3D reconstruction of Amyloid Plaques in Kuru, a Prion Disease Spread by Ritual Endocannibalism.
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Introduction: Kuru was the first transmissible spongiform encephalopathy (TSE) to be identified in humans, occurring in the Fore linguistic group of Papua New Guinea, and brought to medical attention in the middle of the 20th century by D. Carleton Gajdusek. Kuru, spread by ritualistic endocannibalism, was a uniformly fatal and remarkably stereotyped cerebellar ataxic syndrome usually beginning with a slight shivering tremor, followed by choreiform and athetoid movements. Neuropathologically, kuru-affected brains were characterized by a neuronal loss, astrogliosis and spongiosis. The most striking neuropathologic feature of kuru was the presence of numerous amyloid plaques consisting of pathological form of prion protein.

Methods: The main objective of the study was description of confocal microscopic, 3D reconstruction and electron microscopic structure of amyloid plaques in kuru brain, including co-localization of various proteins To elucidate the structure of amyloid in the brain we performed confocal laser microscopy, electron microscopy on archived material from a well documented 1963 kuru case. Formalin fixed and paraffin embedded human brain specimens were analysed by immunohistochemistry and confocal laser microscopy. The antibodies used in the study were GFAP (polyclonal DAKO, PrP, clone 12F10, Cayman, p62 polyclonal, Progen, APP clone 22C11, Chemicon). Z-stack optical sectioning was performed for 3D reconstruction of the amyloid plaques.

Results: The fine structure of plaques was surprisingly well preserved with compact core and radial fibrils at the periphery. Immunohistochemistry and confocal laser microscopy revealed that plaques were built of pathological isoform of prion protein (PrPSc) with abundant astroglial reaction around the core of the plaque. Dystrophic neurites characterized by MAP-tau, APP and p62 immunoreactivity were present but less frequent than in the plaques of other prion diseases. Additionally 3D structure of amyloid deposits was reconstructed. The most interesting finding is that the presence of APP, p62 and MAP-tau immunoreactivity in kuru brain was much more accentuated at the periphery of the amyloid plaques thus we may speculate that the amyloid fibrils influence the appearance of dystrophic neurites. 3D reconstruction revealed close interaction between astroglial cells and amyloid deposits.