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Polyomavirus Nephropathy in Native Kidneys of an Immunocompetent Individual

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 34
Final Diagnosis: Poliomavirus nephropathy
Symptoms: Renal disfunction
Medication: —
Clinical Procedure: Renal biopsy
Specialty: Nephrology

Objective: Rare disease
Background: Polyomavirus nephropathy has emerged as an important cause of graft loss in kidney transplant recipients. Polyomavirus rarely affects the native kidneys of an immunocompetent individual. Until now, polyomavirus nephropathy in native kidneys of an immunocompetent individual has not been reported, as far as we know.
Case Report: A 34-year-old man was transferred from a local clinic to be evaluated for the cause of azotemia. Serum creatinine was 2.85 mg/dL. We performed renal biopsy to identify the cause of azotemia. The result of kidney biopsy was consisted to polyomavirus nephropathy.
Conclusions: We report the first case of polyomavirus nephropathy in native kidneys of an immunocompetent individual.

MeSH Keywords: Immunity • Polyomavirus • Renal Insufficiency, Chronic

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/902031

Background

Polyomavirus nephropathy is recognized as a major clinical problem in kidney transplant recipients. Polyomavirus infection usually occurs during childhood, and as many as 85% of adults have serologic evidence of prior viral exposure [1]. Following primary infection, the polyomavirus preferentially establishes viral latency in the genitourinary tract. Because immunosuppression stimulates viral reactivation and progression to viral disease, polyomavirus nephropathy has emerged as an important cause of renal allograft dysfunction and loss in kidney transplant recipients. Reactivation of the polyomavirus may not only occur in the transplanted kidney but also in native kidneys of non-renal transplant recipients or patients with acquired immune deficiency syndrome or systemic lupus erythematosus as recorded in some case reports [2]. Until now, the polyomavirus in native kidneys of an immunocompetent individual has not been reported. Here, we present a case of an immunocompetent man who developed polyomavirus nephropathy in his native kidneys.

Case Report

A 34-year-old man was referred to our hospital to evaluate the cause of azotemia detected during a medical checkup. He was a hepatitis B carrier and had not been treated for hepatitis B. There was neither a specific family history nor a past history of other diseases, except hepatitis B. He had no subjective symptoms or any abnormal physical examination findings. His initial vital signs were as follows: blood pressure, 120/70 mm Hg; heart rate, 64 beats per minute; respiratory rate, 16 breaths per minute; and temperature, 36.3°C. His white blood cell count was 5,860/mm^3 (neutrophils 60.8%, lymphocytes 29.7%); hemoglobin, 12.2 g/dL; platelet count, 239,000/mm^3; protein, 7.3 g/dL; albumin, 4.2 g/dL; aspartate transaminase (AST), 32 IU/L; alanine transaminase (ALT), 46 IU/L; total bilirubin, 0.9 mg/dL; glucose 90 mg/dL; blood urea nitrogen (BUN), 31.1 mg/dL; creatinine, 2.85 mg/dL; and electrolytes were in the normal range. His urinalysis revealed red blood cells, 0–2/high-power field (HPF), and white blood cells, 0–2/HPF. The protein-to-creatinine ratio in his spot urine sample was 69.6 mg/g. Additional laboratory results were as follows; rheumatoid factor, 6.7 IU/mL (normal range 0.0–18.0 IU/mL); IgG, 1,527.2 mg/dL; IgA, 272.5 mg/dL; IgM, 96.6 mg/dL; Ig E, 1,691.0 IU/mL; IgD, 3.53 mg/dL; IgG subclass 4 at 572.0 mg/L; antistreptolysin O, 60.3 IU/mL (normal range <200 IU/mL); C3, 72.9 mg/dL (normal range 90~180 mg/dL); C4, 17.8 mg/dL (normal range 10~40 mg/dL); Antinuclear antibody, positive (speckled); anti-double-stranded deoxyribonucleic acid antibody, negative; anti-myeloperoxidase antibody, negative; anti-proteinase 3 antibody, negative; anti-glomerular basement membrane antibody, negative; hepatitis B surface antigen, positive; hepatitis B surface antibody, negative; hepatitis C virus antibody, negative; human immunodeficiency virus antibody, negative; hepatitis B e antigen, positive; hepatitis B e antibody, negative; hepatitis B virus DNA real-time polymerase chain reaction, >1.70×10^8. Liver ultrasonography showed no remarkable finding in the liver. AST and ALT were normal and there was no evidence of cirrhosis, so the patient was not treated for hepatitis B. There was no specific finding in either his chest radiography or electrocardiogram. Kidney ultrasonography showed increased renal cortical echogenicity and decreased kidney size (right: 8.3 cm, left: 8.6 cm). Renal biopsy was performed. In the hematoxylin eosin stain and the periodic acid-Schiff stain, tubules revealed focal moderate atrophy and loss with infiltration of mononuclear cells and fibrosis in the interstitium; tubular epithelial cells frequently showed intranuclear inclusion bodies (Figure 1). The Masson trichrome stain showed interstitial fibrosis (Figure 2). Blood vessels were unremarkable. As many as 25 glomeruli

