Dementia with Lewy Bodies and Parkinson Disease with Dementia Within the Spectrum of Lewy Body Disease

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Abstract The history of Parkinson disease (PD) and dementia with Lewy bodies (DLB) is briefly presented. Since Lewy reported Lewy bodies in the brainstem nuclei of the PD brain in 1912, Lewy bodies had been considered an essential pathological finding for the diagnosis of PD. It had been, however, considered that there were almost no Lewy bodies occurring in the cerebral cortex. In 1976, we reported our first autopsied case showing numerous Lewy bodies in the cerebral cortex. In 1978, we reported the detailed characteristics and distribution pattern of cortical Lewy bodies, based on three autopsied cases showing diffuse Lewy body disease (DLBD), a term that we proposed in 1984. We also reported two German autopsied cases showing DLBD in 1979, which were the first DLBD cases reported in Europe. In 1980, we also proposed the term Lewy body disease and classified it into three types: brainstem type, transitional type, and diffuse type. The brainstem type is the same as PD, and the diffuse type was later designated DLBD. In 1990, we reviewed all the 37 DLBD cases reported in Japan and classified DLBD into two forms: a common form with more or less Alzheimer pathology and a pure form without such pathology. Since then, we have reported many papers concerning DLBD. The term dementia with Lewy bodies (DLB) was proposed at the first international workshop held in 1995. CDLB guidelines were published in 1996, and the CDLB guidelines–revised were reported in 2005. In the revised guidelines the term Lewy body disease was used as a generic term that included DLB, PD, and PDD, as we had insisted since 1980.

Keywords Dementia with Lewy bodies (DLB) • Diffuse Lewy body disease • Lewy body disease • Parkinson disease • Parkinson disease with dementia (PDD)

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Introduction

Dementia with Lewy bodies (DLB) is now the second most frequent dementing illness in the elderly, following Alzheimer-type dementia (ATD). The term DLB was proposed at the first International Workshop [1], which was held in Newcastle upon Tyne in 1995. Lewy bodies are essential for the neuropathological diagnosis of Parkinson's disease (PD). PD patients frequently show dementia, and such patients are diagnosed as having PD with dementia (PDD). Recently, it has usually been considered that DLB and PDD are almost the same disease not only clinically but also neuropathologically.

In this chapter, the author briefly introduces the history of PD and DLB, and insists that DLB and PDD should be understood within the spectrum of Lewy body disease, a term that we proposed in 1980 [2].

History of PD and DLB

James Parkinson [3] published the first report detailing the clinical features of "shaking palsy" in 1817. Then, he described that cognition remained intact in this disease. Charcot [4] proposed the term "Parkinson disease" in 1968, and described cognitive disturbance in PD. In 1912, Lewy [5] reported eosinophilic round intraneuronal inclusions in the substantia innominata and dorsal vagal nuclei of PD brain. Tretiakoff [6] nominated these inclusions "Lewy bodies" and indicated the importance of the substantia nigra in PD in 1919. Thereafter, the difference of PD and postencephalitic parkinsonism was discussed for a long time. Hassler [7] reported the difference in the distribution of neuronal loss in the substantia nigra between these two diseases in 1938. In 1953, Greenfield and Bosanquet [8] pointed out for the first time that the presence of Lewy bodies is the essential pathological finding for the diagnosis of PD whereas the presence of neurofibrillary tangles is essential for the diagnosis of postencephalitic parkinsonism. Furthermore, den Hartog Jager and Bethlem [9] described the detailed distribution of Lewy bodies in the brainstem of PD brain in 1960. Thus, the pathological basis of PD was established about one and a half centuries after the first report of Parkinson in 1817. It had been, however, considered that there were almost no Lewy bodies occurring in the cerebral cortex. In 1976, we [10] reported our first autopsied case showing numerous Lewy bodies in the cerebral cortex as well as in the brainstem nuclei. In 1978, we [11] reported the detailed characteristics and distribution pattern of cortical Lewy bodies, based on our own three autopsied cases with "diffuse Lewy body disease (DLBD)," a term that we [12] proposed in 1984. We [13] also reported two German autopsied cases showing DLBD in 1979, which were the first DLBD cases reported in Europe. In 1980, we [2] proposed the term "Lewy body disease" and classified it into three types: brainstem type, transitional type, and diffuse type. The brainstem type is the same as PD, and the diffuse type was later designated DLBD

[12]. Furthermore, we [14] reviewed all 37 DLBD cases reported in Japan and classified DLBD into two forms: a common form with more or less Alzheimer pathology and a pure form without such findings. Since then, we have published several papers concerning DLBD. The term "dementia with Lewy bodies" (DLB) was proposed at the first international workshop in 1995 [1]. The CDLB guidelines were published in 1996 [15], and the CDLB guidelines–revised were reported in 2005 [16].

