

JC Viral Disease in Renal Transplantation

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JC virus (JCV) is now a recognized pathogen for progressive multifocal leukoencephalopathy (PML). Lately, several reports have shown that JCV may also be an important viral pathogen in renal transplant (Tx). However, only limited information is available on the epidemiology of JCV associated renal allograft dysfunction. We assessed JCV load in patients suspected to have BK viral disease and present clinical data on two patients with renal allograft dysfunction with significant JCV loads.

Methods: We screened blood and urine samples from 242 patients suspected to have BK viral disease with a quantitative PCR assay for JCV based on TaqMan chemistry. Simultaneous BKV load was also assessed. Retrospective clinical data was obtained on two patients by chart analyses.

Results: The JCV assay did not detect other polyoma viruses or various herpes and adenoviruses. Of the 242 patients suspected to have BKV disease, 97% had a positive test for either BKV or JCV or both. Whereas, 9 patients were (4%) tested positive for JCV alone and 22% for both BKV and JCV. The range of urine viral load was similar for both BKV and JCV (500 to >10X10¹⁰ copies/ml) and generally, but not always, a high JCV load was associated with BKV load. The maximum blood viral load for JCV (2.2 x10⁶ copies/ml) was one log order less than BKV (7 x10⁷ copies / ml). The patient with the highest JCV blood load had a coexistent but 3 log order less BKV blood load. Two renal allograft recipients presented with JCV loads also had neurological manifestations. Pt 1, 43 yr, F with LRD for FSGS had a rising creatinine level 2 years post Tx (3.9 ng/dl) and a biopsy showed few glomeruli with mesangial expansion, diffuse tubular atrophy with hyperchromasia and enlargement but no viral inclusions. She also had depression and excessive sleepiness and was found to have a JCV load of 5x10² copies/ml in blood without any detectable BKV. Pt 2, 21 yr, F, had a cadaveric renal transplant 4 years ago, and a rising creatinine level (3 ng/dl). Biopsy evidence showed sclerotic glomeruli, patchy tubular atrophy, mononuclear infiltrates and interstitial fibrosis but no viral inclusions. She also had short-term memory dysfunction, episodes of upper extremity numbness, tingling, irritability, hyper-reflexia of the upper extremity and depression. MRI also showed remote silent right cerebral infarct and some evidence of demyelination. Although no BKV was detected, she had a JCV load of 8.8x10³ in her urine.

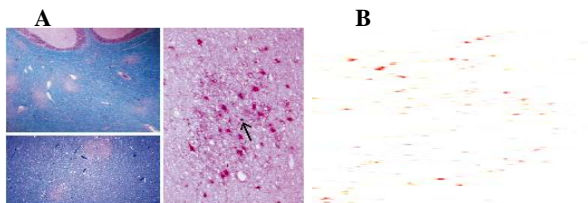


Fig 1: Progressive multifocal leukoencephalopathy (PML) as evidenced by demyelinated lesions in cerebellar white matter (A) was known as early as in 1958. However, the association of this disease with polyomavirus was not established until 1971 when a new type of polyomavirus was detected in the brain of a PML patient, named JC. The virus was subsequently named after the patient's initials (JC).

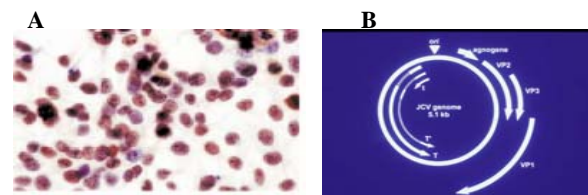


Fig 2: In addition to PML, JC virus also possesses oncogenic potential as detected in tumors (A). The genomic sequence of JC virus reveals that this virus has 70-80% sequence homology with other polyomaviruses (BK & SV 40) and similar genomic organization (B).

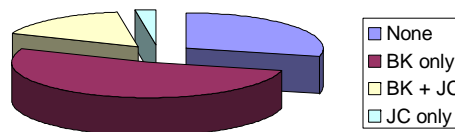


Fig 3: In order to determine the prevalence and distribution of JC virus in kidney transplant patients, we screened 537 clinical specimens (of which 218 were urine and 319 were blood specimens) from 242 patients that were suspected of having BKV infection. Out of 537 clinical specimens, 71% had polyomavirus (either BK or JC), 69% had BK only, 16% had BK and JC co-infection, and 2.6% had JC only.

Conclusions: This study identifies that a significant proportion (up to 26%) of patients with suspected BKV can have coexisting or isolated JCV infection. The JCV infection, however, may have a course that is independent of BKV infection and may be associated with neurological findings in addition to renal allograft dysfunction. Such coexistent and / or independent JCV infection may contribute to clinical course of polyomavirus associated syndromes. Further studies are needed to clarify the clinical and biological correlates of JCV infection in renal transplantation.

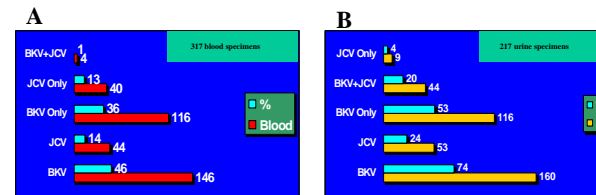
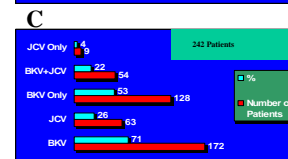


Fig 4: We further analyzed our results by specimen types [blood (A) and urine (B)], and patients (C).



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- The JCV infection, however, may have a course that is independent of BKV infection.

Patient 1:

- 43 yr, F with LRD for FSGS
- A rising creatinine level 2 years post Tx (3.9 ng/dl)
- Few glomeruli with mesangial expansion, diffuse tubular atrophy with hyperchromasia and enlargement but no viral inclusions in biopsy
- Had depression and excessive sleepiness
- JCV load of 5x10² copies/ml in blood, but no detectable BKV

Patient 2:

- 21 yr, F, had a cadaveric renal transplant 4 years ago
- a rising creatinine level (3 ng/dl)
- sclerotic glomeruli, patchy tubular atrophy, mononuclear infiltrates and interstitial fibrosis but no viral inclusions in biopsy
- Had a short-term memory dysfunction, episodes of upper extremity numbness, tingling, and irritability, hyper-reflexia of the upper extremity and depression
- MRI showed remote silent right cerebral infarct and some evidence of demyelination
- JCV load of 8.8x10³ in her urine but no detectable BKV