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Progressive Dementia with 'Diffuse Lewy-Type Inclusions' in Cerebral Cortex

A Case Report

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Summary. A 69-year-old male suffering from progressive dementia died 3 years after the beginning of his disease. The neuropathology of this case revealed the coexistence of senile changes, typical for Alzheimer's disease, and the characteristics of Parkinson's disease, namely, numerous senile plaques and neurofibrillary tangles in the cerebrum and neuronal loss with depigmentation in the substantia nigra and locus caeruleus. Lewy-type inclusions were distributed not only in the pigmented brain stem nuclei, but also diffusely in the CNS. The close nosological relationship between paralysis agitans and Alzheimer's disease is discussed.

Key words: Lewy bodies – Dementia – Senile changes – Parkinson's disease.

Zusammenfassung. Ein 69jähriger Mann mit progressiver Demenz verstarb 3 Jahre nach Beginn der Erkrankung. Die Neuropathologie dieses Falles ist gekennzeichnet durch die Koexistenz bekannter seniler Veränderungen in Form von zahlreichen senilen Drüsen und Alzheimerschen Neurofibrillenveränderungen im Großhirn (Morbus Alzheimer) und leichter Nervenzellausfälle mit Depigmentation in Substantia nigra und Locus caeruleus (beginnende Paralysis agitans). Bemerkenswert ist ferner ein zahlreiches Vorkommen von Lewy-Körperchen, die nicht nur im Hirnstamm, sondern auch in den Nervenzellen der Hirnrinde verteilt sind. Die engen nosologischen Beziehungen zwischen Parkinsonscher und Alzheimerscher Krankheit werden diskutiert.

Schlüsselwörter: Lewy-Körperchen – Demenz – Senile Veränderungen – Parkinsonsche Krankheit.

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Introduction

Parkinsonism with dementia (Alvord et al., 1974; Hakim and Mathieson, 1979), or conversely, dementia with parkinsonism (Pearce, 1974) are frequently reported. In our case of progressive dementia, neuropathological findings are characterized by numerous Lewy-type inclusions in the cerebral cortex in addition to the well-known changes of Alzheimer's and Parkinson's diseases.

Case Report

The patient (a 69-year-old male) had spent his last 2 years, up to the time of hospitalization, with his daughter's family. During this time slight forgetfulness had been noticed which had progressed gradually. At first, the patient was capable of harmonious integration into the family system, but approximately 6 months before his death his condition worsened rapidly; exhibiting confusion, disorientation, and delirium, especially at night. A month later, he was admitted as an ambulatory inpatient to a mental hospital. On admission, the patient seemed to be alert but restless, he was incontinent and disoriented, and was confused in speech. His mood was rather euphoric. Neurological examination revealed no particular abnormalities. The physical history only mentioned a record of chronic bronchitis with emphysema. There was no history of hypertension. Hepatomegalia and sinus rhythm with extrasystoles were found. He had a habitual intake of two or three 0.33 l bottles of beer per day before his hospitalization. Clinical diagnosis was early senile dementia and suspected predelirant state resulting from alcohol abuse. The physical and mental condition of the patient deteriorated further and he was confined to bed for about 3 months before his death. During this time, somnolentia had alternated with intervals of conscious state with aggressiveness. Later he suffered from recurrent attacks of fever due to therapy-resistant bronchitis and decubitus. He died of circulatory failure caused by septic fever, approximately 3 years after the first memory disturbances.

Neuropathological Findings

Only the brain was available for examination. The brain weighed 1292 g after 4% buffered formalin fixation. There were mild frontal, temporal, and parietal atrophies on the cerebral convexities. The basilar arteries indicated no arteriosclerotic change. Upon coronal section, the atrophy was found to be more predominant in the temporal region. The lateral ventricle was remarkably dilated. No obvious macroscopic changes were noticed in the mammillary bodies, substantia nigra, locus caeruleus, or elsewhere. Histological findings were itemized as follows:

1. Senile Changes. Many senile plaques and neurofibrillary tangles were distributed in the temporal region and were especially numerous in the fusiform parahippocampal and hippocampal gyri (Fig. 2), but not in Sommer's sector. These changes were also sporadically found in other cerebral-cortical regions. Abundant nerve cells with granulovacuolar degeneration were seen in Ammon's horn. In the subcortical nuclei only the amygdaloid nucleus and the supraoptic part of the hypothalamic region were affected by numerous neurofibrillary tangles.