The most important recent findings in this field were (1) alpha-synuclein gene mutation in familial PD [17] and (2) alpha-synuclein as the main component of Lewy bodies [18]. Thereafter, alpha-synuclein has received considerable attention in the research on Lewy body disease.

DLB and PDD Within the Spectrum of Lewy Body Disease

At the first international workshop held in 1995, the difference between DLB and PDD was discussed. In the CDLB guidelines [15], the "1-year rule" was adapted. According to these guidelines, PDD is differentiated from DLB by the appearance of dementia at least 1 year after the onset of PD symptoms. At the third international workshop held in 2003, not a few researchers insisted that this 1-year rule should be abolished. This rule was, however, maintained even in the CDLB guidelines–revised reported in 2005 [16]. Considerable evidence has been reported that DLB and PDD are almost the same not only clinically but also neuropathologically. Therefore, in the revised guidelines, the term "Lewy body disease" was used as a generic term that includes DLB, PD, and PDD [16]. In the report of the DLB and PDD working group in 2007 [19], a similar description was also introduced.

Since our proposal of Lewy body disease in 1980 [2], we have insisted that Lewy body disease is a generic term that includes PD, PDD, and DLBD [12, 14, 20–22].

Lewy body disease is now defined as follows: "Lewy body disease is a chronic neuropsychiatric disease characterized clinically by idiopathic parkinsonism of early- or late-onset, frequently followed by progressive dementia. In many cases, progressive dementia is the main symptom, followed frequently by idiopathic parkinsonism. It is neuropathologically characterized by the presence of numerous Lewy bodies and Lewy neurites in the central and sympathetic nervous systems."

As indicated above, we classified DLBD into two forms: a common form with more or less ATD pathology and a pure form without it [14]. Then, we described differences in the clinical features between the common form and the pure form. In the common form, most cases showed later onset, and the initial symptom was memory disturbance followed by progressive dementia, and about 70% of patients later developed parkinsonism. However, the pure form was characterized by younger onset, idiopathic parkinsonism as the initial symptom and later followed by progressive dementia. Therefore, the pure form can be diagnosed as PDD. In 1992, when the 150th anniversary congress of the German Psychiatry Association was held

in Koeln, I was invited to a symposium and reported the differences in clinical features between Japanese and European-American DLBD cases [23]. The features of the common form do not show any differences between the two regions, while the pure form showed marked differences between regions: most Japanese cases were characterized, as indicated above, by younger onset and initial parkinsonism followed by dementia, whereas most European-American cases demonstrated later onset and progressive dementia followed by parkinsonism, as in the common form. In 2003, when I was invited as a symposist at the annual meeting of the Japan Neurology Association, I [24] reported a neuropathological study of 24 PDD cases. The findings showed that all our 24 PDD cases were pathologically diagnosed as DLB. Thus, PDD did not show neuropathological differences from DLB.

In 1996, we [21] proposed the term "cerebral type" of Lewy body disease. In the cerebral type, the main symptom is progressive dementia without parkinsonism. Neuropathologically, numerous Lewy bodies appeared in the cerebral cortex as in DLBD, but only rare Lewy bodies were found in the brainstem nuclei. Braak's theory [25] insisted that Lewy bodies occur from the medulla oblongata through the pons and midbrain to the cerebral cortex in PD. This cerebral type means suggests that Lewy bodies occur at first in the cerebral cortex and then migrate down to the brainstem nuclei . Therefore, the cerebral type of Lewy body disease should receive more attention.

In conclusion, Lewy body disease is a generic term that includes PD, PDD, and DLB. It is neuropathologically classified into four types: brainstem type, transitional or limbic type, diffuse type, and cerebral type.

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