An autopsy case of neuronal intermediate filament inclusion disease (NIFID)

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Abstract
We herein report an autopsy case of neuronal intermediate filament inclusion disease (NIFID) which presented some different clinicopathological features, compared to previous cases. A 41-year-old Japanese man presented progressive spastic quadriparesis followed by cognitive impairment. His neurological symptoms gradually deteriorated and he died of pneumonia 16 years from onset. His brain showed severe cortical atrophy with enlargement of ventricles. The microscopic examination revealed severe neuronal loss with gliosis and spongiosis predominantly in the frontal, temporal cortices, caudate and putamen. Hyalinated intracytoplasmic inclusions were observed in the remaining neurons which were immunoreactive for alpha-interinemxin, while not for fused in sarcoma protein (FUS). This case confirms the presence of FUS-negative NIFID and extends the clinicopathological spectrum of this disorder.

Case report
A 41-year-old Japanese man first noticed his right lower limb stumbled easily. One year later, he developed gait disturbance, weakness of upper extremities, dysarthria and dysphasia. On hospital admission, 3 years after disease onset, the neurological examination disclosed spastic quadriparesis, saccadic eye movement, mood disturbance and change of personality. Six years after the first symptom, he became drowsy, and cognitive impairment was evident during the alert period. Brain MRI/CT images showed progressive atrophy of bilateral fronto-temporal lobes. He had repeated pneumonia and died at the age of 57.

Materials and methods
Brain and spinal cord were fixed with buffered 10% formalin, embedded in paraffin and prepared for routine examination with H&E, K-B and Bodian stains. Some sections were stained with Bielschowsky’s silver impregnation. A part of the right hemisphere was frozen at -80°C for Brain Bank (Research Resources Network, Japan). Immunohistochemical stains were performed on selected sections using various antibodies (Table 1). To visualize the positive immunoreactions, we used the standard ABC method (Nichirei, Japan), or a Ventana automated immunostaining instrument (Ventana, Tucson, AZ, USA).

Results (Neuropathological study)
The brain weight was 816 g, pre-fixed. His brain showed severe cortical atrophy with enlargement of ventricles. The microscopic examination revealed severe neuronal loss with gliosis and spongiosis predominantly in the frontal, temporal cortices, caudate and putamen. Hyalinated pale eosinophilic inclusions were observed in the remaining neurons of hippocampus, cerebral cortices, as well as in striatum and pontine nuclei at the lesser extent. The outline of those inclusions was stained by Bodian silver impregnation, and few inclusions were positive for Bielschowsky stain.

Immunohistochemistry revealed that the inclusions were positive for Ubiquitin, neurofilaments and most reactive for alpha-interinemxin, but not for alpha-synuclein, phospholylated tau and TDP43. There were intranuclear inclusions in the granular layer of the hippocampus, which were positive for Ubiquitin and negative for TDP43 and polyglutamin. Any inclusion was not immunoreactive for FUS.

Conclusion
This case confirms the presence of FUS-negative NIFID and extends the clinicopathological spectrum of this disorder. More cases of NIFID should be investigated to define the range of FTLD-FUS.

References