Antitumour and pro-apoptotic actions of highly unsaturated fatty acids in glioma.

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Abstract

The highly unsaturated fatty acids (HUFA) of the n-6 and n-3 series are involved in cell signalling in normal and transformed cells and have recently been associated with pathways leading to tumour cell death. The antitumour activity of three HUFA (arachidonic acid, gamma linolenic acid and eicosapentaenoic acid) were studied in glioma cells and tissue. Using five glioma models, including primary cell suspensions prepared from 46 human glioma samples and an in vivo rat C6 glioma model, we obtained evidence that, following exposure to HUFA, either administered into the medium surrounding human glioma cells or in 16 preparations of multicellular spheroids derived from human and rodent glioma cell lines (C6, MOG, U87, U373) or administered intra-tumourally by infusion using osmotic mini-pumps in 48 rats, glioma regression and apoptosis were detected. Additionally, synergy between gamma irradiation and HUFA administration was observed in 13 experiments analyzing C6 glioma cell apoptosis in vitro. These pro-apoptotic and antiproliferative activities were observed using both C18 and C20 fatty acids of the n-6 and n-3 series, but not when saturated and monounsaturated C18 and C20 fatty acid preparations were used. In the glioma infusion model, in addition to the apoptosis detected in glioma tissue infused with HUFA for 3-7 days, preservation of normal neural tissue and vasculature in adjacent brain was observed. Also, there was little evidence of acute inflammatory infiltration in regressing tumours. Our findings suggest that intraparenchymal infusion of HUFA may be effective in stimulating glioma regression.