

## LETTER TO THE EDITORS

# Progressive multifocal leukoencephalopathy cannot be due to liver cirrhosis alone

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We read with interest the article by Almeida et al.<sup>1</sup> on a 57 year-old male with progressive, multifocal leukoencephalopathy (PML) attributed to liver cirrhosis. It was concluded that PML can have multiple clinical manifestations and affect patients with mild or transient immunosuppression.<sup>1</sup> The study is excellent but has concerning limitations that should be discussed.

The main limitation is that causes of immunosuppression other than HIV were not adequately ruled out. It is not mentioned whether the patient had leukemia, lymphoma (e.g., primary central nervous system lymphoma) or other diseases of the reticulo-endothelial system. Wiskott-Aldrich syndrome was also not excluded. Neither is it mentioned whether the patient had a history of multiple sclerosis, organ transplantation (e.g., bone marrow or solid organ), or autoimmune disease. In addition, it should be ruled out that the patient previously received natalizumab, rituximab, efalizumab, eculizumab, or brentuximab, drugs that have been associated with the development of PML.<sup>2,3</sup> Cytomegalovirus encephalitis and toxoplasmosis are other differential diagnoses of PML that must be ruled out.<sup>4</sup>

A second limitation is that the patient was not systemically screened for occult neoplasms. No mention is made of tumor markers, gastroscopy, colonoscopy, or computed tomography of the thorax and abdomen.

A third limitation is that the complete immune status of the index patient was not reported. Which values were measured when determining C-reactive protein, immunoglobulin G, immunoglobulin M, immunoglobulin A, anti-nuclear antibody, complete blood count, CD4 count, CD4/CD8 ratio, secondary humoral response to recall antigen, titers of isohemagglutinins, complement assay,

examination of lymphocyte proliferation, cytokines (interleukins, interferon titers), and chemokines?<sup>5</sup>

A fourth limitation is that the long-term outcome was not reported. Since the prognosis of PML is generally poor, we should know for how long the index patient survived after receiving the diagnosis, as well as the treatment type. Did the patient receive dendritic cell vaccine?<sup>4</sup> Was the patient receiving anti-retroviral treatment and did he develop immune reconstitution inflammatory syndrome while on anti-retroviral treatment?

In summary, this interesting study has limitations that call the results and their interpretation into question. Addressing these issues would strengthen the conclusions and could improve the status of the study. Before PML can be attributed to liver cirrhosis, all alternative causes must be thoroughly ruled out.

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## Disclosure

The authors report no conflicts of interest.

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