ULTRASTRUCTURAL STUDY ON HEMORRHAGIC FEVER WITH RENAL SYNDROME (HFRS) VIRUS INFECTION IN CULTURED CELLS

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This study was done to elucidate the morphogenesis of HFRS virus and the character and significance of intracytoplasmic inclusion bodies related to viral replication. Monolayer cultured Vero E–6 cells were infected with HFRS virus (strain Hantaan 76–118).

HFRS-specific antigenic substances of the infected cells on 4, 8 and 12 days post-inoculation (PI) were examined by the IFA and ABC methods with mouse ascites (HTN) and three monoclonal antibodies (8B6, 1G8 and ECO2) for recognizing G1, G2 and N proteins. After that, the cells were investigated unltrastructurally and immuno-electron microscopically.

Light microscopically, many cells were stained positively with all four antibodies, showing a peak at 8 days PI. However, positive cells for 8B6 and 1G8 decreased in number at 12 days PI. Antigenic substances for HTN and ECO2 were detected in granular patterns in the cytoplasm.

Electron-microscopically, on days 4 and 8 PI, the cytoplasm had mature and/or immature virions, string-like structures resembling the "viral antigen layer" reported previously to be specific for HFRS and structures probably related to the viral morphogenesis. In addition, the cells contained cytoplasmic inclusion bodies consisting of microtubules.

On day 8 PI there were some brush-like bodies consisting of microfilaments, filamentous inclusions enclosing irregular microfilaments, granular round-shaped inclusions and filamentous crystal-like inclusions in the cytoplasm. The latter two types of inclusions were similar to those described in the literature. No mature virions were detercted in such inclusions. On day 12 PI, giant inclusions were prominent in the cytoplasm.

Immuno-electron microscope findings suggested that the granular round-shaped inclusions were composed of N protein.

From the findings obtained here, it was considered that the viral formation reached its peak day 4 to 8 PI and the inclusions found at 8 and 12 days PI consisted of N protein without viral particles, as a result of persistent infection. The character and significance of the inclusion bodies, except for the granular round-shaped ones, could not be determined. The HFRS virus appears to be able to mature in the cytoplasm.