Energy metabolism of glial tumors

GERARD M. LEHRER, M.D., AND HOWARD S. MAKER, M.D.
Division of Neurochemistry, Department of Neurology, The Mount Sinai School of Medicine, City University of New York, New York City, New York, U.S.A.

When cytologically homogeneous areas of human and experimental glial neoplasms were examined by quantitative microanalysis of frozen-dried sections, consistent results were obtained within homogeneous areas of the same tumor, but adjacent regions often varied widely. The enzyme spectra of several human gliomas, as well as of an experimental mouse ependymoblastoma resembled that of immature brain. Hexokinase and malate dehydrogenase were lower, and lactate, glucose-6-phosphate, and NAD-linked isocitrate dehydrogenases and β-D-glucuronidase were higher in the tumors than in whole adult human or mouse brains. The lactate dehydrogenase isoenzyme pattern of the ependymoblastoma also closely resembled that of immature brain.1,2

The ependymoblastoma, which had originally been produced in the laboratory of Dr. Harry Zimmerman and was propagated by serial subcutaneous transplantations, showed amazing constancy of both its histological characteristics and its enzyme spectrum through more than 300 generations. The steady-state fluxes of glycolytic metabolites and high-energy phosphates were studied in the experimental tumors under conditions of intracranial and subcutaneous growth.

Both tumors and brains of the tumor-bearing animals were assayed after exposure to varying periods of ischemia prior to freezing.3 Steady-state levels of lactate, ADP, and AMP were higher, and ATP and creatine phosphate levels were lower in the tumor than in brain. During an ischemic period of 10 minutes, progressive anaerobic metabolic changes in glucose, glycogen, lactate, glucose 6-phosphate, creatine phosphate, ATP, ADP, and AMP occurred in all tissues in these animals.

However, the metabolic flux was slower in the subcutaneously growing tumor than in the other tissues. The steady-state levels of most substrates in the tumors resembled those of ischemic brain. When ATP levels were assayed in various areas of frozen-dried sections from the subcutaneously growing ependymoblastoma, large variations in the concentrations of this substrate were found. In regions closest to the blood supply, the ATP concentration was similar to that in normal brain, while lower levels were found in viable-appearing adjacent areas.

The results of our studies confirm the hypothesis that environmental factors are an important determinant in the mode of metabolism of tumor as a whole and of regions within it.4 Studies of tumor metabolism should therefore be confined to specific, physiologically and histologically identified regions which can be related to growth, blood supply, and other parameters susceptible to local variation. The mode of metabolism of the neoplasm is more clearly related to local factors than it is to the enzymatic potential of the tissue. Under optimal conditions, e.g., a small tumor growing in the brain, the tumor metabolism closely resembles that of immature brain. There is no evidence to suggest that a tumor-specific metabolism exists which is related to the neoplastic process. The metabolism of glial tumors growing under optimal conditions so closely resembles that of the stem cell that the tumor may serve as a chemical model of some glial functions.
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References