Parkinsonism and Related Disorders 46 (2018) S6–S9

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Dementia with Lewy Bodies and Parkinson Disease Dementia: It is the Same Disease!

Joseph H. Friedman, MD [a, b, *]

[a] Dept. of Neurology, Butler Hospital, 345 Blackstone Blvd, Providence, RI 02906, USA
[b] Dept of Neurology, Warren Alpert Medical School of Brown University, Providence, RI 02906, USA

ARTICLE INFO

Article history:
Received 15 July 2017
Accepted 15 July 2017

Keywords:
Dementia with Lewy bodies
Parkinson's disease dementia
Disease classification
Parkinson's disease progression
Dementia with Lewy bodies disease progression

ABSTRACT

Introduction: The question whether DLB and PDD are distinct disorders has been debated in several forums. The two disorders, once parkinsonism is present in DLB, cannot be distinguished on clinical or pathological grounds. The conundrum exists for those DLB patients who do not yet have parkinsonism, and raises the parallel with patients who have Rapid Eye Movement Behavior Disorder but have not yet manifested parkinsonian signs.
Methods: A literature review was summarized to justify classification as a single disorder.
Results: Most clinical observations and trials point to these disorders, once parkinsonism is present in DLB, are identical.
Conclusion: This article notes the advantage to clinical research and treatment by considering these two syndromes as the same so that medications approved for PDD and for PD psychosis can be extended to DLB patients and that resources for PD research and support can be also used for DLB.
© 2017 Elsevier Ltd. All rights reserved.

1. Introduction

The first description of DLB was published in 1961 [1]. Two men, ages 69 and 70, one with a 12 month course and the other of unclear duration, had developed dementia associated with severe flexion and rigidity. One had visual hallucinations. The medical histories were not well known to the physicians so that clinical details were slight. The occurrence of Lewy bodies (LB) in the cortex, they noted, had been described previously but only in the elderly and had unknown significance. The recognition that this disorder was a significant cause of dementia, was a surprise to the original authors, who had thought their cases a "curiosity." (personal communication).

Clinically defined DLB is now thought to constitute about 5% of dementia cases in the elderly [2] and autopsy studies have found that 3–10% of older dementia patients meet pathological criteria for the diagnosis of DLB [2]. Parkinson's disease (PD) is the second most common neurodegenerative disorder in resource wealthy parts of the world and DLB is the second most common neurodegenerative dementing disorder.

Whether DLB and PD with dementia (PDD) are the same disease or not has been the subject of debate [3]. The Movement Disorders Society convened a panel to suggest a revised clinical definition of idiopathic PD, which suggested that DLB, once parkinsonism is present, should be considered the "DLB subtype" of PD [4], and that the presence of dementia should no longer be exclusionary for the diagnosis of PD. The U.K. Brain Bank criteria use "severe dementia" as an exclusionary criterion, not mild dementia. While both sides of the argument agree that the two clinical syndromes are extremely close in all aspects, other than for the timing of the onset of dementia, several expert groups have taken the position that it is "useful" to consider the entities as separate [3,5,6], without an explicitly stated rationale. A summary of arguments against the MDS revised criteria that suggested DLB classification as a variant of PD was published in 2017 [7]. The current distinguishing feature between the two disorders remains the temporal sequence of dementia versus motor signs. If dementia precedes or occurs within 12 months of the onset of motor features, the disorder is labeled DLB, the "12 month rule" [8].

There are two questions to consider in attempting to reach an answer to the question. What criteria should be used to classify a disease: does the answer to the DLB vs PDD question matter?

The conundrum arises because DLB often presents before motor features of PD. Fifteen to 40% die without motor signs [8]. It is

* Dept. of Neurology, Butler Hospital, 345 Blackstone Blvd, Providence, RI 02906, USA
E-mail address: joseph_friedman@brown.edu.

http://dx.doi.org/10.1016/j.parkreldis.2017.07.013
1353-8020/© 2017 Elsevier Ltd. All rights reserved.

difficult to distinguish from Alzheimer's disease (AD), a distinction important for prognosis and clinical trials. It is difficult [3] for patients to understand that they have a variant of PD when no motor features are present. Analogies might be made to patients with REM sleep behavior disorder [7] who lack motor features of an alpha synucleinopathy, those with progressive supranuclear palsy who lack the required eye movement abnormality by the time of death, those with autonomic dysfunction prior to developing diagnosable multi-system atrophy, etc.

2. What is a disease and what is the role of disease classification?

There are a number of definitions of disease (see Table 1) but they share the unifying requirements of "distinguishing signs and symptoms" and a "particular," or distinguishing process.

The first International List of Causes of Death was published in 1893 and later taken over by the World Health Organization as The International Classification of Disease. This was always considered an evolutionary process, as understanding of epidemiology, pathophysiology and pathology improved with time. ICD 11 is in progress, and "experts and stakeholders are invited to participate in the ICD revision" (WHO ICD Revision website 2017).

