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Case report

Subcortical neurofibrillary tangles and argyrophilic grains in a case of familial frontotemporal dementia with parkinsonism

Katsuji Kobayashi [a,b,*], Satoru Sudo [c], Rokurou Matsubara [d], Hiroyuki Nakano [a,b], Yoshifumi Koshino [a,b]

[a] *Department of Psychiatry and Neurobiology, Graduate School of Medical Sciences, Kanazawa University, 13-1 Takara-machi, Kanazawa 920-8641, Japan*

[b] *Department of Psychiatry, Awazu Neuropsychiatric Sanatorium, Wo-88 Yatano-machi, Komatsu-shi, Ishikawa-ken 923-0342, Japan*

[c] *Department of Psychiatry, Fukui University School of Medicine, Matsuoka-tyou, Fukui-ken, Japan*

[d] *Fukui Matsubara Hospital, Bunkyou, Fukui, Fukui-ken, Japan*

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Abstract

A case of familial frontotemporal dementia with parkinsonism (FTDP) similar to progressive supranuclear palsy (PSP) was reported. A 58-year-old man developed personality change followed by parkinsonism and dementia. Three family members showed similar symptoms. Cerebral atrophy was marked on the anterior frontotemporal lobes. The substantia nigra, hippocampus, peri-aqueductal gray matter and pontine nucleus were affected with globose neurofibrillary tangles (NFT) and glial tangles. Argyrophilic grains were distributed in the CA1–CA2. NFT, glial tangles and argyrophilic grains expressed four-repeat microtubule-associated protein tau (MAPT). *MAPT* gene had no mutation. Familial occurrence of FTDP with PSP-like tauopathy is rare.

Keywords: Argyrophilic grains; Frontotemporal dementia; Microtubule-associated protein tau; Neuropathology; Parkinsonism; Progressive supranuclear palsy

1. Introduction

Frontotemporal lobar degeneration (FTLD) is characterized by abnormalities in personality and behavior, dementia and language disturbance. Three different clinical syndromes: frontotemporal dementia (FTD), progressive aphasia, and semantic dementia are recognized [1–4]. Histologically FTLD is currently classified as a tauopathy and non-tauopathy disorders, based on the presence or absence of abnormally phosphorylated microtubule-associated protein tau (MAPT) in neuronal and glial inclusions [5]. FTLD with tauopathy includes Pick's disease, corticobasal degeneration (CBD), progressive supranuclear palsy (PSP) and frontotemporal dementia and parkinsonism linked to chromosome 17. But PSP as a pathological variation of familial FTLD with tauopathy was very rare [4] and only two non-familial cases have been reported [6,7]. The present case manifested initially FTD symptoms and later parkinsonism. Autopsy revealed globose NFT and glial tangles distributed in the subcortical gray matter and argyrophilic grains in the hippocampus in addition to frontotemporal lobe atrophy. Three family members showed parkinsonism but *MAPT* gene mutation was absent. The present case is a familial FTD with parkinsonism (FTDP) that showed PSP-like pathological profile.

2. Clinical history

A 45-year-old man had been in good health until he was arrested on a charge of train resistance. His mother, sister

* Corresponding author. Department of Psychiatry, Awazu Neuropsychiatric Sanatorium, Wo-88 Yatano-machi, Komatsu-shi, Ishikawa-ken 923-0342, Japan. Tel.: +81 761 44 2545; fax: +81 761 43 1877.

E-mail address: k-koba@ta2.so-net.ne.jp (K. Kobayashi).

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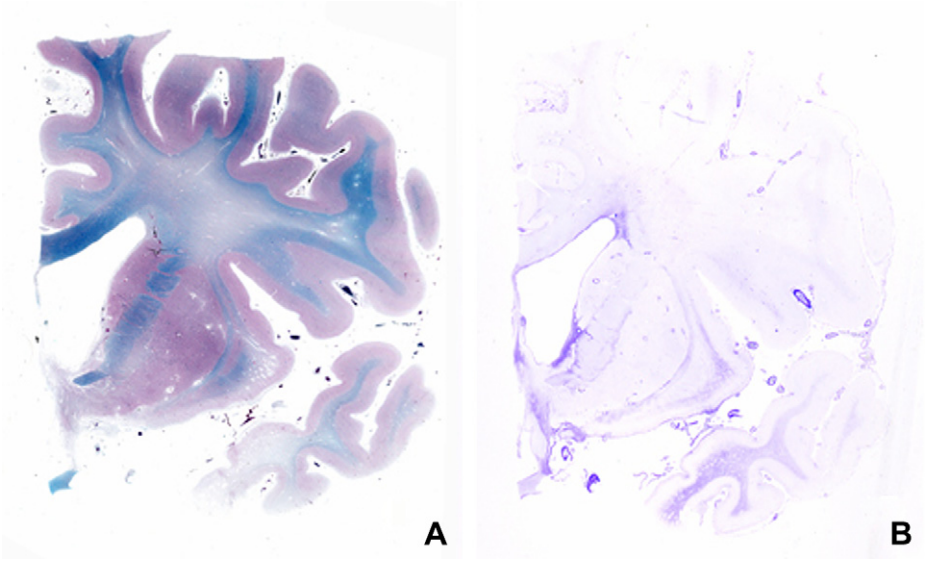