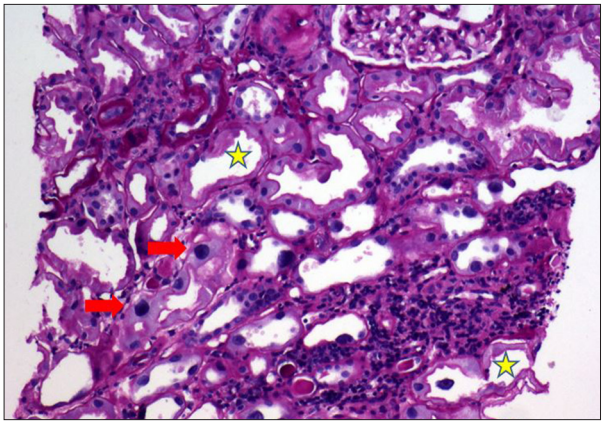

Figure 1. PAS stain revealed typical intranuclear viral inclusion (red arrow) and necrosis (yellow star) of tubular epithelial cells (×100). It is also noted that moderate interstitial inflammation by mononuclear cells.

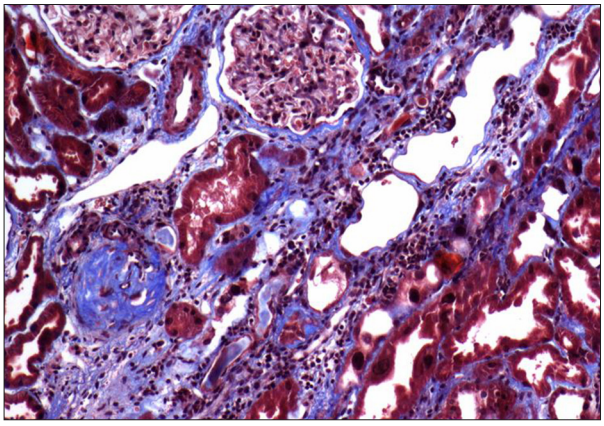

Figure 2. Masson trichrome stain showed interstitial fibrosis with tubular atrophy and interstitial inflammation (×100). These findings are consistent with polyoma (BK) virus nephropathy, sclerosing phase.

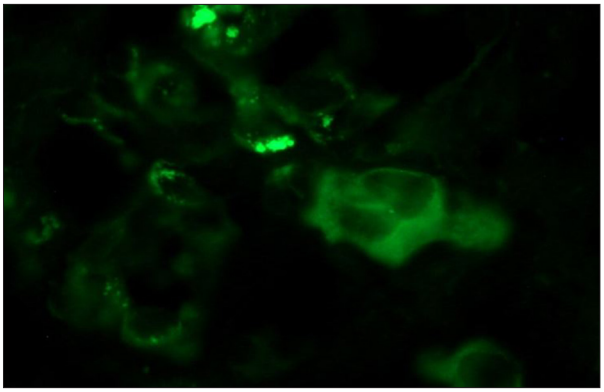

Figure 3. Green fluorescence is noted in the tubular epithelial cells (simian virus 40 immunofluorescence, ×400).

