Growth-inhibitory effect of diphenylhydantoin on murine astrocytomas.

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Abstract
In previous work reported from this laboratory we found that diphenylhydantoin (DPH) inhibited the growth of 7 of 10 tissue-cultured human astrocytoma cell lines in a microtiter system. In this report we describe significant growth inhibition by DPH of two murine astrocytoma tissue cultures and correlate these in vitro findings with the in vivo activity of DPH in rat subcutaneous and intracranial tumor models. In the in vivo studies, rats were inoculated either subcutaneously or intracranially with RT9 or C6 rat gliomas. DPH or placebo was injected intraperitoneally in doses ranging from 50 to 150 mg/kg daily for 15 days. The DPH-treated rats showed significantly slower rates of tumor growth than untreated rats (p less than 0.01) in both the subcutaneous and intracranial models. At sacrifice, the tumor volume of the rats with subcutaneous tumors treated with DPH (100 mg/kg daily) was 62% less than the tumor volume of the control rats. Also, the number of "clonogenic" cells and thus, indirectly, the number of actively dividing tumor cells was 54% less in the intracranial tumors of the DPH-treated rats. These findings indicate that DPH may be a potentially useful adjunctive agent in the clinical chemotherapy of astrocytic tumors. Furthermore, the data presented indicate that in vitro test results are predictive for in vivo effects, supporting the idea that tissue culture can be used to screen for the effectiveness of clinically used chemotherapeutic agents.

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