Tottori J. Clin. Res. 8(2), 202-209, 2017

Brief Communications

Brief literature review on the pathology of argyrophilic grain formation:

Based on an experience of a case of elderly dementia given a clinical diagnosis of Alzheimer's disease, in whom argyrophilic grains and neurofibrillary tangles were concomitantly observed at autopsy

Yoshihiro Konishi[1)]* Hirotake Nishimura[2)]

1) Department of Clinical Research, NHO Tottori Medical Center

2) Department of Pathology I, Kawasaki Medical School

*Correspondence: ykonishi@tottori-iryo.hosp.go.jp

We encountered an autopsy case involving a 93-year-old woman (at the time of death) in whom memory disturbance had gradually progressed over an 11-year course. Both argyrophilic grains (AGs) and neurofibrillary tangles (NFTs) were histopathologically observed, which may be generally reported as complications of argyrophilic grain dementia (AGD) or dementia with grains (DG) and senile dementia of the neurofibrillary tangle type (SD-NFT)[1,2)]. We extensively searched the literature on AGs in Japan and other countries; they indicated that AG lesions are additive and the pathology that we call AGs or AGD is a part of SD-NFT rather than a unique, distinct tauopathy causing dementia. Tottori J. Clin. Res. 8(2), 202-209, 2017

Key Words: argyrophilic grains (AGs), neurofibrillary tangles (NFTs), pretangles, Gallyas-Braak (GB) silver staining

Two hours after a natural death due to aging, an autopsy was conducted of the brain only. The brain weighed 986 grams before fixation with formalin solution. Macroscopically, gyral atrophy of the frontal and temporal cortices was observed. Coronal slices showed that the amygdala, hippocampal head and body, and parahippocampal gyrus were all extremely atrophic (Fig. 1). The hippocampal trail was relatively preserved.

Microscopically, neuronal loss, astrocytosis, and ghost tangles were noted in this region over the hippocampal C1 subfield (Fig. 2). These changes were more prominent in the anterior than in the posterior hippocampus.

On Gallyas-Braak (GB) silver impregnation and immunohistochemical staining with anti-phosphorylated tau antibody AT8 (Innogenetics), pretangles, NFTs, and neuropil threads (NTs) were mainly observed in these atrophic regions (Fig. 3) and only slightly in the temporal isocortex. Most of the isocortical areas lacked these abnormal findings. The distribution of AT8-positive NFTs/NTs in the present case corresponded to Braak NFT/NT stage III[3,4)].

On GB silver and AT8-immunohistochemical stainings, AGs were present not only in the amygdala, ambient gyrus, hippocampus, and parahippocampal gyrus but also in the insular cortex and the anterior cingulate cortex (Figs. 3 and 4), corresponding to Saito's stage III[5)]. On immunostaining with antibodies specifically recognizing 3-repeat tau (3R-tau) (RD3, Merck Millipore) and 4-repeat tau (4R-tau) (TIP-4RT-P01, Cosmo Bio, Tokyo)[6,7)], AGs were positive for 4R-tau, NFTs were positive for both 3R- and 4R-tau, and ghost tangles were positive for 3R-tau (Figs. 5 and 6). On immunohistochemistry with anti-amyloid β-peptide (Aβ) antibody Aβ11–28 (IBL, Takasaki, Japan), positive plaques were observed mainly in the isocortices, but not in the hippocampus or the visual cortex (Fig. 7), corresponding to Thal's Aβ-phase 1[8)]. Most of the Aβ-positive deposits were diffuse plaques and not senile plaques with cores or neuritic haloes.

On Western blot analysis of tau protein, a 60-, 64-, and 68-kDa triplet pattern was detected in the hippocampal formation, subiculum, near the sulcus collateralis in the transentorhinal area, the base of the temporal lobe, and the amygdaloid nucleus, showing accumulations of 3R-tau (60 and 64 kDa) and 4R-tau (64 and 68 kDa) to similar levels in all regions. In the middle temporal and anterior cingulate gyri, a 64- and