

# High-level polyomavirus JC viruria following long-term steroid therapy

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## SUMMARY

C virus is a highly seroprevalent ubiquitous polyomavirus which is acquired at an early age through respiratory or oral route. Thereafter JCV establishes persistent, but mainly asymptomatic, infections in various tissues, including the genitourinary tract and brain.

In individuals with altered immunity, viral replication can occur leading to serious organ diseases. In contrast to polyomavirus BK, that is found infrequently in the urine of healthy adults, JC viruria occurs universally. Herein we describe a case of an otherwise immunocompetent patient who presented a very high-level asymptomatic polyomavirus JC viruria following long-term steroid therapy.

**KEY WORDS:** Polyomavirus JC, Viruria, Steroids

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## CASE REPORT

JC virus is a highly seroprevalent ubiquitous polyomavirus which is acquired at an early age through respiratory or oral route. Thereafter JCV establishes persistent, but mainly asymptomatic, infections in various tissues, including the genitourinary tract and brain (Knowles *et al.*, 2006). In individuals with altered immunity, viral replication can occur leading to serious organ diseases such as progressive multifocal leukoencephalopathy and polyomavirus-associated nephropathy in renal transplant recipients (Cavallo *et al.*, 2009). Polyomaviruses BK and JC are closely related to each other with 72%-81% nucleotide homology and 59%-83% amino acid homology (Barbanti-Brodano *et al.*, 2006). In contrast to BK, that is found infrequently in the urine of healthy adults, JC viruria occurs universally,

increasing with age, with adult prevalence rate often between 15% and 60% (Behzad-Behbahani *et al.*, 2004; Knowles *et al.*, 2006; Bialasiewicz *et al.*, 2009).

Herein we describe a case of an otherwise immunocompetent patient who presented a very high-level asymptomatic polyomavirus JC viruria following long-term steroid therapy. The subject was a 55-year-old man who underwent urinary cytology analysis as a part of a routine check-up in the absence of any signs and/or symptoms. By Papanicolaou stain on fixed urine, abundant cells with irregular shape and enlarged nucleus occupied by a basophilic inclusion surrounded by a condensed rim of chromatin, thus conferring a ground-glass appearance, were detected. PCR assay resulted negative for serum BKV-DNA and JCV-DNA and urine BKV-DNA and disclosed a viral load of  $2.54 \times 10^8$  JCV-DNA Genome Equivalents (GEq)/ml on urine. The patient had no clinical condition possibly associated with JC viruria, except for a vertebral disc hernia for which he had taken betamethasone (4 mg/die) and diclofenac (undefined amount) for approximately 6 months before undergoing surgery, approximately 3.5 months before the PCR assay findings. No data on urine JCV load or urine cy-

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tology before starting or immediately after discontinuing steroid and diclofenac therapy were available. The subsequent evaluation of renal function by serum creatinine level measurement excluded the likelihood that JC viruria can turn into established nephropathy, as expected in a non-transplant patient. In a recent study by Egli and *et al.* (2009), JCV load was investigated in 400 healthy blood donors and asymptomatic urinary shedding was observed in 19% of subjects, with median viral load of 4.8 log GEq/ml and 75<sup>th</sup> percentile of values approximately of 5x10<sup>7</sup> GEq/ml. In another study on a mixed immunocompetent/immunocompromised population, the occurrence of JC viruria has been described in 14% of cases, although no data on viral load are reported (Bialasiewicz *et al.*, 2009). Slight changes in immune status and/or an immunocompromised condition can lead to the reactivation of latent polyomaviruses, especially along the uroepithelium, resulting in the shedding of viral particles and infected cells into the urine, with the detection of the typical decoy cells (Singh *et al.*, 2006). A role of steroids in polyomavirus reactivation has been postulated and seems plausible, although poor evidence is available. In a study by Barzon *et al.* (2008), adrenal steroid hormones overproduced in human adrenal tumors represented a trigger for polyomaviruses reactivation. On the other hand, in a study we performed on BKV reactivation in lupus nephritis patients, BKV reactivation tended to be associated with immunosuppressive treatment other than steroids and inversely correlated with the use of steroids (Colla *et al.*, 2007). Data obtained by Egli *et al.* (2009) indicate significant differences between BKV and JCV with respect to virus-host interaction and epidemiology. They hypothesized that JCV shedding is not necessarily a sign of cellular immune dysfunction but suggests a difference between BKV- and JCV-infected cells with respect to anatomic location and/or accessibility to T cells in mucosal sites.

Knowles and coll. found that the correlation between failing T-cell immunity in HIV-infected patients and JC viruria was poor (Knowles *et al.*, 1999). In a study on kidney transplant, Drachenberg *et al.* (2007) noted that the reduction of immunosuppression in patients with JCV-mediated polyomavirus-associated nephropathy

resulted in clearance of graft involvement but not clearance of urinary shedding. It is likely that differences in polyomavirus-host balance between BKV and JCV exist. In the individual herein described, a transient immunosuppression determined by the steroid therapy had been present and a high-level JC viruria was detected in the absence of BKV reactivation and other clinical findings. A study investigating this issue could provide information potentially useful to correctly interpret JC viral load in urine specimens from different categories of patients and the urine cytological analysis.

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