No Consistent Relationship of Glioblastoma Incidence and Cytomegalovirus Seropositivity in Whites, Blacks, and Hispanics

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Abstract. *Glioblastoma multiforme is the most common and most aggressive type of primary brain tumor, accounting for 52% of all primary brain tumor cases and 20% of all intracranial tumors. Recently, evidence for a viral cause has been postulated, possibly cytomegalovirus (CMV). In one report, 80% of patients with newly diagnosed glioblastoma multiforme had detectable cytomegalovirus DNA in their peripheral blood, while sero-positive normal donors and other surgical patients did not exhibit detectable virus. However, another study reported that five glioblastoma patients showed no circulating CMV detected either with RT-PCR or blood culture. Materials and Methods: We utilized Cytomegalovirus Seroprevalence in the United States data from the National Health and Nutrition Examination Surveys, 1988-2004. Glioblastoma Incidence Rates 2004-2008 by race and gender are from Cancer of the Brain and Other Nervous System - SEER Stat Fact Sheets (http://seer.cancer.gov/statfacts/html/ brain.html). Statistical significance was determined from published 95% confidence intervals. Results: CMV seroprevalence rates are not consistently related to glioblastoma incidence rates. CMV seroprevalence is significantly lower in whites than in blacks or Hispanics (Mexican Americans), while glioblastoma incidence is higher. However, both CMV seroprevalence and glioblastoma incidence are higher in Hispanics than in blacks. CMV seroprevalence rates are significantly higher in women, 55.5% (53.3-57.7, mean±95% CI) than men, 45.2% (42.4-48.0), although glioblastoma is more common in men. Conclusion: A possible CMV-glioblastoma association cannot be readily substantiated with CMV seropositivity rates.*

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Glioblastoma multiforme is the most common and most aggressive type of primary brain tumor, accounting for 52% of all primary brain tumor cases and 20% of all intracranial tumors. Glioblastoma multiforme is more common in males and appears to be sporadic, without any genetic predisposition. No conclusive links have been found between glioblastoma multiforme and smoking, diet, cellular phones, or electromagnetic fields. Recently, evidence for a viral cause, cytomegalovirus (CMV), has been postulated (7).

Cobbs *et al*. reported that a high percentage of malignant gliomas are infected by CMV and multiple CMV gene products are expressed in these tumors (4). Prins *et al*. found CMV immunity after vaccination with autologous glioblastoma lysate (8). Mitchell *et al*. reported that 80% of patients with newly diagnosed glioblastoma multiforme have detectable cyto-megalovirus DNA in their peripheral blood, while sero-positive normal donors and other surgical patients did not exhibit detectable virus (7). Mitchell *et al*. suggested an association of CMV with malignant glioma and proposed that subclinical CMV viremia is a previously unrecognized manifestation of glioblastoma multiforme. However, Lehrer *et al*. reported that five glioblastoma patients showed no circulating CMV detected either with RT-PCR or blood culture (5).

In this study, we examine CMV seropositivity data and glioblastoma incidence.

Materials and Methods

We utilized *Cytomegalovirus Seroprevalence* in the United States data from the National Health and Nutrition Examination Surveys, 1988-2004 (1). Glioblastoma Incidence Rates 2004-2008 by Race and gender are from Cancer of the Brain and Other Nervous System - SEER Stat Fact Sheets (http://seer.cancer.gov/statfacts/html/brain.html). Statistical significance was determined from published 95% confidence intervals.

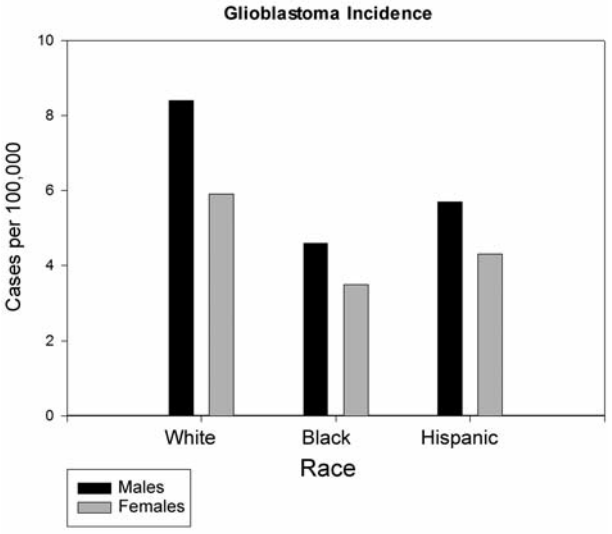

Figure 1. *Glioblastoma incidence in males and females by race, data from Cancer of the Brain and Other Nervous System - SEER Stat Fact Sheets (http://seer.cancer.gov/statfacts/html/brain.html). Glioblastoma is more common in males than females and in whites when compared with blacks and Hispanics.*

Results

Glioblastoma incidence rates are presented in Figure 1. Glioblastoma is more prevalent in males than females, and in whites compared to non-whites (10).

