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Abstract

Ultrastructural Characterization of the Frontal Lobe in the Case of Human Herpes Virus-6 Infection †

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Abstract: The vast majority of the world's population is exposed to beta-herpesviruses during early childhood. After the primary infection, human herpesvirus-6 (HHV-6) can establish a lifelong persistence. The role of HHV-6 in the development of neurodegenerative disorders is not completely clarified. Postmortem samples of brain tissue obtained from 24 elderly subjects with unspecified encephalopathy were used in the study. Nested (nPCR) and real-time polymerase chain reaction (RT PCR) were used for the qualitative and quantitative detection of viral genomic sequences in isolated DNA from frontal lobe samples. For ultrastructural examination, transmission electron microscopy (TEM), nPCR, and immunohistochemically confirmed HHV-6-positive tissue samples were used. Immunogold (IG) labeling using anti-HHV-6 (20) mouse monoclonal antibodies, raised against viral lysate (Santa Cruz Biotechnology, dilution 1:30), was performed. HHV-6 DNA was detected in 38% (9/24) of the frontal lobe tissue samples. The HHV-6 load in the nPCR-positive samples ranged from 10 to 3878.5 (copies/10^6 cells). A TEM examination of the frontal cortex revealed lipofuscin containing neurons, glial cells, unmyelinated and small myelinated axons, and symmetric synapses. Subcortical brain regions revealed glial cells interspersed by myelinated axons. The expression of viral proteins was found in the nuclei of neurons, demonstrating disarranged chromatin. HHV-6 positivity was detected between the adjacent cisternae of the rough endoplasmic reticulum of neurons displaying IG labeling. Furthermore, products of IG labeling were found in nuclei and cytoplasm of oligodendrocytes. The cytoplasm of astrocytes was IG labeled as well. IG labeling was used to determine the presence and intracellular localization of HHV-6 proteins in the human brain. HHV-6 possibly contributes to the demyelination process via entry into and affection of oligodendrocytes. Finally, neural susceptibility to HHV-6 may be linked to an invalid cellular immune response, followed by the development of a persistent viral infection.

Keywords: human herpes virus-6; human brain; electron microscopy; PCR