AXOLEMMAL AND CYTOSKELETAL ULTRASTRUCTURAL PATHOLOGY IN TRAUMATIC HUMAN BRAIN EDEMA.

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Traumatic axonal injury in human is a phenomenon particularly important that seems to be a major determinant of clinical outcome dominated by executive and memory dysfunction. (Graham et al., 2000; Fork et al.; 2005). The submicroscopic changes of axolemma and cytoskeleton of degenerated/myelinated of 11 patients with complicated head trauma have been studied with transmission electron microscopy using cortical biopsies of frontal, parietal and temporal regions. Microtubules appeared disrupted and absent in most cases, actin-like filaments appeared disrupted and showing granular disintegration (Fig. 1-4). Most degenerated myelinated axons exhibited deep invaginations, formation of endocytic vesicles and fragmentation of axolemmal membrane (Fig. 3-4). In some cases a differential response was observed characterized by absence of microtubules and presence of fragmented bundles of actin-like filaments. The degenerated myelinated axons showed myelin sheath vacuolization and distortion, formation of myelin ovoids, mitochondrial edema, and protein aggregation of the level of axoplasmic matrix (Fig. 1-4), suggesting interruption of axoplasmic transport (Maxwell, 1996; Povlishock and Petus, 1996). Loss of microtubules and neurofilaments are associated with compromised axonal transport (Graham et al., 2000). The infoldings and /or fragmentation of axolemma occur after traumatic brain injury by means calpain-mediated cytoskeletal proteolysis (Povlishock et al., 1999; Graham 2000). Severe disruption of neuronal Ca2+ homeostasis leading to lethal Ca2+ overload as occurs in brain ischemia, can initiate a cascade of destructive processes (Graham et al., 2000; Pashen 2000), which induce axolemmal membrane and cytoskeletal damage. Previous studies have identified axolemmal disruption and impaired axonal transport as key mechanisms in the evolution of traumatic axonal injury (Stone et al., 2004). The axolemmal and cytoskeletal changes are correlated with the neurological deficit exhibited by the patients under study.

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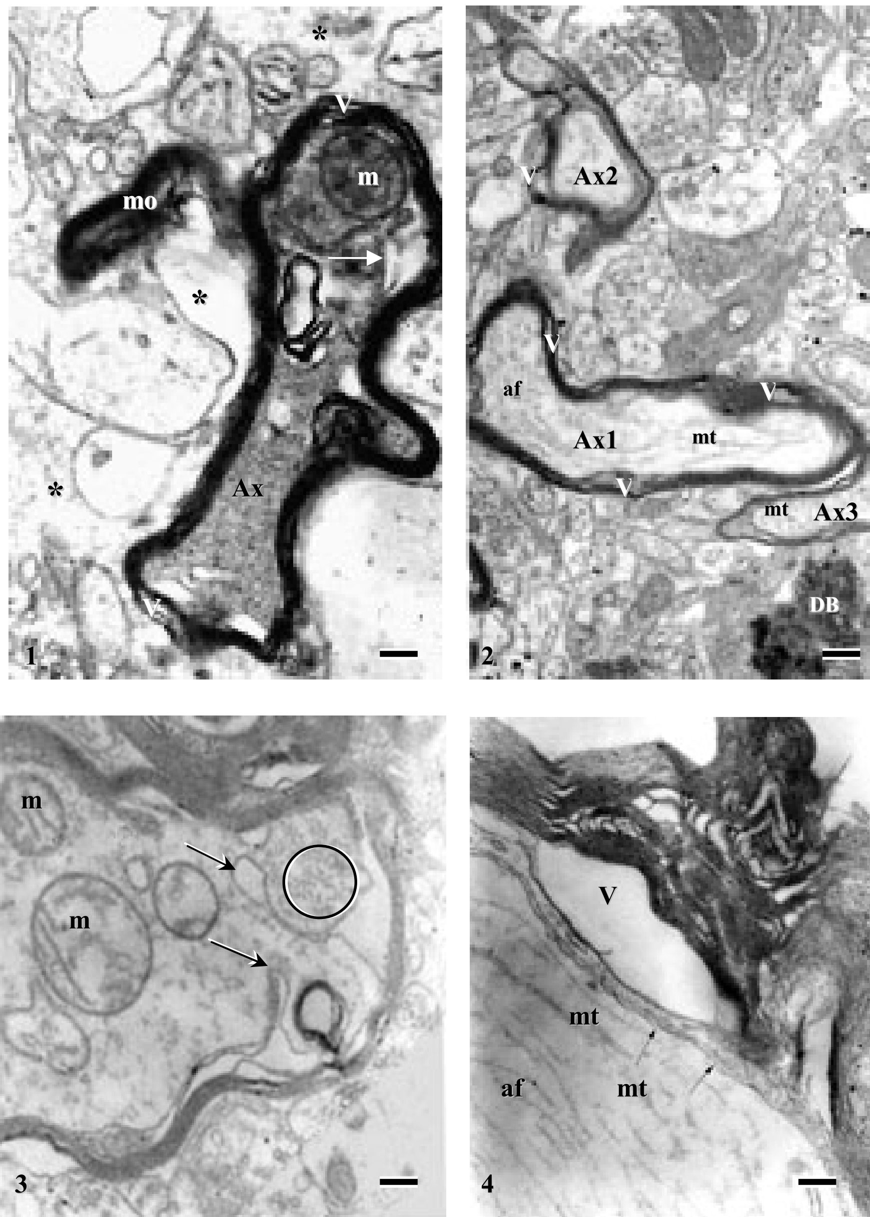

Fig. 1. Right epidural hematoma. Degenerated myelinated axon (Ax) showing granular disintegration of axoplasmic matrix, fragmentation of axolemma (arrow), swollen mitochondria (m), and myelin sheath vacuolization (V), with formation of myelin ovoids (mo). The asterisks label the enlarged Extracellular space. Bar: 0,125 μm.

Fig. 2. Subdural hematoma. Three edematous axons (Ax1; Ax2; Ax3) that present fragmented and disintegrated microtubules (mt) and actin-like filaments (af), vacuolization of myelin sheath (V). Note the dense body (DB) in a vicinity cell process. Bar: 0,14 μm.

Fig. 3. Subdural hygroma. Degenerated myelinated axon showing deep invaginations of axolemmal membrane (arrows), fragmented actin-like filaments (circle), disappearance of microtubules and edematous mitochondrion (m). Bar: 0,08 μm.

Fig. 4. Subdural hematoma. Axon that exhibit discontinuities of axolemmal membrane (arrows), fragmented microtubules (mt) and actin-like filaments (af), and myelin sheath vacuolization (V). Bar: 0,05 μm.