

Early-onset Alzheimer Disease Mimicking Frontotemporal Dementia: Hippocampal-sparing And Cerebellar Amyloid (autopsy)



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【Background】

- Behavioral variant Alzheimer disease (bvAD) is an atypical form of AD that may closely mimic behavioral variant frontotemporal dementia (bvFTD).
- Its clinicopathological basis remains incompletely defined, requiring further autopsy-based studies.

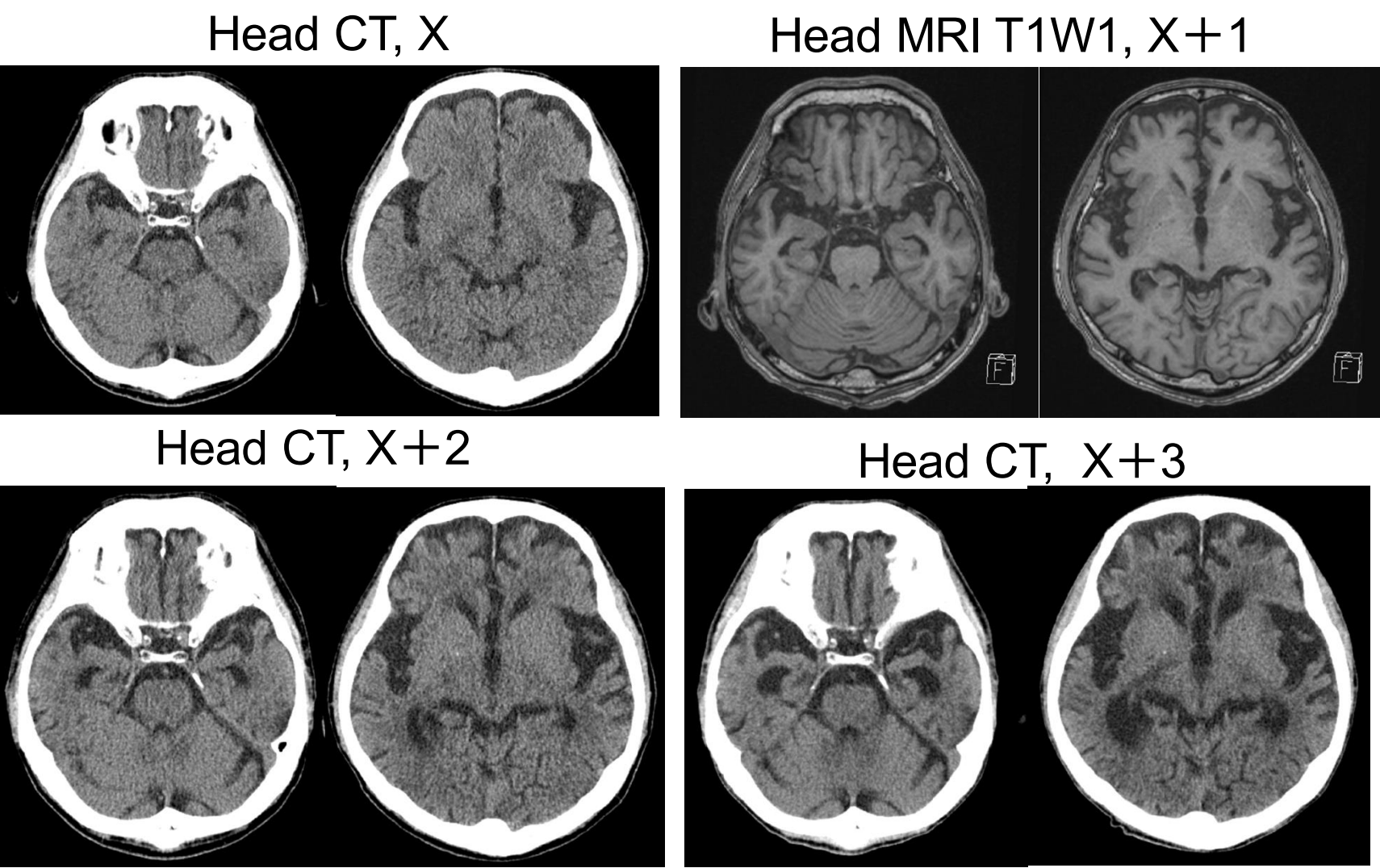
【Objective】

To describe the clinical and neuropathological features of an autopsy-confirmed case of early-onset Alzheimer disease presenting with a bvFTD-like behavioral syndrome.

