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CASE REPORT

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Coexistence of paired helical filaments and polyglucosan bodies in the same neuron in an autopsy case of Alzheimer's disease

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Abstract The coexistence of polyglucosan bodies (PBs) and paired helical filaments (PHFs) in the same neuron is reported in an autopsy case of Alzheimer's disease. The patient was a 56-year-old Japanese male with a typical clinical course and pathological findings of Alzheimer's disease. Electron microscopically, numerous neurofibrillary tangles, mainly composed of PHFs, were observed in the neuronal cytoplasm, axons and dendrites. Some of them coexisted with other filamentous structures, which comprised randomly oriented branching filaments with a diameter of 5–10 nm. These structures were compatible with PBs. Glial tangles could not be found. Coexistence of these two structures was thought to occur in neurites.

Key words Paired helical filament · Polyglucosan body · Alzheimer's disease · Ultrastructure

Introduction

Bodies in the human nervous system which mainly consist of polyglucosan are known as corpora amylacea [2], Bielschowsky bodies [3, 20] and Lafora bodies [5], called en bloc polyglucosan bodies (PBs) [14]. Corpora amylacea generally exist in the processes of astrocytes, while the latter two exist in neurons. However, corpora amylacea also exist in the cytoplasm or axons of neurons and are called intraneuritic corpora amylacea [1, 15–17, 19]; they have no disease specificity and are thought to be related to aging [9, 16]. We present what we believe to be the first report of the coexistence of PBs and paired helical filaments (PHFs) in the same neurite in Ammon's horn in an autopsy case of Alzheimer's disease.

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Case report

The patient was a 56-year-old Japanese man with no significant family or past history. He developed an impairment of memory relating to recent events at the age of 50 years and became gradually more forgetful. He was admitted to Numazu Chuo Hospital 3 years later. Subsequently, he developed euphoria and focal signs of high cerebral functions. The neurological examination showed no remarkable abnormalities. His condition rapidly deteriorated until in 1994 (55 years old) he became bedridden. He had recurring ileus and died aged 56 years.

Materials and methods

For light microscopy, representative sections were embedded in paraffin wax. The routine stains employed were hematoxylin-eosin (HE), Klüver-Barrera for myelin, Holzer for glial fibers and Bodian silver impregnation. In addition, periodic acid-Schiff (PAS) stain was also employed.

For electron microscopy, small fragments of Ammon's horn were taken from the fresh brain at autopsy, 6 h post mortem. The specimens were immediately fixed in 2.5% glutaraldehyde solution, and post-fixed in 1% osmium tetroxide. After dehydration in graded alcohol series, the tissue was embedded in Epon mixture. Ultrathin sections were contrasted with uranyl acetate and lead citrate. In addition, they were also stained using the thiosemicarbazide (TSC) method [18] and observed using a JEOL 2000FX electron microscope.

Result

Neuropathological findings

The brain weighed 1120 g and revealed diffuse atrophy of the cerebral cortex, especially in the temporal region. The brain stem and cerebellum showed no gross abnormality. On sectioning, the cerebral cortex and the white matter were atrophic. The lateral ventricles were markedly dilated. Histologically, numerous senile plaques and tangles were distributed throughout the cortex. Moreover, numerous thread-like tangles were prominent in senile plaques and neurites on the HE preparations. In addition, moderate neuronal loss and gliosis were seen in the cerebral cor-

