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ON THE BIOLOGICAL SIGNIFICANCE OF APOPTOSIS IN GLIOMAS

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Apoptosis in gliomas occurs in direct relation with histological malignancy and in malignant gliomas it appears to correlate with cell proliferation, even though it is abundantly present in regressive areas. Its interpretation must take into account, for prognostic purposes, not only a possible transcriptional origin, but also a receptorial one. In a series of malignant gliomas, the demonstration of apoptotic nuclei by in-situ end-labeling methods and morphology showed that apoptotic index (AI) has a linear correlation with mitotic index (MI) only in proliferative areas and not in regressive areas. Using cleaved caspase-3, -7 and PARP for the demonstration of apoptosis it was observed that in proliferative areas the number of caspase-3 positive nuclei roughly corresponded to that of ISEL-positive nuclei, whereas in regressive areas they were less numerous. It is possible that transcriptional apoptosis prevail in proliferative areas and the receptorial one in regressive areas.

In well differentiated astrocytomas, apoptotic nuclei are found in a very low number. In the transition from these tumors to anaplastic astrocytomas many genetic changes have been described, associated with some phenotypic features, whereas little is known on the transition from precursor cells to astrocytomas. One hypothesis is that beside a PDGFR amplification, a failure of apoptosis may be responsible. A series of astrocytomas which recurred as such and a series of astrocytomas which recurred as anaplastic tumors or glioblastomas have been studied for apoptosis as before mentioned. If the hypothesis of apoptosis failure was true, the number of apoptotic nuclei should have been higher in tumors which preserved benign features than in those which transformed. However, a difference was found , but not statistically significant. The main point to be emphasized in this regard is the destiny of cells which escaped apoptosis, taking into account that DNA breaks in living cells mean accumulation of mutations. This possibility must be discussed in relation with radiotherapy of gliomas.

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