Fig. 1. Hemispheric sections stained with Bodian and luxol-fast blue stain (A) and with Holzer's stain (B). White matter gliosis was found from the rostral temporal lobe to the medial temporal lobe. The medial septal nucleus, diagonal band of Broca, nucleus basalis of Meynert were gliotic.

and brother had been affected with parkinsonism showing hypokinesia, muscle rigidity, and tremor. In his mother and brother parkinsonism preceded psychotic symptoms and dementia and died at a mental hospital. But his sister initially developed apathy and inertia followed by severe parkinsonism. At the age of 46 years old, his gait became unsteady and tremor was noted in his right hand. He developed general slowness, uncooperativeness, and indifference. He showed marked rigidity and tremor in his extremities, gait disturbance, hypokinesia, and impaired postural reflex. Dysautonomia was not observed and brain CT was unremarkable. He was diagnosed as Yahr's grade III of PD. L-Dopa and dopamine agonist minimally improved his parkinsonism. He became euphoric and showed frequently uninhibited and stereotypical behaviors. He scored 25 on MMSE at age 49 with rigidity in his right upper extremity and no gaze palsy. On MRI bilateral inferior horn of the lateral ventricle was dilated and temporal poles were atrophied. He was hospitalized in a mental hospital at age 51. He showed dysarthria and gait instability with backwards falls. He scored 13 at age 56 and 11 at age 58 on MMSE. He died at age 58.

3. Pathological findings

The fresh brain weighed 1270 g. The anterior temporal and frontal lobes showed bilateral atrophy. Visible blood vessels had no atheromatous changes. Representative hemispheric sections were stained with hematoxylin and eosin, luxol-fast blue, cresyl violet, Holzer and Bodian stain and examined. Immunolabelings of ubiquitin, alpha-synuclein, MAPT (AT8, RD3 and RD4), beta amyloid protein (4G8) and glial fibrillary acidic protein was performed.

The prefrontal and orbitofrontal cortex and the medial and lateral occipitotemporal gyri, particularly their anterior parts, showed a decrease in cortical thickness with white matter myelin pallor (Fig. 1). These cortices showed spongiform

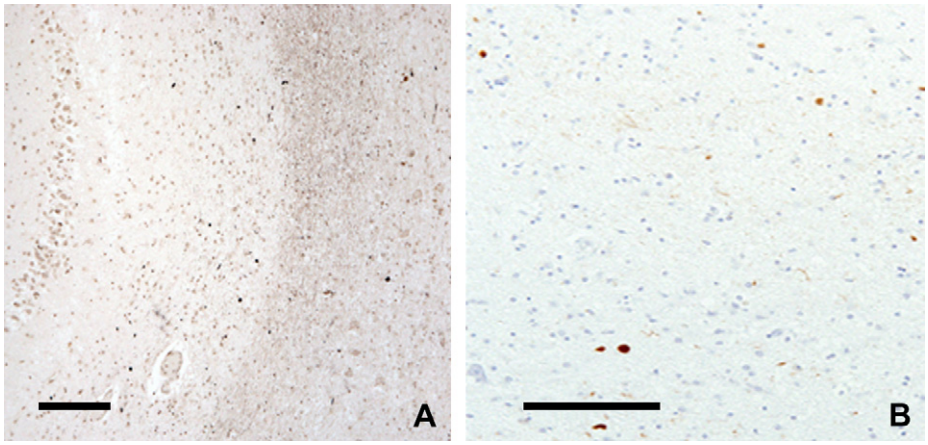

Fig. 2. Gallyas-impregnated minute round materials in CA1 (A). These structures were labeled with RD4 (B). Bars = 100 μm in A, and 10 μm in B.