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Letters to the Editor

Towards an unbiased, collaborative effort to reach evidence about the presence of human cytomegalovirus in glioblastoma (and other tumors)

The question of whether most gliomas are infected with human cytomegalovirus (HCMV) has been under dispute for more than 10 years. We recently reported our failure to detect HCMV in gliomas in Neuro-Oncology.[1] Our article was accompanied by 2 related editorials,[2,3] one of which boldly criticized our approach.[3] Instead of fighting a petty, ivory tower dispute, we would like to lobby for a serious collaborative approach to providing conclusive evidence on the presence of HCMV in glioma (and other cancers). Since we developed the concept of oncomodulation (ie, that HCMV may increase tumor malignancy by infecting established tumor cells and/or tumor-associated cells) in 1996,[4,5] we have been confronted with requests from desperate cancer patients who wanted to know whether they should be treated with antiviral drugs. Eighteen years later, we still do not have an answer to this question.

The accusation that we are ignorant of the evidence supporting that HCMV infects gliomas[3] is, in our opinion, not justified. We initially tried to use the highly sensitive techniques for HCMV detection that were described by Charles Cobbs and other groups.[3] However, the staining results looked the same in glioma samples from HCMV seropositive and seronegative patients. We then contacted 3 groups that reported the detection of HCMV infection in glioma. The principal investigator of one group responded that the responsible postdoc, who had performed the experiments, had left and that no materials or data were available anymore. The 2 other groups agreed to stain our samples for us. However, again there was no difference between glioma tissues from seropositive and seronegative patients. Upon our request, the 2 groups refused to publish these data. After these experiences, we developed the methods described in our article[1] and could not detect HCMV.

We are aware of reports on HCMV-positive tumors in HCMV seronegative patients,[6] but we doubt the validity of these findings. The diagnostic tests for HCMV are very reliable for identifying HCMV-infected immunocompromised patients who are at risk of HCMV disease. Moreover, we and others neither found a difference in the glioma prevalence in HCMV-seropositive and –negative patients nor in disease severity.[1] If there was a substantial difference in the individual immune response to HCMV that resulted in an antibody response in some cases but not in others, we would expect some differences in both disease course and outcome.

Taken together, this is about patients in need, and we do not have any time to lose. We need a collaborative, interdisciplinary approach among neuro-oncologists, virologists, and pathologists that includes the open (and open-minded) exchange of data and techniques in order to achieve a broad consensus. We are prepared to be convinced, and we hope that everybody working in the field is also.

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