The increased glioblastoma incidence in whites, when compared with blacks and Hispanics, is also confirmed by data from cancer registries, which suggest that glioblastoma incidence is proportional to socioeconomic status. The 2004-2007 age-adjusted incidence rate of glioma per 100,000 persons varies considerably by race (6.5 among whites, 3.3 among blacks) (2). One study of glioblastoma demonstrated higher rates among persons residing in high socioeconomic areas, even after statistical adjustment for confounding factors (3). A Swedish study reported increased odds of glioma among those with a higher family income adjusted for gender, age, and geographic region (11).

CMV seroprevalence rates are not consistently related to glioblastoma incidence rates (Figure 2). CMV seroprevalence is significantly lower in whites than in blacks or Hispanics (non-white Mexican Americans), although glioblastoma is more common in whites. However, both CMV seroprevalence and glioblastoma incidence rates are significantly higher in Hispanics, 76.9% (74.1-79.6, mean±95% CI) than blacks, 70.6% (68.5-72.8). CMV seroprevalence rates are significantly higher in women, 55.5% (53.3-57.7) than men, 45.2% (42.4-48.0) (1), though there are more cases of glioblastoma reported in men.

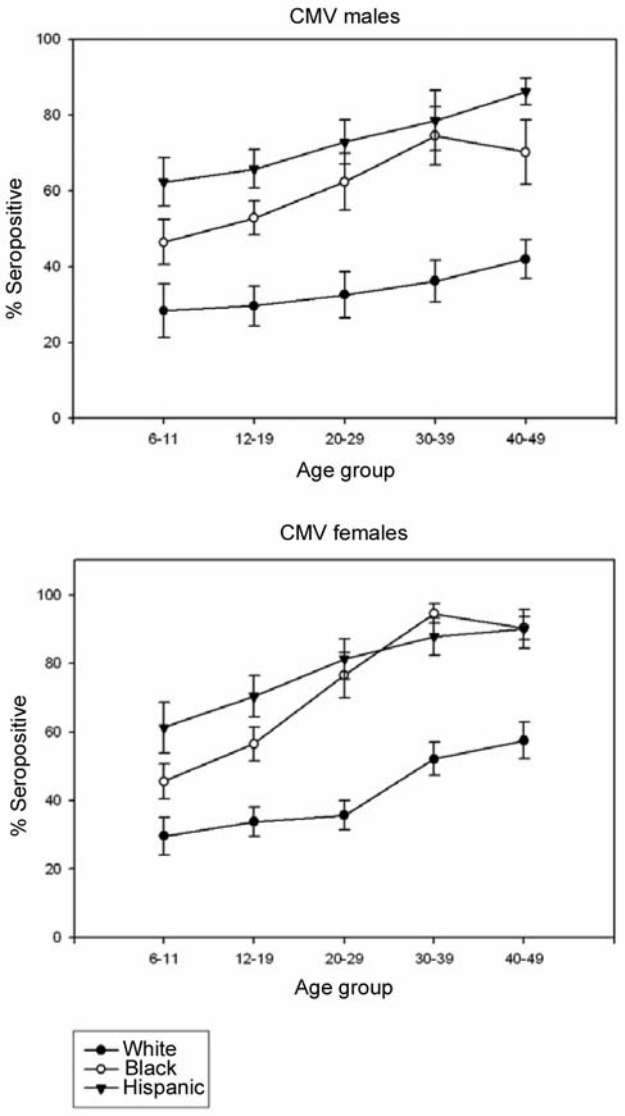

Figure 2. *CMV seroprevalence in males (Mean±95% CI) and females, data from table 2, reference (1). CMV seroprevalence is significantly lower in whites than in blacks or Hispanics (Mexican Americans), but higher in females than males.*

Discussion

CMV is one of the eight human herpesviruses. CMV infects at least half of the population in developed countries, and nearly everyone in developing countries, where poor sanitation and poor hygiene abet its transmission. Although it generally does not produce problems in healthy adults, CMV is a common cause of birth defects, and it can cause serious problems in immuno-compromised people, particularly AIDS patients, who often develop CMV chorioretinitis (6). Moreover, increased CMV antibody levels are associated with impaired cognition,

frailty, functional impairment, and increased mortality among community-dwelling older adults (9).

The CMV-glioblastoma association is controversial. It is unclear why CMV, a common virus, would cause glioblastoma in only a small subset of individuals infected, especially since *in vitro* studies have failed to show that CMV transforms normal cells into cancerous cells. Yet some preliminary results indicate Valcyte (Roche), an antiviral drug, may improve prognosis in glioblastoma patients, despite the questionable CMV association (6).

Certainly, a CMV-glioblastoma multiforme association deserves further investigation; but the data above suggest that a possible CMV-glioblastoma association cannot be readily substantiated with CMV seropositivity rates.

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