How commonly is JC virus detected in the cerebrospinal fluid of patients with HIV?

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Introduction:

Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection caused by JC virus (JCV) in immunodeficient individuals. The pathological hallmark is irreversible white matter demyelination. The diagnosis is supported by the clinical presentation (subacute motor deficits, ataxia, cortical visual symptoms), characteristic findings on MRI of the brain (bilateral, asymmetric, well-demarcated, T2 hyperintense white matter lesions with no oedema) and JCV detection by polymerase chain reaction (PCR) in the cerebrospinal fluid (CSF)[1]. We investigated how frequently JCV was detected in the CSF from HIV seropositive patients with findings on brain MRI suggestive of PML compared to those lacking MRI features of PML.

Methods:

We obtained retrospective data of all JCV PCR test results performed on CSF samples between March 2002 and November 2011 from our cohort of HIV seropositive patients. These results were correlated with results from contemporaneous MRI imaging of the brain (see table).

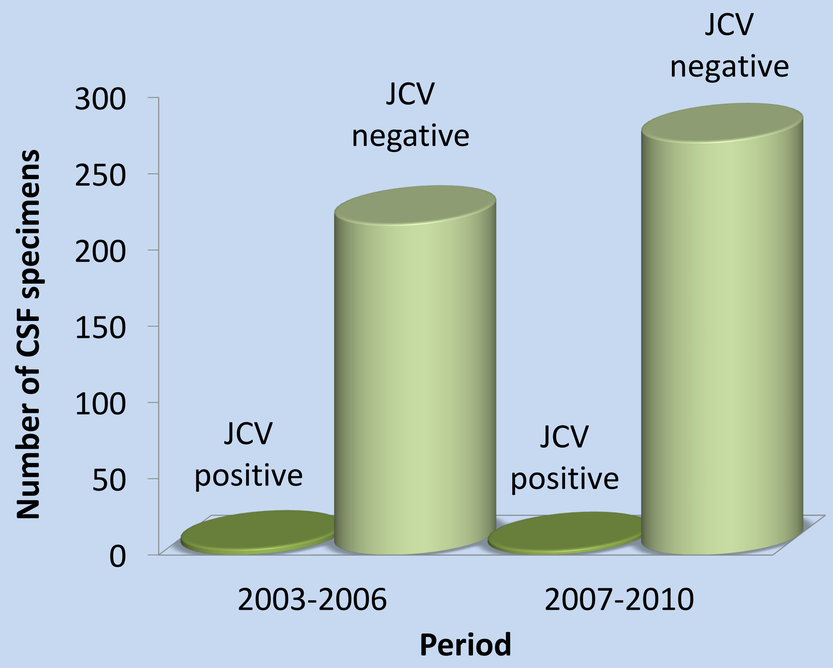
Results:

In total, 564 CSF samples from HIV-positive patients were tested for JCV during 117 months, of which 7 (1.24%) were positive. Contemporaneous MRI imaging of the brain was performed in 360/564 (63.8%) patients. The distribution of JCV PCR results with time is shown in figure 1. The table below shows the correlation of JCV positive results with MRI brain findings.

Discussion:

The gold standard for diagnosis of PML is brain biopsy. However, this is often unsafe, unethical or unnecessary. The combination of an appropriate clinical presentation and typical findings on MRI brain is often sufficient to make the diagnosis, for which HAART is the evidence-based treatment[1]. The utility of JCV PCR testing in the CSF of HIV seropositive individuals is under question (sensitivity for MRI-proven PML = 24-89.5%[2,3]). Unsurprisingly, the use of HAART has been shown to reduce the sensitivity of this test (57.5% vs. 89.5%[3]). Our data suggest that the sensitivity is even lower than previously thought (<5%). This raises the question whether this expensive laboratory test should continue to be ordered routinely.

Fig. 1: Distribution of JCV PCR results with time



Limitations:

It is acknowledged that our data would become more useful after correlation with contemporaneous CD4 counts, HIV viral loads and whether therapy with HAART had been initiated. The retrospective analysis of MRI reports has also been assumed to be consistent, which may not be the case.

Contemporaneous MRI of the brain report	Number of CSF samples tested for JCV	Number of positive JCV tests	Percentage of positive samples
Suggestive of PML	64	3	4.69%
Suggestive of an infectious, but non-PML, pathology	77	2	2.60%
Normal or suggestive of a non-infectious pathology	219	1	0.46%
MRI not performed	204	1	0.49%

Conclusion:

JCV was infrequently detected in the CSF of HIV-positive individuals over a 9-year period. Although JCV was more frequently found in the CSF of patients with MRI findings suggestive of PML, the detection rate was still <5% suggesting a very high false negative rate for this test. CSF JCV testing should not be performed routinely when MRI of the brain is normal or suggestive of a non-infectious pathology. Even when PML is suspected on MRI of the brain, JCV CSF is unlikely to be positive. We conclude that the majority of these tests are unnecessary, offering a potential to significantly reduce costs without compromising patient care.

References:

1. British HIV Association and British Infection Association guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011, *M Nelson, DH Dockrell and S Edwards on behalf of the BHIVA Guidelines Subcommittee.*
2. Effective use of JC virus PCR for diagnosis of progressive multifocal leukoencephalopathy, Y. Wang *et al.; Journal of Medical Microbiology, 58, 253–255, 2009.*
3. Reduced Rate of Diagnostic Positive Detection of JC Virus DNA in Cerebrospinal Fluid in Cases of Suspected Progressive Multifocal Leukoencephalopathy in the Era of Potent Antiretroviral Therapy, A. Marzocchetti *et al*.; *Journal of Clinical Microbiology, Vol. 43, No. 8, p. 4175–4177, Aug. 2005.*