26 Effects of Treatment on Brain Tumors and Normal Nervous Tissue

26.1 Effects of Radiotherapy and/or Chemotherapy on Human Brain Tumors

The effects of radiotherapy and chemotherapy on malignant gliomas have been studied extensively [3050, 902, 1295, 334, 2505, 2506, 2508, 1034A]. Since they are not specific, it is difficult to separate them from those developing spontaneously in the tumor during its natural course. An example is glioblastoma central necrosis. The frequency of the changes depends on the material available for study, biopsy or autopsy, time elapsed between treatment and death, and radiation dose. Macrophagic areas, monstrous and giant cells (Fig.26.1), atypical mitoses and bizarre astrocytes are maximally represented at a short distance from the irradiation and, therefore, might be considered as "short-term effects". Vessel wall changes, e.g., hyalinization and fibrinoid necrosis, increase both with the radiation dose and the distance from treatment. Also, the disappearance of morphologic features typical of active growth such as endothelial proliferations and mitoses, parenchymal mitoses and circumscribed necroses with pseudopalisading can be attributed to radiotherapy. All these features reappear along with the tumor regrowth that most frequently happens for glioblastomas between 6 and 12 months after doses of about 6000 cGy [2508, 336]. Interesting but not specific are the morphologic patterns of regrowth: An overgrowth of a population of small anaplastic cells may take place and tumor repopulation may start again both from cells in the brain adjacent to the tumor (BAT) and from cells close to the central necrosis. The tumor builds up new vessels from those of the normal nervous tissue already damaged by irradiation, as demonstrated by the occurrence of endothelial hyperplasia in vessels with fibrous-hyalin degeneration of the wall. In long term survivors, more commonly after 1 year past the end of radiotherapy, a population of fibroblastic-like cells develops from thickened hyalinized vessel walls [2522]. These cells have been interpreted as an expression of a sarcomatous transformation, even though true fibrosarcomas from irradiated glioblastomas have never been observed, perhaps because of the associated short duration of survival.

Morphologic changes produced by chemotherapy on malignant gliomas are hardly distinguishable from those produced by radiotherapy. An increase of monstrous and giant cells and, less frequently, of nuclear hyperchromasia and nuclear-cytoplasmic inclusions after treatment with different drugs are reported [1297].

In all autopsy series of malignant gliomas treated with radiotherapy after surgery [334, 2505, 2506] or intraarterial chemotherapy [2363], there are patients with no sign of tumor regrowth but with severe damage of the normal nervous tissue.
Very few data are available on the effects of radiotherapy on well-differentiated astrocytomas. In a personal series [2510], astrocytomatosous areas of glioblastomas were studied, and the only change was chronic edema. In one case, small necrotic foci were found, probably representing small anaplastic foci sterilized by radiation. In the case of brain tumors more radiosensitive than gliomas, such as medulloblastomas, germinomas, lymphomas, leukemias, and metastases, an almost complete sterilization of the neoplastic cells may sometimes be observed.

26.2 Effects of External Radiotherapy on the Human Brain

Adverse effects of external radiotherapy on the normal human brain may be divided into three types according to the latency period [2618, 1607A]: acute, early delayed, and late delayed. Acute effects occur during irradiation and clinically are variably characterized by headache, nausea and vomiting, somnolence, temperature elevation and an exacerbation of neurologic symptoms and/or signs, being transitory and reversible with steroids. The acute syndrome is more frequent when the previous neurological status of patients was poor and when treatments with high doses per fraction (>200 cGy) are used. No pathologic data are available on this syndrome.

Early delayed effects appear between 2 weeks and 4 months after irradiation, with a variety of reversible neurologic symptoms, and the incidence may approach 25%