【Case Summary】 (X denotes the year of first clinical assessment)

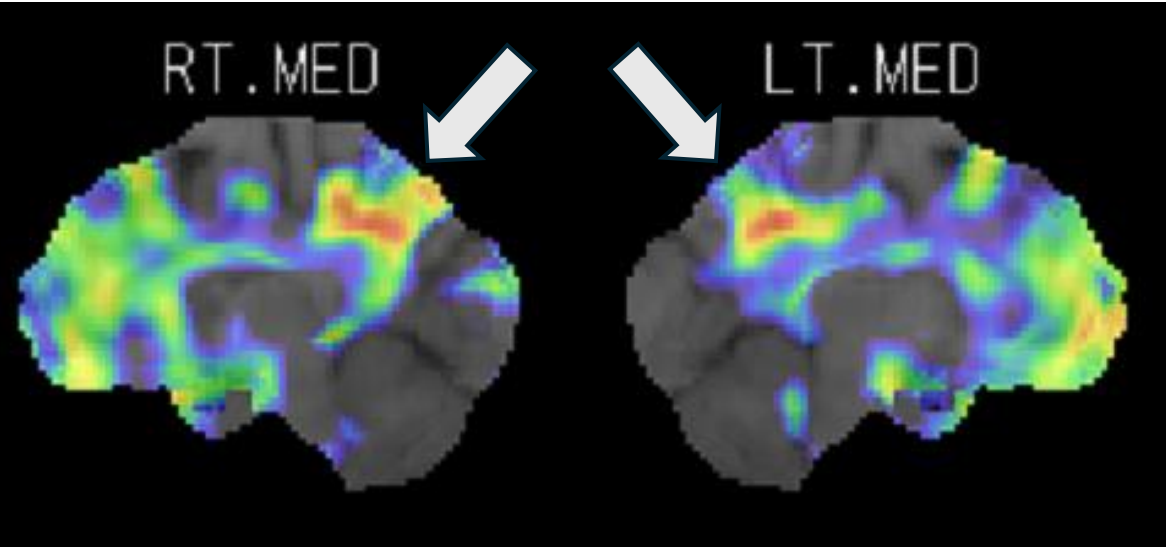
- A man died at age 68 after a 10-year disease course.
- Symptom onset occurred at age 58 (X–7), with workplace errors including miscounting change and poor product management.
- At age 64 (X), he went missing after an argument with a customer, prompting psychiatric evaluation.
- Initial cognitive testing showed MMSE 27/30 and Hasegawa’s Dementia Scale-Revised (HDS-R) 16/30. Head CT showed bilateral frontal atrophy with relative hippocampal preservation.
- Brain perfusion SPECT showed hypoperfusion in the bilateral posterior cingulate, precuneus, and medial frontal regions, leading to a clinical diagnosis of early-onset Alzheimer disease.
- Behavioral and cognitive symptoms progressed rapidly, with apraxia, agnosia, wandering, irritability, pica, and resistance to care.
- He died of recurrent pneumonia at age 68 (X+4).

