Department of Neuroscience
Division of Neuropathology

Satoshi Kurihara, *Professor and Director*
Junko Fujigasaki, *Assistant Professor*
Takahiro Fukuda, *Assistant Professor*

General Summary

Our research projects have concerned neurodegenerative disorders caused by intracellular accumulation of abnormal proteins. We are also studying mouse models of neurodegenerative disorders and autopsy cases by means of standard morphologic analysis and molecular biological analysis.

Research Activities

Pathophysiological study of neuronal organelles in lysosomal diseases
Objective: The aim of this study was to investigate the pathophysiology of neuronal organelles in lysosomal disorders.
Material and methods: We analyzed the central nervous system (CNS) of Niemann-Pick disease type C and prosaposin deficiency model mice by means immunohistochemical studies with antibodies against early endosome antigen 1 (endosomes), trans-Golgi network 38 (Golgi apparatus), cytochrome c oxidase subunit IV (mitochondria), calnexin (endoplasmic reticulum), S6 ribosomal protein (ribosomes), lysosome-associated membrane protein 2 (lysosomes), and catalase (peroxisomes).
Results: In the CNS neurons of Niemann-Pick disease type C and prosaposin deficiency mice, swollen lysosomes accumulated. Structurally preserved peroxisomes and Golgi apparatuses decreased slightly in number. Mitochondria, endosomes, endoplasmic reticulum, and ribosomes decreased markedly in number.
Discussion: After being sorted in endosomes, most proteins are rapidly recycled. Degraded proteins are packaged into lysosomes and then processed into the ubiquitin-proteasome system or the autophagy-lysosome system. In lysosomal storage diseases, recycled endosomes are inhibited, and degraded proteins accumulate in lysosomes. Mitochondria depletion leads to an energy crisis and decreases in the synthesis activity of proteins and lipids in ribosomes and endoplasmic reticulum.

A case of chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids syndrome diagnosed with brain biopsy
A 28-year-old woman consulted our hospital due to ataxia, diplopia, and facial paresthesia. Magnetic resonance disclosed patchy spotlike gadolinium enhancement with a "salt-and-pepper"-like appearance in the cerebellum and pons. Brain biopsy was performed before corticosteroids were administered. The biopsy specimens showed a scattered and perivascular infiltration of small, mature lymphocytes in the white matter of the cerebellum.

The lymphocytes were predominantly T cells admixed with CD4-positive and CD8-positive cells. Cells immunoreactive for Olig2 with slightly enlarged nuclei appeared; however, an inflammatory reaction rather than a neoplastic lesion was suspected. After biopsy, treatment with corticosteroids lead to symptomatic improvement and the reduction of lesions on magnetic resonance. The pathological findings and the clinical course led to a diagnosis of chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) syndrome. In 2010, this syndrome was identified as a rare chronic inflammatory CNS disorder responsive to immunosuppressive therapy. The diagnosis in this case required careful assessment of the clinical course and pathological findings.

Publications

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Inagaki T, Fukuda T, Ohta A, Hano H. No oncogenic role of WT1 in the peripheral nerve sheath tumors. *Jikeikai Med J.* 2011; **58:** 95-102.