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Glial proliferation and glial cell death in the spinal cord of the hypomyelinated jimpy mutant mice.

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The jimpy mouse is a sex-linked recessive mutant that dies within 4 weeks of age and is characterized by a severe hypomyelination throughout the central nervous system associated with a variety of glial abnormalities. In the present study, we investigated the proliferative capability and apoptotic degeneration of glial cells in the jimpy spinal cord. Proliferating cells were visualized by PCNA immunostaining and apoptosis was demonstrated by in situ labeling of nuclear DNA fragmentation (TUNEL method). Identification of proliferative and apoptotic cells was achieved through double labeling with selective markers for glial cells. Oligodendroglial and astroglial cells were demonstrated by immunocytochemical detection of MBP and GFAP, respectively, and microglial cells by tomato lectin histochemistry.

Our results revealed that the density of PCNA-positive cells was higher in jimpy than in normal spinal cord, this difference being more pronounced in white matter than in gray matter and at 20-22 days than at 10-12 days. Double labeling showed that about 50% of PCNA-positive cells in the jimpy white matter were cells from the oligodendrocyte line, 30% were microglial cells and 20% were astrocytes.

When compared to normal littermates, the spinal cords of jimpy mice showed a significantly higher number of apoptotic cells. Double labeling techniques enabled us to demostrate that glial cell death in jimpy is restricted to oligodendrocytes. Apoptotic oligodendrocytes appeared as isolated cells ubiquitously distributed throughout the jimpy spinal cord, although they were more numerous in white matter than in gray matter. Noteworthy, microglial cells were frequently found closely attached to and even surrounding apoptotic oligodendrocytes.