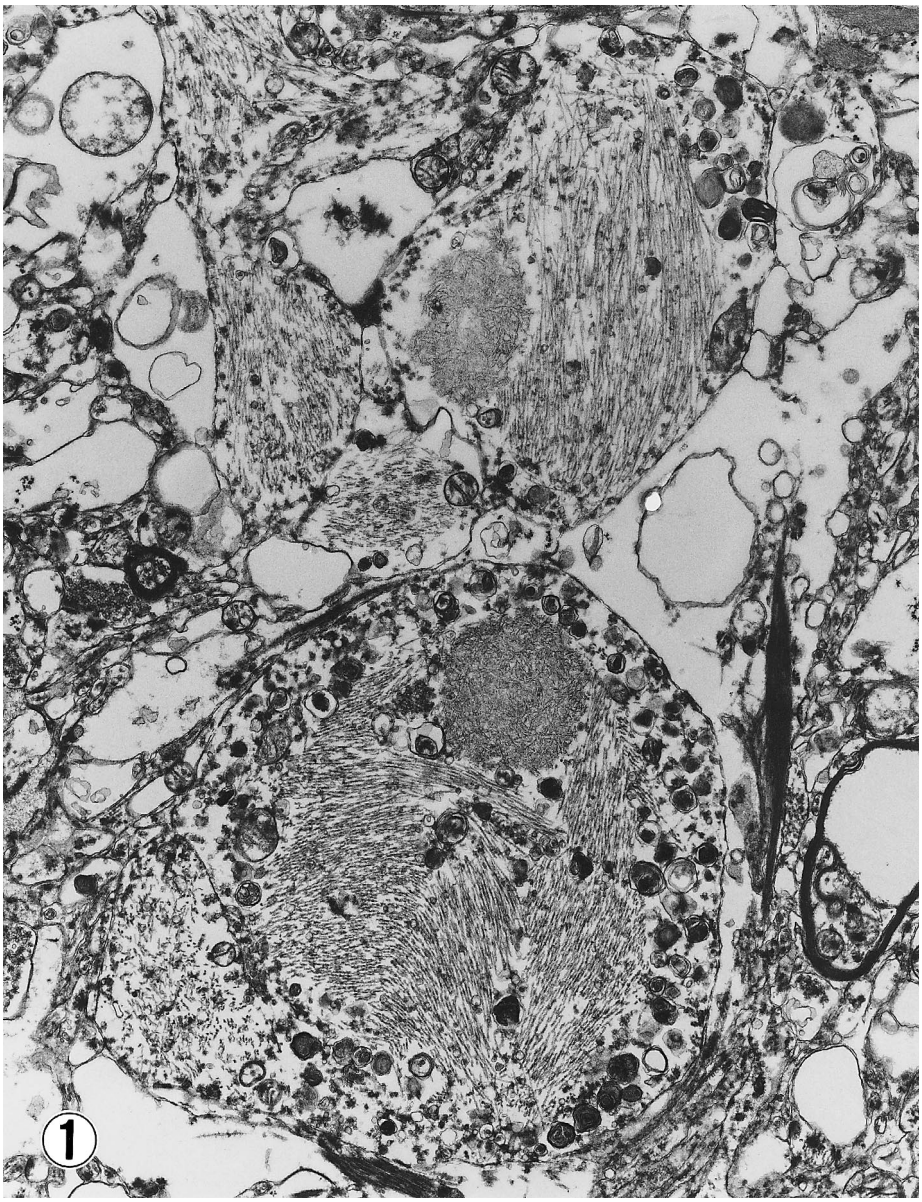

Fig. 1 Both a polyglucosan body and a skein of paired helical filaments are seen in a neuronal process in Ammon's horn. × 10,500

tex. These histological pictures were compatible with those of Alzheimer's disease.

Electron microscopic findings

Numerous neurofibrillary tangles, mainly composed of PHFs, were observed in the neuronal cytoplasm, axons and dendrites. Some of them coexisted with other filamentous bodies (Fig. 1), which comprised randomly oriented, slightly bent, branching filaments about 5–10 nm thick (Fig. 2). These bodies did not have a central core, peripheral radiation or glycogen granules. No limiting membrane could be discerned between the two structures. They were surrounded by small organellaes, for example degenerating mitochondria and small vesicles. These structures were thought to be compatible with PBs. The astrocytes examined, including their processes, did not bear any PHF structures.

As electron microscopic examination revealed the existence of polyglucosan, the consecutive sections of paraffin-embedded blocks were also stained with PAS. On PAS staining, in addition to lipofuscin granules in neuronal perikarya, numerous small PAS-positive granules were seen in the neuropil of Ammon's horn, particularly in the CA4 region of the hippocampal formation. Their size were usually less than 1 μm.

Electron microscopically, TSC-positive structures were scarcely observed; histologically small PAS-positive structures were mostly lipofuscin granules in the neurites.

Discussion

PBs occur in various conditions in the human nervous system, especially corpora amylacea in the aging brain [2, 13], Bielschowsky bodies in a syndrome of double atheto-

