A new polyomavirus-related dermatosis in a pancreatic transplant patient

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INTRODUCTION

Solid organ transplant recipients require constant immunosuppression to prevent graft failure of the transplanted organ. As a result, patients are at high risk for infections, some that are extremely rare and uncommon with unusual presentations. Herein, we describe a pancreatic transplant patient who suffered from an infection from a novel polyomavirus resulting in a unique constellation of symptoms and skin manifestations. This patient and novel polyomavirus have been previously reported but we revisit the case to highlight the dermatologic manifestations for dermatology providers who may similar patients.1

CASE REPORT

A 33-year-old woman who received a pancreatic transplant for type 1 diabetes mellitus 11 months prior presented with a 3-week history of fatigue, myalgias, decreasing visual acuity, and progressive motor weakness in her torso and lower extremities. Her posttransplant course was complicated by cytomegalovirus (CMV) viremia treated with a course of valganciclovir, which was completed 6 months before presentation. She was in excellent health, working as a teacher and exercising 3 days a week. Two weeks before presentation, Hurricane Sandy damaged her home in Hoboken, New Jersey with more than a foot of floodwater forcing her to evacuate on foot. For 3 weeks, she experienced progressive fatigue, myalgias, and decreasing visual acuity. She had no history of international travel, illicit drug use, or direct exposure to domestic animals or wildlife. Her medications included 2.5 mg of prednisone daily, mycophenolic acid, 180 mg twice daily, and tacrolimus, 6 mg twice daily.

On presentation, she had symmetric motor weakness in her upper and lower extremities and was blind with the ability to detect only bright light. Multiple 1- to 2.5-cm necrotic ulcers on the scalp, face, and hands with pseudovesicular, inflammatory borders (Fig 1) were present. Her workup was notable for elevated aldolase to 325 U/L (normal, 1.0 to 7.5 U/L) and creatine kinase to 8000 U/L (normal, 60 to 174 U/L). Her polymerase chain reaction (PCR) test for HIV, Epstein Barr virus, parvovirus, and CMV was negative, and there was no evidence of antibodies to influenza, adenovirus, mycoplasma, human T-lymphotropic virus or human herpesvirus 6. Her serologic workup for autoimmune and connective tissue disease was also negative. Electromyography indicated widespread myopathy. A deltoid muscle biopsy found focal acute vasculitis, microthrombosis, focal chronic perivasculitis, and chronic myofiber changes including myonecrosis, large hyperchromatic vascular endothelial atypia, and myoatrophy consistent with nonspecific myositis. Immunostaining for CMV, herpes simplex virus, adenovirus, BK virus and John Cunningham (JC) virus were negative.

Ophthalmologic examination found bilateral optic neuropathy of ischemic or inflammatory origin and extensive retinal vascular occlusions bilaterally. A skin biopsy found ischemic dermopathy without vasculitic or thrombotic features.

The patient was initially treated for a presumptive diagnosis of systemic vasculitis of unknown cause with 500 mg/d of methylprednisolone intravenously without improvement. She underwent a 5-day...
course of plasmapheresis with some improvement of muscle strength but no recovery of her vision. Repeat deltoid muscle biopsy failed to detect CMV, enteroviruses, cardioviruses, human polyomaviruses, parvovirus B19, mycoplasma, and a broad range of herpesviruses by PCR.

Because no cause could be found for these symptoms, a search for a novel viral cause was initiated. The W. Ian Lipkin virology laboratory at Columbia University tested total nucleic acid samples from the patient with high throughput sequencing (Ion Torrent) after ribosomal RNA depletion to enhance sensitivity for virus detection. For further details of the methodology, please see Mishra et al.1 Ultimately, the Lipkin laboratory was able to clone a circular double-stranded DNA viral genome, comprising 5108 base pairs, with 80.7% overall nucleotide homology of genome to the closest known related chimp polyomaviruses. The virus identified in this patient meets criteria for classification as a novel polyomavirus and was tentatively named New Jersey polyomavirus 2013 (NJPyMv-2013). In situ hybridization confirmed the presence of viral signal in the deltoid muscle and skin biopsies.1

The patient was discharged to a rehabilitation facility where her motor strength continued to improve but without recovery of her vision. Blood collected 10 months after the onset of illness tested positive for NJPyMv-2013 DNA. Assays of banked sera from 35 multiple transfusion patients from the New York Blood Center, 15 rhesus macaques housed at Columbia, the patient’s roommate in Hoboken, and her sexual partner found no evidence of NJPyMv-2013 infection by PCR or serology.