Disease classification has followed a standard progression. A syndrome was first described, usually based on symptoms and signs, but possibly by changes in laboratory markers or by pathology. With increased knowledge came refinements. Classification runs into trouble when pathology, or pathological mechanisms, incompletely understood, produce different syndromes with the same pathology or when different pathologies produce clinically indistinguishable syndromes. There are family members with clinical PD, but not all of whom have LB, for example [9]. There are currently three "variants" of FTD and several variants of Alzheimer's disease, phenomenologically quite dissimilar.

The importance of classification is in avoiding confounding one disease with another. Pre-motor DLB is often indistinguishable from Alzheimer's disease [6], but observations on one do not translate to the other.

3. Are DLB and PDD the same? (see Table 2)

3.1. Clinical manifestations

DLB may present with purely behavioral symptoms or purely motor signs, with dementia being recognized later. The rationale for the 12 month designation [8] were not provided with the consensus guidelines. The most recent Consensus statement [8] simply notes that "this arbitrary cutoff remains useful, particularly in clinical practice." Sensitivity for pre-motor DLB has been low, but promises to be much higher with the addition of dopamine transporter (DaT) imaging [8]. Thus, studies of DLB are hampered by the need to have either autopsy results or the presence of motor features to correctly identify those with the disorder. Increasing use of dopamine transporter (DaT) scanning may allow for a higher degree of confidence and sensitivity in the diagnosis of pre-motor DLB, which will increase the number of subjects available to study.

Dementia eventually affects about 80% of PD patients. PDD is characterized primarily by executive dysfunction [10]. Patients have problems with planning and multi-tasking. They have a reduced ability to abstract and to adjust to changing requirements. Visuo-spatial dysfunction is an early feature, often preceding the onset of dementia or memory loss. Cortical functions such as language and praxis are generally not involved early. Memory problems tend to be more a problem of recall than a failure to lay down a memory trace. The neuropsychological profile on formal testing of the two disorders is the same [6,11]. As the dementia progresses however, the overlap with "cortical" dementias, particularly Alzheimer's disease became more pronounced, with language dysfunction, apraxia and failure to lay down a memory trace becoming more evident [5].

Behavior problems, particularly depression, anxiety, fatigue, apathy and sleep behavior disorder are so common in PD, that their absence is considered a "red flag" for its diagnosis [4]. These are common in DLB as well [8].

Psychotic symptoms, hallucinations and delusions are common in PDD. These are typically visual hallucinations, although other sensory hallucinations also occur [12]. Although hallucinating PDD patients are almost always on medications known to psychotic symptoms, this is not always the case [13]. These psychotic symptoms are common in DLB, as well, although these patients are usually *not* on medications for PD motor dysfunction. Minor hallucinations," transient peripheral field hallucinations or "presence" hallucinations," are not uncommon in early, untreated PD patients even without dementia [14]. These symptoms, occurring prior to diagnosis, illustrates the continuum of the psychotic syndrome, analogous to the presence of MCI in 10–20% of PD patients at the time of PD diagnosis [15].

Cognitive fluctuations, a diagnostic feature of DLB is seen commonly in PDD [16]. REM sleep behavior disorder is also common in both. Even the prevalence of daytime sleepiness appears to be the same [5]. Thus, the core [8] features of DLB, dementia, cognitive fluctuations, hallucinations and parkinsonism are present in both disorders.

Autonomic dysfunction is equivalent in the two conditions [17,18].

Table 1
Definitions of "disease".

1. "A condition of the living animal or plant body or one of its parts that impairs normal functioning and is typically manifest by distinguishing signs and symptoms" Merriam Webster Unabridged Dictionary 2017 (www.merriam-webster.com/dictionary/disease)
2. "A particular abnormal condition, a disorder of structure or function, that affects part or all of an organism" Wikipedia 2007
3. A particular destructive process in an organ or organism, with a specific cause and characteristic symptoms. Webster's New World College Dictionary (www.websters.yourdictionary.com)
4. A definite pathological process having a characteristic set of signs and symptoms. [Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing and Allied Health, Seventh Edition. 2005. Saunders Press.

Table 2
Quotes from expert reviews.

"When the clinical picture is fully developed they are indistinguishable" [29]
.,"there is no rational clinical or pathological basis to dictate a definite time interval between development of motor symptoms versus onset of dementia" [5]
"We did not find evidence of or a definitive pathological substrate to support the categorical clinical distinction between PDD and DLB despite the findings of higher cortical NFT, NP and SYN pathology in DLB compared with PDD, [20].
The MDS suggested criteria for the dx of PD "do not consider dementia an exclusion criterion for PD regardless of when it occurs in relation to parkinsonism onset" [7].
"no major difference between DLB and PDD have been found in any variable examined including cognitive profile, attentional performance, neuropsychiatric features, sleep disorders, autonomic dysfunction, type and severity of parkinsonism, neuroleptic sensitivity, and responsiveness to cholinesterase inhibitors" [Third report of the DLB consortium]
"The Working Group agreed unanimously that PDD and DLB are more similar than different. The main difference between the two entities is the timing of onset of dementia in relation to motor symptoms." [6]
"Neuropathologic findings do not support an arbitrary cut off between the two disorders." [30]

Download English Version:

https://daneshyari.com/en/article/8285602

Download Persian Version:

https://daneshyari.com/article/8285602

Daneshyari.com