【Neuroimaging Findings】



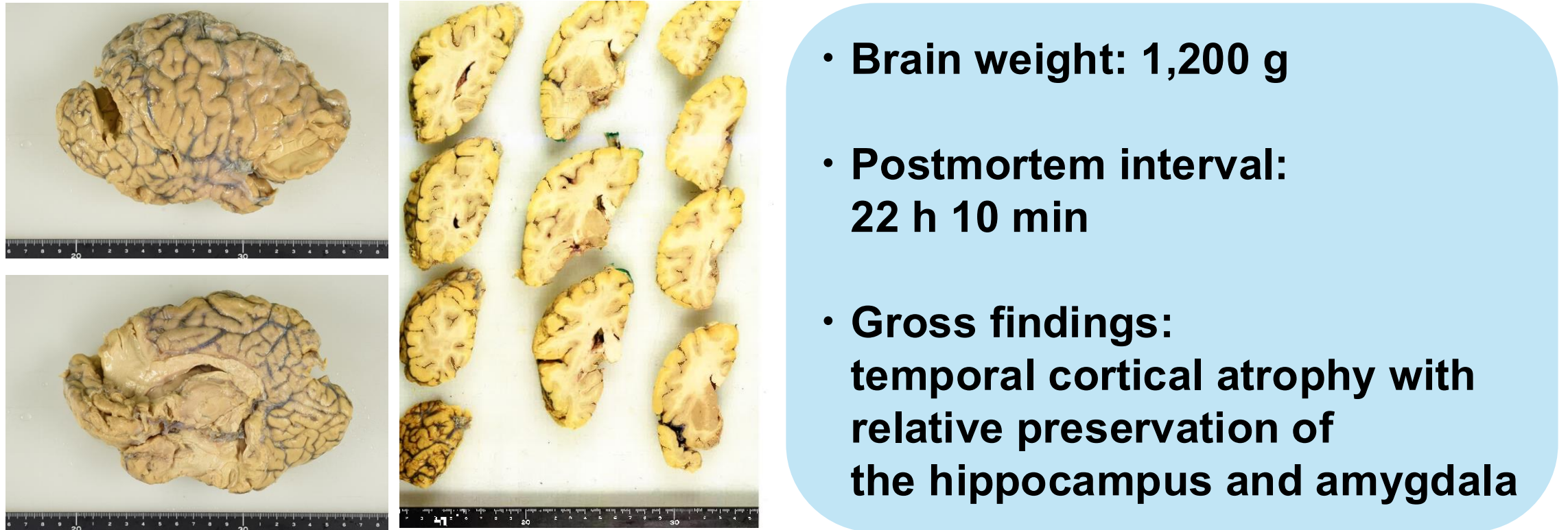
- At X: prominent bilateral frontal atrophy with relative hippocampal preservation
- X to X+3: progressive diffuse cerebral atrophy over time

