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Distribution of 4-hydroxynonenal-protein conjugates as a marker of lipid peroxidation and parameter of malignancy in astrocytic and ependymal tumors of the brain

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ABSTRACT

Aims and background. Lipid peroxidation (LPO) is an autocatalytic process caused by oxidative stress. It results in the production of 4-hydroxynonenal (HNE), which plays a crucial role in hypoxic brain injury, neuronal degeneration and apoptosis. The aim of this study was to evaluate the expression of HNE in 120 astrocytic and 40 ependymal tumors in relation to tumor type, grade of malignancy, angiogenesis, and presence of necrosis and apoptosis.

Methods. Immunohistochemical staining was performed using a monoclonal antibody for the detection of HNE-modified proteins.

Results. HNE-protein adducts were found in all tumors. The incidence of HNE-immunopositive tumor cells increased with increasing grades of malignancy. Significantly higher HNE expression was found in tumor cells of glioblastomas multiforme than in cells of pilocytic astrocytomas (P <0.005), and in anaplastic ependymomas than in benign ependymomas (P <0.01). HNE-immunopositive tumor cells were distributed more diffusely than in perivascular locations (P <0.05). Pronounced HNE-protein adducts were detected in mitotic, necrotic, and apoptotic cells. HNE was expressed in the endothelium of almost all tumor vessels, but its expression in the walls of the vessels was significantly higher in diffuse and anaplastic astrocytomas than in pilocytic astrocytomas and glioblastomas multiforme (P <0.05). The number of microvessels containing HNE in their endothelium and walls was significantly associated with the grade of malignancy in both astrocytic (P <0.001) and ependymal tumors (P <0.05), although microvessels in pilocytic astrocytomas were significantly more numerous (P <0.05) than in diffuse astrocytomas.

Conclusions. LPO seems to be a common pathological process in astrocytic and ependymal glial tumors, proportional to the level of malignancy and neovascularization. Therefore, HNE might be involved in the damage of brain cells and the induction of malignancy.

List of abbreviations

AA = anaplastic astrocytoma; AE = anaplastic ependymoma; CAT = catalase; CNS = central nervous system; DA = diffuse astrocytoma; DAB = diaminobenzidine; DNA = deoxyribonucleic acid; E = ependymoma; GBM = glioblastoma multiforme; GPx = glutathione peroxidase; GRx = glutathione reductase; GST = glutathione-S-transferase; HNE = 4-hydroxynonenal; HNE-dG = 4-hydroxynonenal deoxyguanosine; IMD = intratumoral microvessel density; LPO = lipid peroxidation; MDA = malondialdehyde; PA = pilocytic astrocytoma; PUFA = polyunsaturated fatty acid; ROS = reactive oxygen species; SOD = superoxide dismutase; VEGF = vascular endothelial growth factor

Key words: 4-hydroxynonenal, astrocytomas, ependymomas, angiogenesis.

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