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Hyperoxia retards growth and induces apoptosis, changes in vascular density and gene expression in transplanted gliomas in nude rats.

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This study describes the biological effects of hyperoxic treatment on BT4C rat glioma xenografts in vivo with special reference to tumor growth, angiogenesis, apoptosis, general morphology and gene expression parameters. One group of tumor bearing animals was exposed to normobaric hyperoxia (1 bar, pO(2) = 1.0) and another group was exposed to hyperbaric hyperoxia (2 bar, pO(2) = 2.0), whereas animals housed under normal atmosphere (1 bar, pO(2) = 0.2) served as controls.
All treatments were performed at day 1, 4 and 7 for 90 min. Treatment effects were determined by assessment of tumor growth, vascular morphology (immunostaining for von Willebrand factor), apoptosis by TUNEL staining and cell proliferation by Ki67 staining. Moreover, gene expression profiles were obtained and verified by real time quantitative PCR.Hyperoxic treatment caused an approximately 60% reduction in tumor growth compared to the control group after 9 days ($p < 0.01$). Light microscopy showed that the tumors exposed to Hyperoxia contained large "empty spaces" within the tumor mass. Moreover, hyperoxia induced a significant increase in the fraction of apoptotic cells (approximately 21%),with no significant change in cell proliferation. After 2 bar treatment, the mean vascular density was reduced in the central parts of the tumors compared to the control and 1 bar group. The vessel diameters were significantly reduced (11-24%)in both parts of the tumor tissue. Evidence of induced cell death and reduced angiogenesis was reflected by gene expression analyses. Increased pO(2)-levels in experimental gliomas, using normobaric and moderate hyperbaric oxygen therapy, caused a significant reduction in tumor growth. This process is characterized by enhanced cell death, reduced vascular density and changes in gene expression corresponding to these effects.

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