



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Virology

ESPS manuscript NO: 22039

Title: Neuropathology of JC virus infection in progressive multifocal leukoencephalopathy in remission

Reviewer’s code: 03197139

Reviewer’s country: United States

Science editor: Shui Qiu

Date sent for review: 2015-08-11 15:06

Date reviewed: 2015-08-18 04:25

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

JCV is a human polyomavirus that infects greater than 60% of the human population during childhood, and establishes a latent infection in healthy individuals. Replication of the neurotropic strain of JCV in glial cells causes the fatal demyelinating disease of the central nervous system, progressive multifocal leukoencephalopathy (PML), which is seen in patients with underlying immunocompromised conditions. PML has also been described in patients with autoimmune diseases treated with immunomodulatory therapies. PML is a mortal disease and there is no specific therapy. Long-term survivors have been reported with no sign of viral reactivation and replication. There is little known about neuropathologic description of long-term survivals. In this manuscript, authors provided an interesting case report of a long-term PML survivor with immunohistological evaluation. These observations are interesting for the readers of the Journal. However, the following issues needed to be addressed. Major comments: 1. Authors stated in the discussion (the first paragraph-lane 8-10) that “polyomaviruses integrate into the host DNA”. Polyomaviruses mostly stays episomal and do not commonly integrate with host chromosomes.



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

Unlike retroviruses, polyomaviruses do not carry or encode integrase. 2. Unlike the conclusion made by authors, the postmortem histological evaluation of cerebellar lesions points demyelination, viral antigen (T-antigen) expression, enlarged bizarre astrocytes, and p53 expression that all indicates JCV reactivation and PML lesions. 3. Authors indicate that the T-antigen staining in Fig. 2E and p53 staining in Fig. 2F are nonspecific. It is important to have a non-PML cerebellar section as a control in parallel to make this conclusion. Additionally, the SV40 T-antigen antibody used in the study can recognize all the early gene products of polyomaviruses including small t antigen and T' proteins. Some of these proteins including small t antigen exclusively localizes to the cytoplasm. Therefore, the observed cytoplasmic staining does not exclude that these cells are not infected. Additionally if examined carefully, the panel E in Fig.2 also shows nuclear staining of some cells for T-antigen. 4. In order to make the case and conclusions based on JCV remission, the postmortem CSF viral loads with strain sequencing (if possible) should be analyzed. Minor comments: The antibody "middle T antigen" in several places (including figure legends) in manuscript must be corrected with T-antigen and stayed consisted. The antibody used recognizes all the early products of JCV T antigens.



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		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

excellent article, informative and to the point. could you include a radiograph (or two? - at diagnosis, and prior to death if possible)