Photoirradiation therapy of experimental malignant glioma with 5-aminolevulinic acid

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Purpose: 5-aminolevulinic acid (5-ALA) induces the accumulation of protoporphyrin IX in malignant gliomas. Since protoporphyrin IX is a potent photosensitizer, the present experiments seek to elucidate whether accumulation might be exploited for photoirradiation therapy of experimental brain tumors without injuring normal or edematous brain.

Method: Rats were craniotomized for (a) photoirradiation of cortex (200 J/cm², 635 nm argon-dye laser), (b) photoirradiation (200 J/cm²) of cortex 6 hours after intravenous 5-ALA (100 mg/kg b.w.), (c) cortical cold injury for edema induction, (d) cortical cold injury with simultaneous administration of 5-ALA (100 mg/kg b.w.) and photoirradiation (200 J/cm²) 6 hours later, or (e) irradiation of cortex (200 J/cm², 635 nm) 6 hours after intravenous 5 mg/kg b.w. Photofrin II®. C6 tumors were induced by cortical inoculation of C6 cells. 9 days later, magnetic resonance images were obtained. On day 10, animals were given 100 mg/kg b.w. 5-ALA. Their brains were irradiated with 100 J/cm² 3 or 6 hours later. 72 hours after irradiation, brains were removed for histology.

Results: Irradiation of brains after administration of 5-ALA resulted in superficial cortical damage not different to irradiation alone. Cold injury in combination with 5-ALA and irradiation slightly increased damage depth. The depth of damage inflicted by irradiation after intravenous Photofrin II® however, was significantly greater. The extent of damage in response to 5-ALA and irradiation in brains harboring C6 tumors corresponded to the extent of tumors as determined from pretreatment magnetic resonance images.

Conclusions: Photoirradiation therapy with 5-ALA appears to selectively damage experimental brain tumors, with negligible damage to normal or perifocal edematous tissue.