Electron microscopic (EM) evidence of ER stress in Purkinje cells (PC) of a patient with Type 6 of Ceroid Lipofuscinosis (CLN6)

S.I. Bannykh[1]

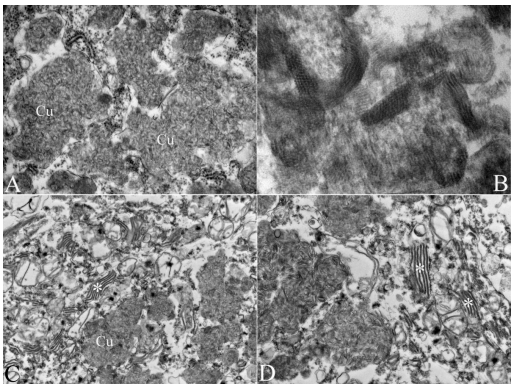
[1] Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, Los Angeles, CA, United States.

Abstract

13-year-old female with a history molecularly confirmed CLN6 passed away and full autopsy was performed. Brain (685 g) showed severe diffuse cortical and especially cerebellar atrophy, hydrocephalus ex vacuo and compensatory thickening of a skull. There was extensive neuronal loss and gliosis but no alterations in myelinated fibers. The most striking loss of neurons and synapses was detected in the molecular cell layer of cerebellar vermis.

EM of frontal and occipital cortices and cerebellar vermis was performed. Cortical neurons and PC showed large collections of membrane bound of predominantly curvilinear inclusions. Additionally, rims of some inclusions occasionally contained twisted skeins of beaded shoelace-like inclusions composed of 60-80 nm in diameter spiraling crystalline arrays of 9.8 nm particles (up to 7 per row). Additionally, PC but not neocortical neurons also contained stacked cisternae of ER, lacking ribosomes.

Discussion: Little is known about a pathogenesis of CLN6. This disease is caused by mutations in a transmembrane protein, which resides in ER. Mutations lead to a loss of CLN6 protein expression. Here, we find that in the areas of the greatest synaptic and neurons loss the persistent PC show evidence of ER stress response, which might be relevant to their capacity to survive.



EM of cortical neurons (A & B) and PC (C & D). Curvilinear (Cu) inclusions are predominant type of lipofuscinosis-associated lysosomal abnormalities in all neuronal populations. Beaded shoelace skein inclusions (B) at rims of curvilinear inclusions are less common. PC also show striking proliferations of stacked ER membranes adjacent to curvilinear inclusions, suggestive of ER stress.