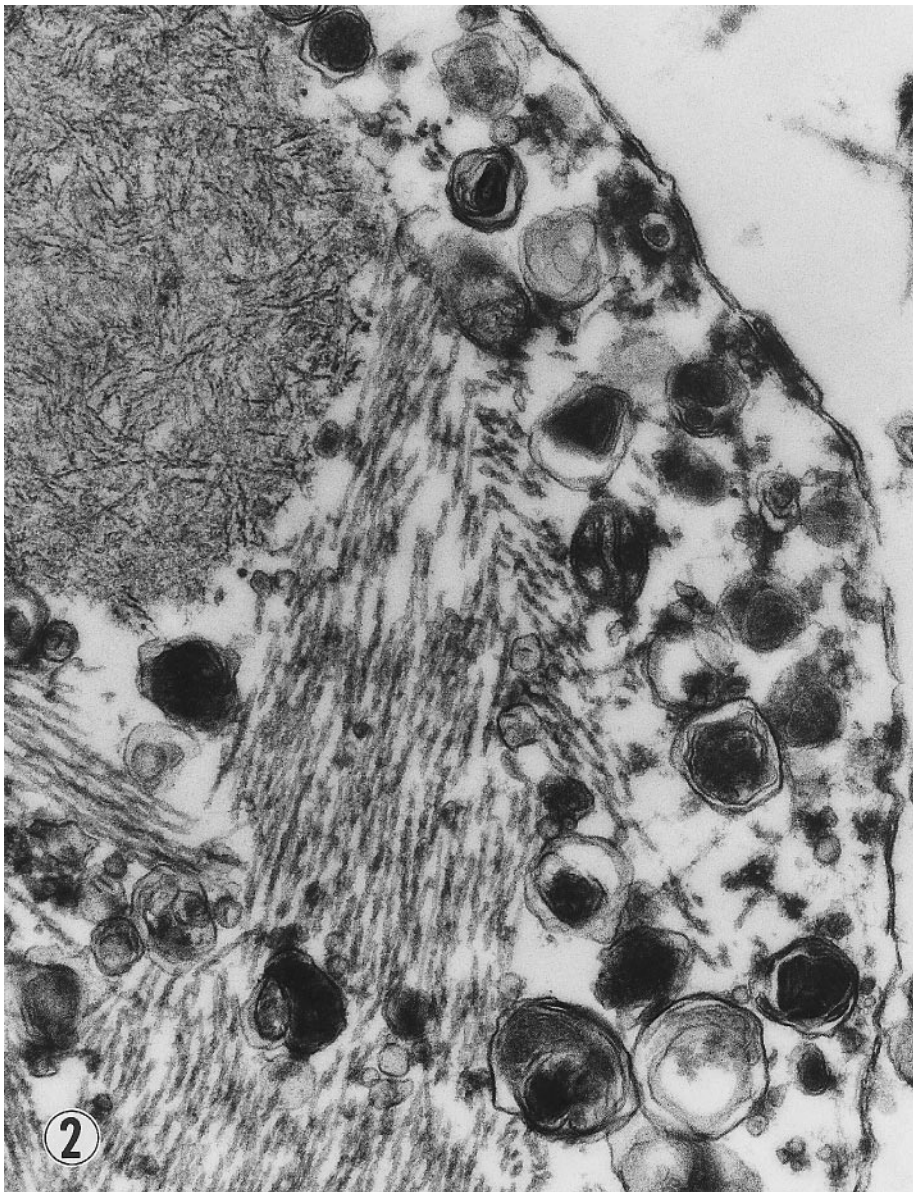

Fig. 2 Higher magnification of Fig. 1. A polyglucosan body is composed of irregularly arranged, branching filamentous structures with a diameter of 5–10 nm. × 42,000

sis [3, 20] and Lafora bodies in Lafora's disease [5]. PBs in neurons are non-specific and also occur in type IV glycogenosis [7], adult polyglucosan disease [14] and other conditions [1, 11, 12, 15–17, 19]. However, PBs in neurons are a rare phenomenon.

On the other hand, PHFs are the main component of neurofibrillary tangles and exist in the neuronal cytoplasm, dendrites and axons in normal aging, Alzheimer's disease and several other neurodegenerative diseases.

PHFs have been reported to exist in the astrocytes of a case of atypical Alzheimer's disease [10], in which the lesion of the cerebral cortex was very severe. In our case there were no tangles in glial cells. Moreover, there were no glial filaments in processes bearing both PBs and PHFs. There were also degenerating mitochondria around PHFs and PBs. These findings are usually made in dystrophic axons or degenerative dendrites [4]. It is therefore untenable that PHFs exist in glial cells in our case. It might be that PHFs and PBs coexisted in neurites, although synaptic vesicles or synaptic junctions could not be found in the processes bearing PHFs and PBs.

In this case, numerous small PAS-positive structures were observed in the hippocampal formation, but ultrastructurally TSC-positive structures were scarcely observed, suggesting that most small PAS-positive structures could not be polyglucosan or glycogen granules, and might be lipofuscin granules in the neuropil. Therefore, it is impossible for this case to be diagnosed as adult polyglucosan body disease.

Mizutani et al. [9] reported the relationship between intra-axonal polyglucosan in the ventral posterolateral nucleus of the human thalamus and aging, but they did not mention the existence of PHF. Mann et al. [6] reported accumulation of granular glycogen bodies in the cerebral cortex of 11 cases of Alzheimer's disease, but no reference was made to polyglucosan bodies.

PHFs and PBs are of different origin, because chemically PHFs are made mainly from abnormal tau protein, whereas polyglucosan is a polymer of beta-glucosan, which is an anhydride of glucose [2, 8]. Although PHFs are commonly present in neurons and PBs are rare in neurites in Alzheimer's disease, the coexistence of two substances of different origin is thought to have no significant correlation and to be a very rare coincidence in this case.

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