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May New Biomarkers Help us to Predict Progressive Multifocal Leukoencephalopathy in HIV Positive People?

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Date of Submission: May 6, 2011

Date of Acceptance: Jan 27, 2012

How to cite this article: Aminzadeh Z. May new biomarkers help us to predict progressive multifocal leukoencephalopathy in HIV positive people?. Int J Prev Med 2012;3:515-6.

Letter to Editor

Dear Editor,

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the brain caused by the JC virus (JCV).[1] PML is caused by lytic infection of glial cells in severely immunosuppressed patients and is often fatal.[2] JCV infects most people in childhood and is usually asymptomatic. Afterwards, the virus persists in the body in a latent state, where viral protein expression cannot be detected and replication occurs only episodically and at the low levels.[3,4]

Blood samples taken from healthy individuals indicate that 50–90% of adults have been exposed to this virus, with 19–27% shed JC virus in their urine.[5,6] The JC virus can be detected by PCR in the urine of a third of healthy individuals or immunosuppressed patients with or without PML.[5,7,8] However, the JC virus is not usually found in the blood of immunocompetent individuals. Detection of JCV in blood is correlated with immunosuppression and not with PML.[8] Currently, there is no blood biomarker of JCV activity that may be used to diagnose PML.[1]

A failure to detect JCV DNA in the CSF sample does not rule out the possibility of having PML, particularly in the earlier stages of the disease.[1] However, a false positive JCV test happens in 1–4% of HIV positive people.[9,10] Wollebo[11] also pointed out the presence of robust levels of TNF-α and TNFR1 in clinical samples of PML lesions from an HIV patient.

Table 1 gives the comparison of various diagnostic methods which have been assessed and also shows that how and where a new biomarker can be placed if a special biomarker for JCV reactivation is detected. The author proposes a

Table 1: Comparison of various diagnostic methods in healthy people and HIV patients with and without PML

Diagnostic methods	Normal people	HIV without PML	HIV with PML
PCR-JCV in urine	Positive	Positive	Positive
PCR-JCV in blood	Negative	Positive or negative	Positive
JCV DNA in peripheral blood monocytes	Positive	Positive	Positive
JC antibody	Positive	Positive	Positive
JCV DNA in CSF	Negative	Negative	Positive
		False positive (1-4%)	False negative in early stage
Characteristic findings in brain biopsy	Negative	Negative	Positive
Biomarker TNF-α in brain sample	Negative	Positive slightly	Positive significantly
Biomarker TNFR1 in brain sample	Negative	Negative	Positive significantly

PML - Progressive multifocal leukoencephalopathy, JCV - JC virus

new idea on measuring cytokine (TNF-alfa) and its receptor TNFR1 in blood and CSF samples of HIV patients as a predictor of JCV reactivation and PML. It would be helpful to diagnose PML in early stage and start special treatment for patients to have longer survival.

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Source of Support: Nil. **Conflict of Interest:** None declared.