient outcomes following kidney transplantation.
References


Highlights

- First case report of isolated neurogenic bladder without features myelopathy/tropical spastic paraparesis, attributable to HTLV-1 infection in an Aborigine renal allograft recipient.
- Isolated bladder dysfunction is a rare manifestation of HTLV-1 infection associated with high proviral load.
- Adversely affect graft and patient outcomes following kidney transplantation.
ISOLATED NEUROGENIC BLADDER ASSOCIATED WITH HUMAN T-LYMPHOTROPIC
VIRUS TYPE 1 INFECTION IN A RENAL TRANSPLANT PATIENT FROM CENTRAL
AUSTRALIA.

Abstract

Background: Human T-Lymphotropic virus type 1 (HTLV-1) is endemic amongst the Aborigines of the Northern Territory of Australia. HTLV-1 associated Myelopathy/Tropical Spastic paraparesis (HAM/TSP) has been associated with this infection. In general population, isolated neurogenic bladder dysfunction in HTLV-1–infected individuals without HAM/TSP has been reported and the HTLV-1 proviral load has been found to be higher in such patients compared with asymptomatic carriers. In solid organ transplantation, few cases of HAM/TSP have been reported worldwide but not an isolated neurogenic bladder.

Case: A 50-year-old indigenous women from Alice Springs with end stage renal disease secondary to diabetic nephropathy with no prior history of bladder dysfunction received a cadaveric renal allograft following which she developed recurrent urinary tract infections. The recipient was seropositive for HTLV-1 infection. HTLV-1 status of donor was not checked. Urodynamic studies revealed stress incontinence and detrusor overactivity without urethral intrinsic sphincter deficiency. She had no features of myelopathy. There was elevation of the serum and cerebrospinal fluid (CSF) HTLV-1 proviral load. The MRI myelogram was normal. Pyelonephritis was diagnosed based on clinical features, positive cultures and renal allograft biopsy. Continuous suprapubic catheter drainage helped preventing further episodes of allograft pyelonephritis in spite of chronic colonisation of the urinary tract.

Conclusion: Isolated bladder dysfunction is a rare manifestation of HTLV-1 infection and is probably associated with high proviral loads. This may adversely affect renal allograft and patient outcomes.