

MITOCHONDRIAL ULTRASTRUCTURE IN HUMAN ASTROCYTIC TUMORS.

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Astrocytic tumors are demoralizing in the clinical setting because they are difficult to treat and may cause disabilities and the survival is still poor (Ohgaki and Kleihues, 2005). Hypoxic microenvironment is a characteristic of astrocytic tumors (Collingridge et al., 1999; Arismendi and Castellano, 2005), they produce energy by high-level glycolysis to generate their cellular ATP requirements (Oudard et al., 1997). What occurs to mitochondria in cancer cells remains poorly understood, since no consistent pattern in several mitochondrial aspects has emerged (Rossignol et al., 2004). The analysis of morphology of mitochondria in human astrocytic tumors using electron microscopy revealed notable alterations in their structure that had not been previously described. The mitochondria show important transformations: cigar, bowling, "V", and "Y" shapes, mitochondrial swelling and megamitochondria, ghost mitochondria, disarrangement of cristae, partial or total cristolysis, external and inner membranes remarkably electron-dense, and thickened membranes, folds of inner mitochondrial membrane, condensation of mitochondrial matrix, vacuoles, and amorphous matrix densities (Fig. 1-5). Mitochondrial fusion-fission phenomena were seen relatively frequently. The mitochondria usually were localized close to nuclear membrane and rough endoplasmic reticulum. The quantity of swollen mitochondria predominates over the presence of megamitochondria. Nuclear changes suggestive of apoptosis were infrequently observed. Some of these changes in the mitochondria have been earlier reported in human carcinomas (Springer, 1980), in human xenografted gliomas (Oudard et al., 1997), in human malignant glioma cell (Steinbach et al., 2003) in human cancer cell lines (Rossignol et al., 2004, Rui-hua et al., 2005). The alterations observed in astrocytomas suggest the existence of mitochondrial malfunction and non-functional mitochondria; consequently the ability of astrocytomas cells to generate ATP by mitochondrial oxidative phosphorylation is severely compromised. The partial or total cristolysis leads to a severe decrease of ATP production by oxidative phosphorylation, therefore to a low bio-energetic index; this would deteriorate the ability of astrocytomas cells to commit apoptosis. In other hand, hypoxia is a characteristic of human gliomas (Collingridge et al., 1999), mitochondrial swelling and megamitochondria observed herein are associated with hypoxic/ischemic conditions (Wakabayashi, 2002; Steinbach et al., 2003). The intratumoral hypoxia emerges as an important factor responsible of mitochondrial transformations. In addition, the ultrastructural changes in mitochondrial morphology observed in these cases probably are a contributing factor in resistance to chemotherapy of this type of cerebral tumors.

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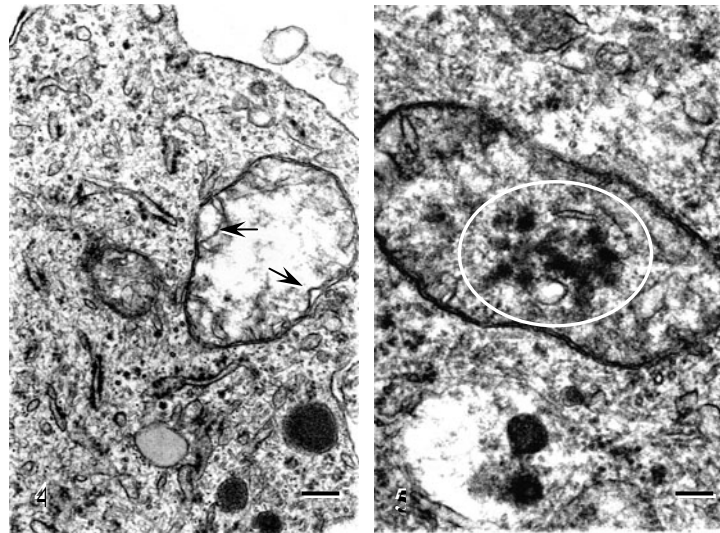
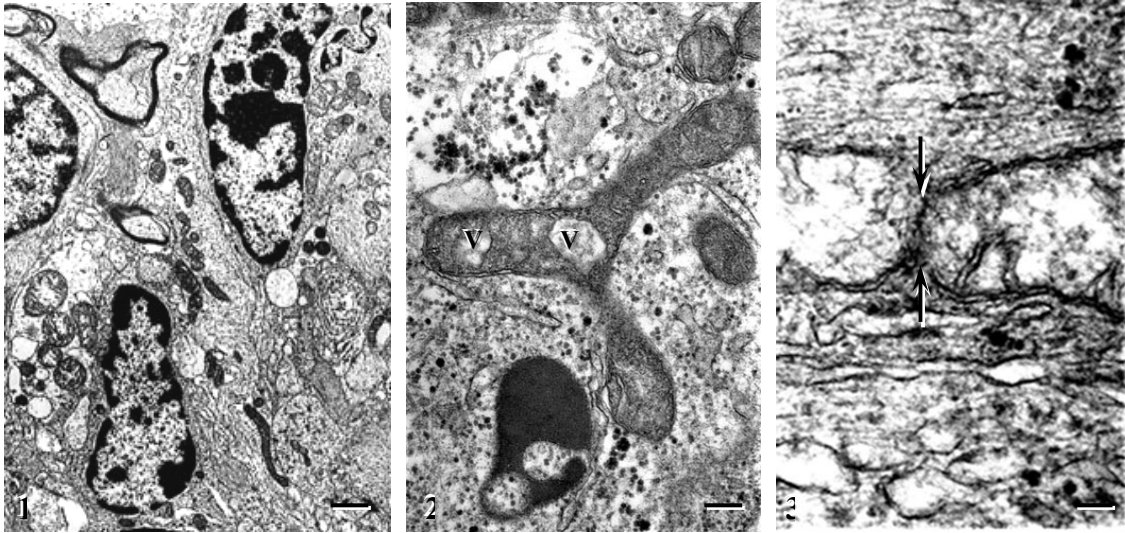


Fig. 1. Presence of megamitochondria, enlarged mitochondria, swelling mitochondria, “Y” shape mitochondrion, and mitochondria with dense degeneration. Bar: 0,625 μm .

Fig. 2. Mitochondrion display “Y” shape, exhibit matrix condensation, cristolysis and vacuoles (V). Bar: 0,165 μm .

Fig. 3. Fusion-Fission mitochondrial phenomena in two swelling mitochondria, both show clear matrix and cristolysis. Note the union of mitochondrial membranes. (opposed arrows). Bar: 0,055 μm .

Fig. 4. Enlarged, piriform mitochondrion that exhibit cristolysis, and clear matrix. Note the inner membrane fold (arrows). Bar: 0,2 μm .

Fig. 5. Enlarged mitochondrion that presents conspicuous amorphous matrix densities (circle), and striking cristolysis. Bar: 0,1 μm .