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Letter to the editor

No circulating human cytomegalovirus in 14 cases of glioblastoma

Cobbs et al have reported that many gliomas contain human cytomegalovirus (HCMV) gene products.[1] Mitchell et al reported that 80% of patients with diagnosed glioblastoma multiforme have HCMV DNA in their peripheral blood; seropositive normal donors and other surgical patients did not.[2] However, Baumgarten et al reported that HCMV infection in tumor cells of the nervous system is not detectable with standardized pathologico-virological diagnostics,[3] calling into question the etiologic role of HCMV in glioblastoma.[4]

In our own studies, we have collected peripheral blood in anticoagulated tubes from 14 patients with newly diagnosed glioblastoma multiforme who were referred for radiation therapy.[5] We used standard methods for detecting HCMV by reverse transcriptase PCR[6] and peripheral blood culture.[7] None of our patients had circulating HCMV detected. Mitchell et al reported that 80% of patients with newly diagnosed glioblastoma multiforme have detectable cytomegalovirus DNA in their peripheral blood.[2] The chance of a single glioblastoma patient not having detectable cytomegalovirus would be 20% or 0.2. Therefore, the chance of none of 14 patients having detectable cytomegalovirus would be 0.2^{14} or $P = 1.6 \times 10^{-10}$.

Moreover, HCMV seropositivity data and glioblastoma incidence data do not support a HCMV-glioblastoma association since HCMV seroprevalence rates are not consistently related to glioblastoma incidence rates.[8] HCMV seroprevalence is, however, related to socioeconomic status. HCMV infection is significantly lower in whites than in blacks or Hispanics (Mexican Americans), while glioblastoma incidence is higher in whites than in blacks or Hispanics. But HCMV seroprevalence rates are significantly higher in women than in men, although glioblastoma is more common in men. Therefore, a possible HCMV-glioblastoma association cannot be readily substantiated with HCMV seropositivity rates.

Age at infection may be involved since the incidence of both glioblastoma multiforme and HCMV infection are related to socioeconomic status, as described above. HCMV infection in early childhood, which is more common in lower socioeconomic groups, may be protective against glioblastoma, whereas HCMV infection in later childhood or adulthood may be a risk factor for glioblastoma. If so, glioblastoma would be similar to paralytic polio, in which low socioeconomic status, poor hygiene, and early infection are protective.[9]

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References

1. Cobbs C. Response to "Human cytomegalovirus infection in tumor cells of the nervous system is not detectable with standardized pathologico-virological diagnostics." *Neuro Oncol*. 2014;16(11):1435–1436.
2. Mitchell DA, Xie W, Schmittling R, et al. Sensitive detection of human cytomegalovirus in tumors and peripheral blood of patients diagnosed with glioblastoma. *Neuro Oncol*. 2008;10(1):10–18.
3. Baumgarten P, Michaelis M, Rothweiler F, et al. Human cytomegalovirus infection in tumor cells of the nervous system is not detectable with standardized pathologico-virological diagnostics. *Neuro Oncol*. 2014;16(11):1469–1477.
4. Huse JT, Aldape K. CMV and glioma - are we there yet? *Neuro Oncol*. 2014;16(11):1433–1434.
5. Lehrer S, Labombardi V, Green S, et al. No circulating cytomegalovirus in five patients with glioblastoma multiforme. *Anticancer Res*. 2011;31(3):959–960.
6. Gozlan J, Salord JM, Chouaid C, et al. Human cytomegalovirus (HCMV) late-mRNA detection in peripheral blood of AIDS patients: diagnostic value for HCMV disease compared with those of viral culture and HCMV DNA detection. *J Clin Microbiol*. 1993;31(7):1943.
7. Shibata D, Martin WJ, Appleman MD, et al. Detection of cytomegalovirus DNA in peripheral blood of patients infected with human immunodeficiency virus. *J Infect Dis*. 1988;158(6):1185–1192.
8. Lehrer S, Green S, Ramanathan L, et al. No consistent relationship of glioblastoma incidence and cytomegalovirus seropositivity in whites, blacks, and Hispanics. *Anticancer Res*. 2012;32(3):1113–1115.
9. Lehrer S. Cytomegalovirus infection in early childhood may be protective against glioblastoma multiforme, while later infection is a risk factor. *Med Hypotheses*. 2012;78(5):657–658.

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