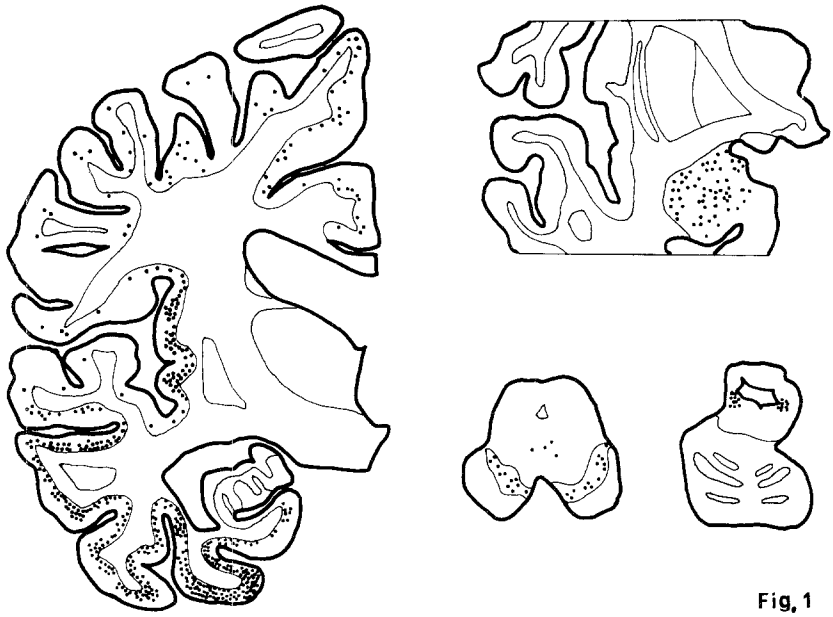

Fig. 1. Distribution of Lewy-type inclusions *(dots)*

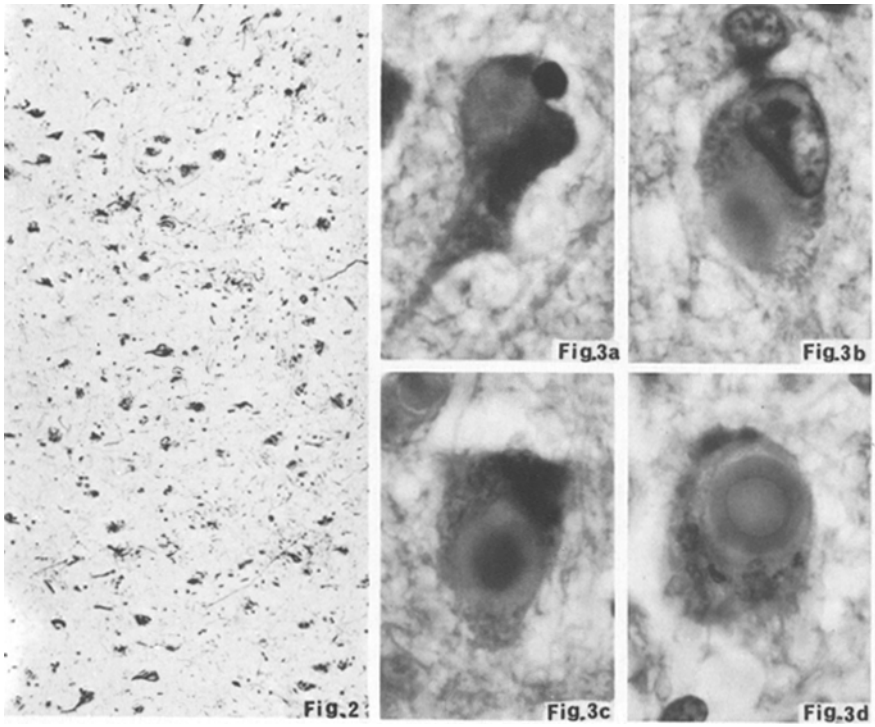

Fig. 2. Neurofibrillary tangles and senile plaques in hippocampus. Bodian, × 100

Fig. 3 a–d. (a–c) Lewy type inclusions in cerebral cortex showing from homogeneous to laminated structure. H & E, × 1200. (d) Typical Lewy body in locus caeruleus. H & E, × 1200