Brain Perfusion SPECT, X

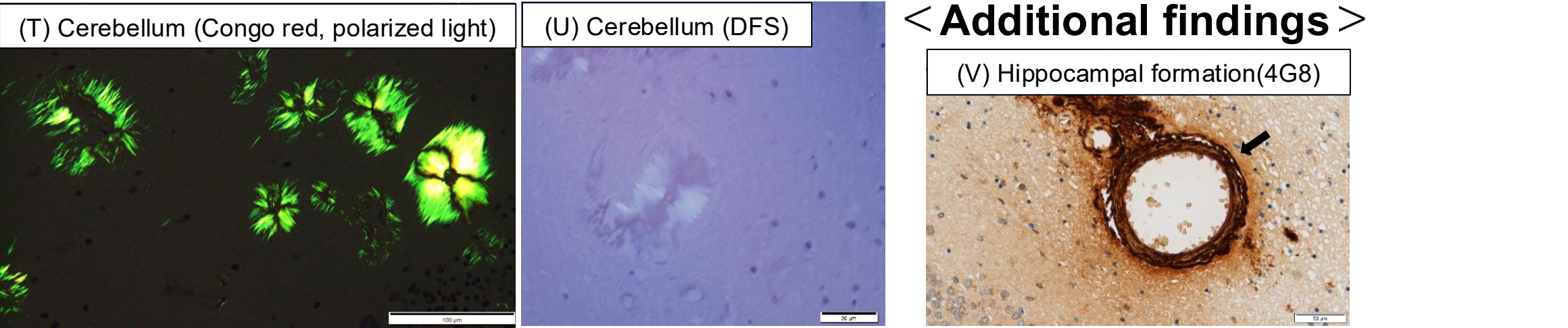
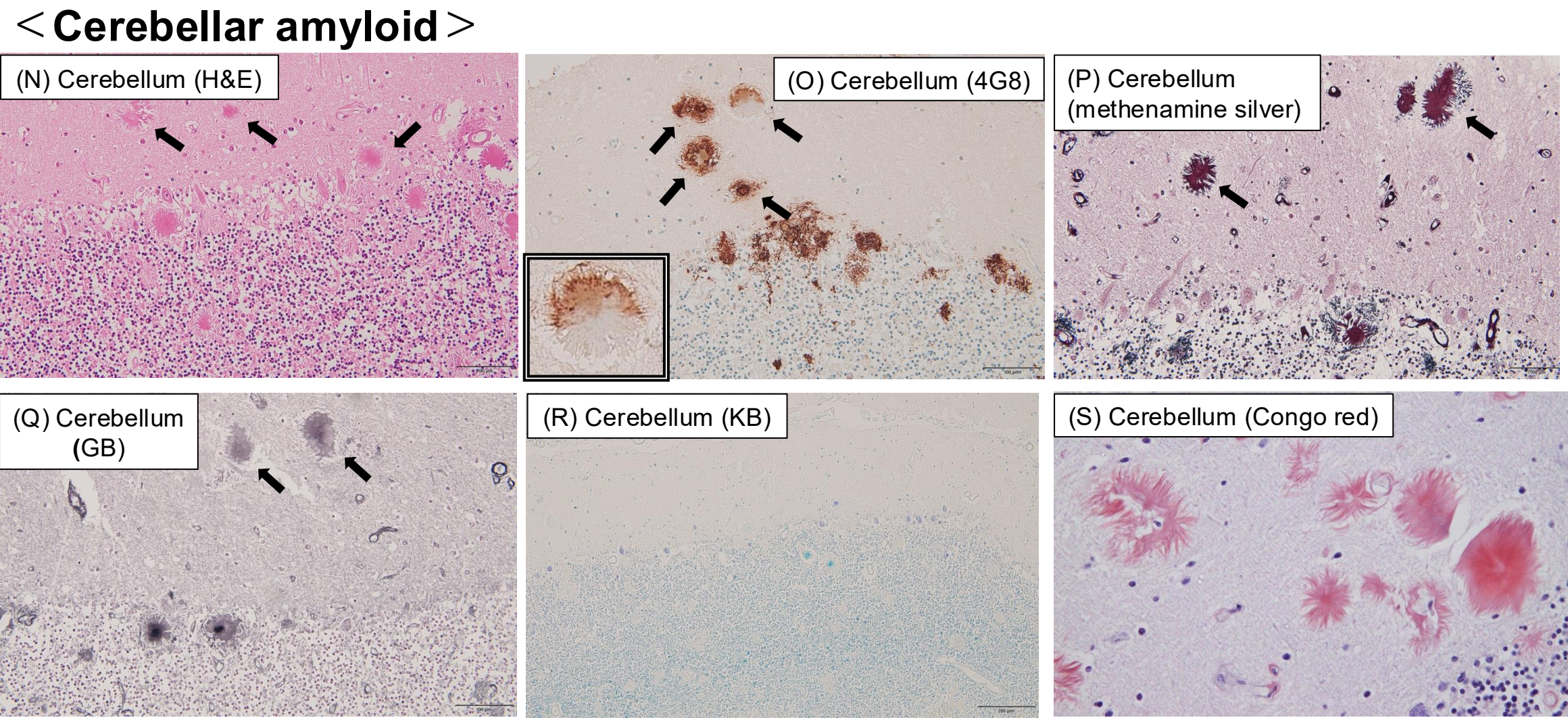
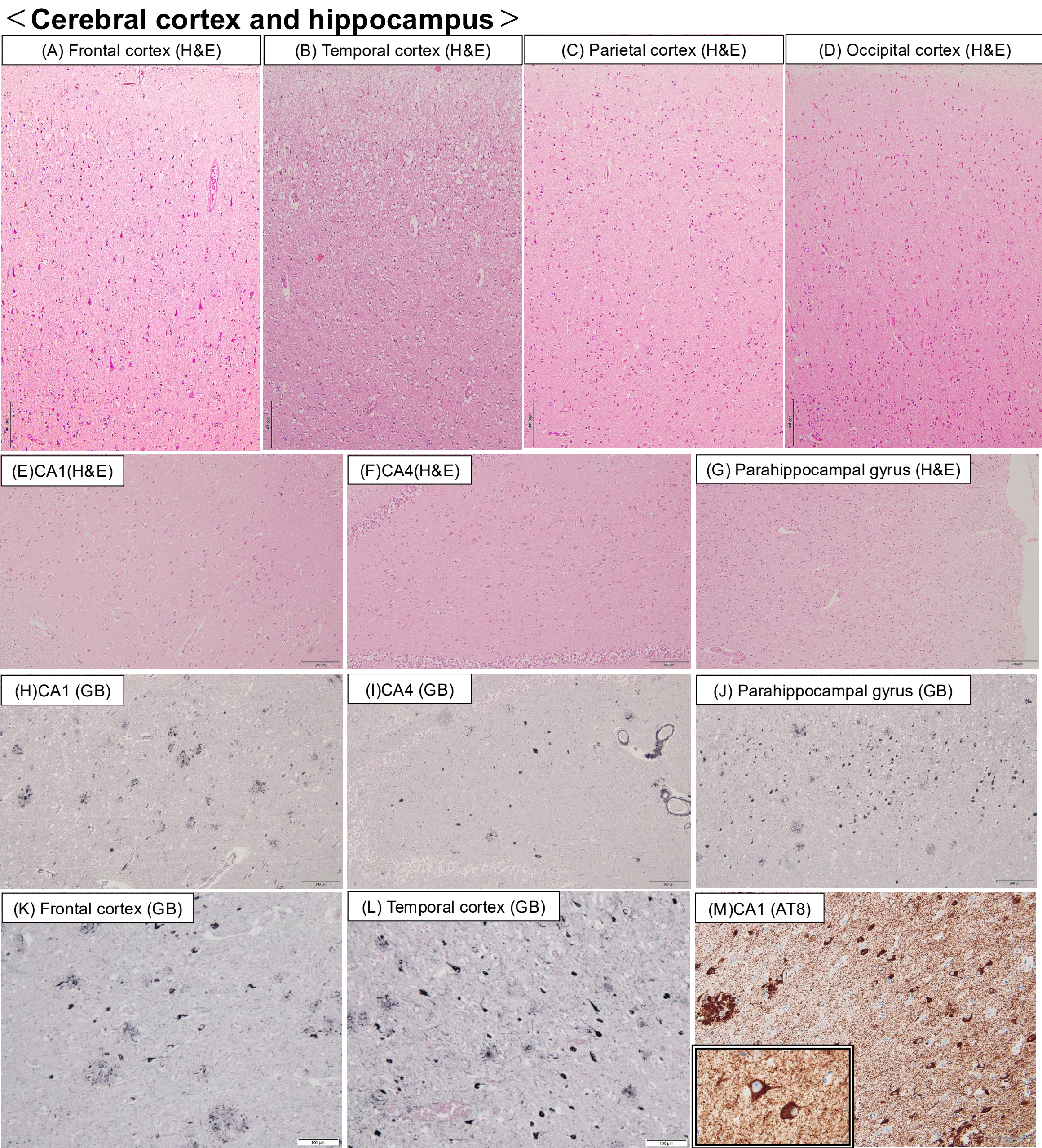