were present in the biopsy, of which 9 (36%) showed global sclerosis. The remaining glomeruli were of normal or slightly increased size and normocellular. Ultrastructurally in the electron microscopy, the glomerular basement membrane measured normal in thickness with partly irregular inner contours. There were localized small electron-dense materials in the mesangium. Epithelial cell foot processes remained relatively patent. The immunofluorescence microscopy showed a strong simian virus 40 large tumor antigen staining mainly in the tubular epithelial cells, confirming the diagnosis of polyomavirus nephropathy (Figure 3). Subsequent tests for BK virus quantitative polymerase chain reaction in blood and urine were negative. However, in accordance with the biopsy results, he was diagnosed with polyomavirus nephropathy.

Discussion

The polyomavirus was first described in 1971, and polyomavirus nephropathy was first described in 1978 in renal transplant recipients [3]. The polyomavirus, especially BK virus which is a member of the polyomavirus family, nephropathy reappeared in the kidney transplantation literature in the late 1990s as a potential cause of graft injury, as a result of the development and use of more potent immunosuppressant agents. The BK virus, JC virus, simian virus 40, and TS virus are the members of polyomavirus [4,5].

Primary infection occurs in childhood, commonly presenting as a respiratory viral infection. Primary entry of the virus into the host results in transient viremia and viral spread to transitional and renal tubular epithelial cells, where the virus establishes latency. Disease caused by the reactivation of latent viruses is typically seen in the immunosuppressive host [2]. Presently, the only widely accepted risk factor for the development of BK virus nephropathy is a degree of overall immunosuppression [6]. There are some differences in other risk factors. BK virus nephropathy mostly occurs in renal allografts, and rarely in native kidneys of non-renal transplant recipients. Additionally some cases reports have shown that BK virus nephropathy occurs in native kidneys of patients with acquired immune deficiency syndrome or autoimmune diseases such as systemic lupus erythematosus.

In kidney transplant recipients, BK virus reactivation predominantly is described as an interstitial nephritis; the most common clinical presentations are asymptomatic deterioration in kidney function [6].

Diagnostic testing for the BK virus relies on evidence of viral replication in the urine and blood and a confirmatory histological examination. Identification of viruria can be performed by using urine cytology or quantitative PCR for DNA. Urinalysis with Papanicolaou staining for inclusion bodies in uroepithelial cells identify decoy cells (>10 cells/cytospin). Urine PCR analysis for BK virus is more sensitive and has the added advantage of quantifying viral ($>1\times10^7$ copies/mL). Detection of viremia is performed by using quantitative PCR for DNA. The viral copy number in blood generally is approximately 1/1,000 that is found in urine ($>1\times10^4$ copies/mL) [6]. However, kidney biopsy remains the gold standard for the diagnosis of BK virus nephropathy, and histological findings in biopsies have been associated with graft outcomes [4,6].

Because of the absence of a proven BK virus-specific antiviral agent and the clear relationship of BK virus nephropathy to the immunosuppression burden, clinicians must first consider the preemptive treatment of patients with BK virus nephropathy to the reduction of immunosuppressive agents. Additional therapies include the antiviral agent cidofovir, the antimetabolite leflunomide, the antibiotics fluoroquinolones, and the immunomodulatory agent such as intravenous immune globulin (IVIG) therapy. Despite the existence of these additional therapies, no randomized prospective clinical trial has tested the value of adding these agents to the strategy of immunosuppression reduction alone. Further, the U.S. Food and Drug Agency has not approved any drugs as a safe and effective treatment for BK virus nephropathy [3].

Conclusions

Until now, polyomavirus nephropathy has been suggested as a cause of renal dysfunction in immunocompromised hosts, especially in the allograft of kidney transplant recipients. However, polyomavirus nephropathy may also be considered a cause of renal dysfunction in the native kidneys of immunocompetent patients.

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