LETTER TO THE EDITOR

Women with Left Frontal Glioblastoma Have a Significantly Shorter Survival—Why?

Dear Editor:

In both experimental and clinical studies, the two cerebral hemispheres have been linked to different immune responses. In patients with stroke, the right frontal cortex-putamen region has been shown to influence the magnitude of immune responses. The delayed-type hypersensitivity reaction is altered in the chronic phase of stroke only in patients with right hemisphere lesion (Tarkowski et al., 1991, 1995). Also, in animal models, indications of a specialization of the right and left sides of the brain have been demonstrated with regard to the modulation of the immune system. Thus, ablation of the left frontoparieto-occipital cortex leads to a decrease of mitogen-induced T-cell proliferation, whereas similar ablation of the right side leads to an enhanced mitogenesis (Renoux et al., 1983). Also, at the subcortical level, an asymmetrical modulation of immune responses may exist. Lesions in the right substantia nigra enhance the proliferation of splenic T-cells, and similar lesions on the left side decrease their proliferation (Neveu, 1992).

The question of whether the immune response is controlled by special areas in the brain might be illuminated by the study of another of its diseases. Malignant gliomas infiltrate and destroy a volume of the brain during a relatively short time period. One could speculate that, if the immune response of the patients is controlled by special brain areas, tumor growth in immunosuppressive areas should allow for longer survival and in immunostimulating areas should lead to a more rapid death.

We have reanalyzed a prospective study from the years 1981 to 1987 (Sandberg-Wollheim et al., 1991) on the effect of chemotherapy with or without radiotherapy on survival time of patients with supratentorial glioblastoma (GBM). One single group of patients differs from all the others. Eleven women with left-sided frontal GBM had a significantly shorter survival time ($P = 0.02; \text{log-rank test}$) than 11 women with right-sided frontal tumors.

A new retrospective study of 369 patients with distinct lobar GBM localization, conducted in our department from 1988 to 1997, shows the same results: 26 women with left-sided frontal tumors have a shorter survival time ($P = 0.002; \text{log-rank test}$) than 21 women with right-sided frontal tumors. When all women studied from 1981 to 1997 are included, 37 with left-sided frontal GBMs have a shorter survival time than 32 with right-sided frontal tumors ($P = 0.0001; \text{log-rank test}$).

How can this be explained? Is an immunostimulating center in the left frontal lobe destroyed by the infiltrating tumor? Why only in women? Hormonal influence? Left-sided GBMs in men do not kill faster than right-sided GBMs, and surgical extensiveness is not related to sex. The literature describes many unexplained differences between the hemispheres and genders in function and in hormonal, transmitter, and immunological situations. However, brain injury has proven to induce immune deficiency syndrome (Meisel et al., 2005), and if studied in detail, the localization of the injury and gender might stratify these effects further.

Continued search for these and other differences may give clues to a better understanding of the battle between the advancing malignant brain tumor and its hosting brain, and thereby possibilities for improved therapies.

Sincerely,

Leif G. Salford, Erik Nordenström, Gunnar Skagerberg, Torgil Möller, Bengt Widegren, and Roland Perfekt

Department of Neurosurgery (L.G.S., E.K., G.S.), the Oncological Centre (T.M., R.P.), and Department of Tumour Immunology (B.W.), Lund University, Sweden


Leif G. Salford is Professor of Neurosurgery at Lund University in Lund, Sweden

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References