- Hypoperfusion in the bilateral posterior cingulate cortex and precuneus (white arrows)
- Additional hypoperfusion in the dorsomedial prefrontal, medial frontal, and orbitofrontal regions

【Gross Neuropathology】



【Microscopic Neuropathology】



Abbreviations: H&E, hematoxylin and eosin; GF, Gallyas-Braak; DFS, direct fast scarlet.

【Microscopic Findings】

- < Cerebral cortex and hippocampus >
 - Neuronal loss and gliosis involved the cerebral cortex, predominantly the frontal and temporal lobes, and the hippocampus (A–G).
 - Modified GB staining showed widespread senile plaques and neurofibrillary tangles(NFTs) in the cerebral cortex (K, L).
 - Hippocampal NFTs were less frequent than those in the frontal and temporal neocortices (H–L).
 - Pretangle-like tau inclusions were more prominent than mature NFTs in the hippocampus (M).
- < Cerebellar amyloid (N–U) >
 - Irregular amyloid deposits were observed in the cerebellar molecular and granular layers.
 - The deposits were eosinophilic on H&E, partially Aβ-positive, methenamine silver- and DFS-positive, and Congo red-positive with green birefringence under polarized light.
 - They were prion-negative and lacked associated glial reaction.
- < Additional findings >
 - Cerebral amyloid angiopathy was present (V).
 - Phosphorylated α-synuclein and phosphorylated TDP-43 immunohistochemistry were negative.

【Neuropathological Diagnosis】

Alzheimer disease
NIA-AA ADNC: High (A3/B3/C3)
Thal phase 4 / Braak NFT stage V / CERAD frequent

【Discussion】

- This case was consistent with atypical early-onset AD, showing features of hippocampal-sparing AD and behavioral variant AD.
- Frontal/temporal-predominant NFT burden and neurodegeneration may explain the bvFTD-like behavioral phenotype.
- The hippocampus showed relatively sparse mature NFTs but prominent pretangle-like tau inclusions, suggesting immature hippocampal tau pathology.
- Numerous irregular cerebellar amyloid deposits were observed, with partial Aβ immunoreactivity and no associated glial reaction. Their pathological significance remains unclear and requires further investigation.

【Disclosure】 The authors have no conflicts of interest to disclose.

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