2. Lewy-Type Inclusions. The most prominent feature was the diffuse distribution of Lewy-type intracytoplasmic inclusions throughout the cerebral cortex, especially in the temporal area (Fig. 1). In contrast to the typical Lewy bodies in the pigmented brain stem nuclei, most of these inclusions were homogeneous and less eosinophilic (Fig. 3a). Some of them, however, had an obscure eosinophilic central core, namely, they showed concentrically laminated structures (Figs. 3b and 3c). These inclusions were negative for PAS, Carmine, and Sudan black B, but slightly argentophilic and found only in the fifth or sixth layer of the cortex. The identical inclusions were frequently present in the amygdaloid nucleus (Fig. 1) and also found, though rarely, in the subthalamic nucleus and Purkinje cell layer of cerebellum. Thus, the distribution of the inclusions was nearly identical with that of the neurofibrillary tangles. A mild nerve cell loss with depigmentation was mainly observed in the central part of the substantia nigra and a moderate one in the locus caeruleus, and the distribution of the typical Lewy bodies (Fig. 3d) was conspicuous (Fig. 1).

3. Further Neuropathological Findings. There was a diffuse cortical nerve cell loss with astrocytic gliosis which was accentuated in the temporal region. The mammillary bodies, the vicinal regions of the third ventricle and other basal ganglia revealed no particular changes except for a slight naked glial proliferation in the pallidum. Mild astrocytic gliosis in the subcortical area of the cerebellum and slight nerve cell loss with gliosis in nucleus dentatus and nucleus olivaris inferior were seen. Neuronal lipofuscinosis in the inferior olivary nucleus was prominent. Neither chromatolytic neuronal nor neuroaxonal swellings were found. No obvious vascular changes except for hyalin degeneration of small vessels in the cerebral cortex.

Discussion

Clinical features of this case were a relatively rapid mental deterioration following mild forgetfulness in senium. The neuropathological findings of this case were characterized by a coexistence of senile changes of the Alzheimer type and pathomorphology of Parkinson's disease. Additionally, Lewy-type inclusions, which are commonly thought to be typical of idiopathic Parkinson's disease with a characteristic localization in the brain stem, showed remarkably widespread occurrence in the cerebral cortex. To our knowledge, such cases with 'diffuse Lewy-type inclusions' in the grisea of the cerebral cortex have only occasionally been reported (Okazaki et al., 1961; Kono et al., 1976; Ikeda et al., 1978; Kosaka, 1978; Ogasawara et al., 1978; Kosaka and Mehraein, 1979). The properties of the inclusions have histochemically and ultrastructurally been confirmed as identical with Lewy bodies by some authors (Ikeda et al., 1978; Kosaka, 1978), though minor differences were also observed. Kosaka and Mehraein (1979), who included their own five cases, recently summarized nine cases with 'diffuse Lewy-type inclusions' in the cerebral cortex. These cases revealed as common features a clinical picture characterized by progressive dementia with muscular rigidity and neuropathological findings including both characteristics of Parkinson's disease and morbus Alzheimer (or senile dementia). They hypo-

thesized that these cases belong to the same category and that they could be considered a new clinicopathological entity subsumed under dementia-parkinsonian syndrome.

Our own case could also be classified under the same syndrome. Since clinically no parkinsonian symptoms were found in our case and neuropathological involvements in the substantia nigra were relatively mild, the dominant features of this case point toward dementia and senile changes. In contrast to this, a previously reported case (Ikeda et al., 1978) of a patient who died at 38 years of age presented parkinsonian symptoms which were not accompanied by dementia and senile changes. Thus, the two processes of dementia and parkinsonism in this group might be regarded as equivalent, i.e., a widespread range and variability of symptoms are characteristic for this dementia-parkinsonian syndrome.

Further, a high incidence of dementia in parkinsonism (Alvord et al., 1974; Hakim and Mathieson, 1979) or the parkinsonian type of extrapyramidal disorders in Alzheimer's disease (Pearce, 1974) was reported. Indeed, it is likely that bradykinesia and/or reactive depression with parkinsonism and hypertonia-hypokinesia arising from the psychiatric disorder of dementia prevent precise recognition of concealed accessory symptoms. According to a neuropathological review by Hakim and Mathieson (1979), 29 of 34 cases of Parkinson's disease revealed various degrees of senile changes associated with Alzheimer's disease in the hippocampus, and only one Parkinson's disease case was free of any senile changes. A comprehensive neuropathological study by Alvord et al. (1974), which aimed to correlate parkinsonism and dementia, also revealed that the frequency of simultaneous cortical degeneration and dementia was higher in the Parkinson's disease group than in the control group.

The following possibilities are suggested: The two processes of dementia and parkinsonism may have a closer nosologic relationship than was previously recognized. Furthermore, involvements in one system may give rise to vulnerability in other systems (Forno et al., 1978).

Future work will very likely provide proof for this hypothesis.

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