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CLINICAL VIGNETTE

Polyomavirus in Immunocompetent Patients

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Case Report

A 59-year-old Asian female with a history of recently diagnosed type 2 diabetes presented with a four month history of lower abdominal pain associated with urgency and dysuria. She noted hourly nocturia with sleep disruption and urge incontinence. She denied hematuria, fever, chills or flank pain or any history of recent urinary tract infections, back pain, constipation, or radiculopathy. She had already sought care with an urgent care physician and was told that she had a urinary tract infection and was prescribed a seven day course of ciprofloxacin. She noted no improvement with the antibiotics.

Past medical history was significant for hypertension, gout, and a remote history of endometrial cancer twenty years prior. Her medications included an ace inhibitor, metformin and allopurinol. Surgical history was notable for TAH BSO. Family history was notable for diabetes and hypertension.

On physical examination she had a temperature of 98.6; blood pressure of 145/85 and heart rate of 75/minute. She appeared in no acute distress. Notably on the exam was that she had mild pain in the suprapubic area. She had no masses, guarding or rebound. Pelvic exam and vaginal exam was significant for atrophy and anterior vaginal pain. No masses were noted.

Urinalysis was performed and was without leukocytes, protein or hematuria. Culture was negative. Post void residual was 75 cc. Subsequent ultrasound of the pelvis, ovaries, bladder, kidneys and ureters was without abnormality. Urine cytology on three specimens was notable for urothelial cell atypia and cells suggesting viral changes consistent with Polyomavirus. Cystoscopy was performed. The uroepithelium was normal without evidence of

lesions, foreign body, tumors or granulomas. The trigone was slightly hyperemic but no specific lesions were noted. The ureteral orifices were normal and patent with good ureteral reflux. The bladder capacity was normal. Bladder irrigation was without evidence of malignant cells however had reactive and atypical urothelial cells. Subsequent CT of the abdomen/pelvis and urogram was performed without any renal or bladder abnormality. The patient's renal function, electrolytes, white blood count, hemoglobin, and platelets were all normal. JC Polyomavirus DNA was noted in urine. JC Polyomavirus was not detected in blood and BK Polyomavirus was not detected in either blood or urine. HIV test was negative. CD counts were normal as was T cell function by lymphocyte mitogen and antigen proliferation assay.

Discussion

Polyomaviruses are nonenveloped viruses with a double stranded DNA. BK virus and JC Polyomavirus are two common Polyomaviruses that infect humans. Primary infection with BK virus occurs early in childhood, while JC virus seroconversion occurs in adolescence¹. BK virus seroprevalence reaches 98% by 9 years of age, and JC virus seroprevalence reaches 72% by 25 years of age². The reason for the difference in the epidemiologic profiles of BK and JC infections is unknown but may be related to differences in the routes of transmission. A fecal oral route of transmission is suspected in both³. Infection is cell specific in the host. Entry mechanism of Polyomaviruses into cells is only partially known. The pathogenesis of tissue damage in Polyomavirus infected tissues is unknown, but depends on immune status³.

The primary infection with the Polyomaviruses are considered to be largely asymptomatic in the immunocompetent. The BK virus has been implicated in short lived infections such as urinary tract infections and nephritic syndrome⁴. The virus remains in a latent state most often in the urogenital tract. Viruria occurs in reactivation of the BK virus and is implicated in renal transplant patients causing ureteric stenosis, transient allograft dysfunction, and irreversible graft failure due to tubulointerstitial nephritis⁵.

JC virus is largely considered an asymptomatic infection in adolescence and adulthood. Reactivation of the JC virus is the causative agent for Progressive Multifocal Leukoencephalopathy in immunocompromised patients, most commonly in HIV patients. Isolated JK virus and co-infection with BK virus has been associated with post transplant nephritis⁶. Notably, JC frequently is excreted in the urine of healthy individuals, and older individuals show a higher viral load^{7,8}. Reactivation of JC virus has been suggested to occur more commonly in diabetes³.

The data to date suggest a possible relationship with Polyomaviruses and malignancy. It has been suggested that Polyomaviruses may serve as co-factors for malignancy⁹. Malignant transformation due to specific Polyomaviruses has been identified. The presumed causative agent for Merkel cell skin cancer has been linked to the Merkel cell Polyomavirus¹⁰. JC virus role in urothelial cancers is controversial at this time. One recent small study did not support an involvement of Polyomavirus in transitional bladder cell cancer in immunocompetent individuals¹¹. Shen CH, Wu JD, et al have found a significant association with JK virus and urothelial cells in a Taiwanese cohort¹². BK virus infection after transplantation is known to cause graft failure, but the association with malignancies has been controversial based on a recent study¹³.

Reactivation of BK and JC viruses with asymptomatic viruria occurs in 10-50% of hematopoietic stem cell and bone marrow transplant recipients and in 30% of renal transplant recipients¹⁴. Pathological transformation due to the JC virus is presently being studied in patients using anti-tumor necrosis alpha inhibitors. Although Infliximab treatment did not directly affect JC reactivation in one study, further investigation on host factors

regulated by it will be important in understanding the mechanisms that may affect viral persistence with Infliximab or immunosuppression overall¹⁵.

To date it is unclear if the patient had a reactivation of the JK virus causing symptoms or chronic viruria unrelated to her symptoms. One could postulate that she had reactivation related to her diabetes. This patient underwent extensive evaluation based on her chronic and progressive urinary symptoms and abnormal urinary cytology. This is appropriate based on current studies which have demonstrated it is difficult to distinguish benign Polyomavirus infected cells from their malignant counterparts by cytology¹⁶. Additionally, the risk factors for atypia have not been clearly identified and will require further study.

Clinicians should remember that asymptomatic Polyomavirus viruria is common in immunocompetent patients. In certain circumstances patients may demonstrate symptoms related to the Polyomavirus. Additionally, clinicians should be aware that abnormal urine cytology demonstrating Polyomavirus should lead to further evaluation as urine cytology can be misleading. Increased surveillance may be recommended pending further study.

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