**DISCUSSION**

The polyomaviruses most commonly associated with human infection are BK virus and JC virus.2 BK virus and JC virus infections occur in early life with an exposure prevalence that exceeds 75% in adults and can persist throughout life. Reactivation most commonly occurs in immunosuppressed patients,
such as those who are pregnant, suffer from HIV/AIDS or cancer, have had organ transplantation, or are undergoing multiple sclerosis treatment.

Polyomavirus infection is typically asymptomatic or results in only a mild respiratory disease; however, reactivation of BK virus has been implicated in renal transplant allograft failure and hemorrhagic cystitis in allogeneic hematopoietic stem cell transplant recipients. BK virus is believed, in these cases, to infect endothelial cells leading to ischemic vasculopathy, similar to the ischemic vasculopathy observed in our patient.

Recently, several dermatologic diseases attributable to polyomaviruses have been reported. A polyomavirus was found to be the causative agent of Merkel cell carcinoma. A novel polyomavirus was found to be associated with trichodysplasia spinulosa, a condition characterized by erythematous to skin-colored papules with spiny projections usually on the mid portion of the face, seen almost exclusively in immunosuppressed patients. Human polyomavirus 7 was recently reported to cause a distinctive epidermal hyperplasia resulting in pruritic, brown plaques on the trunk and extremities in 2 lung transplant recipients. Our case highlights the clinical presentation of a unique polyomavirus infection in a diabetic pancreatic transplant patient who presented with myositis, blindness, and distinctive necrotic ulcers with pseudovesicular inflammatory borders on the scalp and face.

Dermatologists who care for immunosuppressed patients should be aware of human polyomaviruses as potential agents of disease. Moreover, the close temporal relationship between Hurricane Sandy and the onset of illness in our patient should not be overlooked, particularly in light of the observation that other polyomaviruses associated with human disease have been identified in sewage-contaminated water. We present this novel case to highlight the potential risk in immunosuppressed patients in the aftermath of natural disasters so that dermatologists who care for transplant patients are aware of this pathogen should there be future transmission of NJPyMv-2013.

REFERENCES

1. Mishra N, Pereira M, Rhodes RH, et al. Identification of a novel polyomavirus in a pancreatic transplant recipient with retinal blindness and vasculitic myopathy. J Infect Dis. 2014;210(10):1595-1599.
2. Jiang M, Abend JR, Johnson SF, Imperiale MJ. The role of polyomaviruses in human disease. Virology. 2009;384:266-273.
3. Pinto M, Dobson S, BK and JC virus: a review. J Infect. 2014;68(suppl 1):52-58.
4. Pham PT, Schaenman J, Pham PC. BK virus infection following kidney transplantation: an overview of risk factors, screening strategies, and therapeutic interventions. Curr Opin Organ Transplant. 2014;19(4):401-412.
5. Feng H, Shuda M, Chang Y, Moore PS. Clonal integration of a polyomavirus in human Merkel cell carcinoma. Science. 2008;319:1096-1100.
6. van der Meijden E, Janssens RW, Lauber C, Bouwes Bavinck JN, Gorbalenya AE, Feltkamp MC. Discovery of a new human polyomavirus associated with trichodysplasia spinulosa in an immunocompromized patient. PLoS Pathog. 2010;6(7):e1001024.
7. Ho J, Jedrych JJ, Feng H, et al. Human Polyomavirus 7-Associated Pruritic Rash and Viremia in Transplant Recipients. J Infect Dis. 2015;211:1560-1565.
8. Fratini M, Di Bonito P, La Rosa G. Oncogenic papillomavirus and polyomavirus in water environments: is there a potential for waterborne transmission? Food Environ Virol. 2013. doi: 10.1007/s12560-013-9134-0. Published online November 30, 2013.
9. Sidhu JP, Ahmed W, Gernjak W, et al. Sewage pollution in urban stormwater runoff as evident from the widespread presence of multiple microbial and chemical source tracking markers. Sci Total Environ. 2013;463:488-496.