

CORTICOBASAL DEGENERATION (CBD) AND PROGRESSIVE SUPRANUCLEAR PALSY (PSP) ARE VARIETIES OF THE SAME DISEASE

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Recent clinical experience and advances in molecular biology made this thesis a possibility although not universally acceptable. Stating it another way, such as CBD and PSP are similar and overlap clinically and pathologically would encounter much less opposition. Is this then just the matter of the extent of the overlap? I shall examine the clinical and the biological evidence and demonstrate the practical advantage of the thesis

Dementias and movement disorders are clinically and biologically overlapping manifestations of neurodegenerative disorders. Atypical Parkinsonism has been described since Charcot's time and the loose concept of Parkinson "plus" syndromes was applied liberally to cases with extension posture dystonia, absence of tremor and often dementia.. The extrapyramidal variety of Pick's disease (PiD) was also recognized in the 30-s and 40-s and subsequently as variety B with ballooned neurons, but this "Akelaitis" variety has been largely forgotten until recent descriptions of PSP and CBD.

In 1964 Steel, Richardson and Olszewski described Progressive Supranuclear Palsy with vertical gaze palsy as a prominent feature as a distinct clinicopathological syndrome. When corticodentatonigral degeneration was first described in 1968, Rebeiz et al. also considered it a new entity clinically characterized by unilateral rigidity; cortical sensory loss, apraxia and alien hand but recognized the resemblance of the pathological features to Pick's disease (PiD). The hallmark ballooned neurons were identical to Pick cells. After being neglected for 20 years, the disease was renamed corticobasal degeneration (CBD) and corticobasal ganglionic degeneration (CBGD). The extrapyramidal-apraxic syndrome, unresponsive to levodopa, was subsequently described mainly in movement disorder clinics. Diagnostic criteria for the movement disorder of CBGD required evidence of both cortical and basal ganglia involvement and initially dementia was exclusion. However, well-documented behavioral, cognitive, and language disturbances suggestive of frontal and temporal lobe involvement seem to be frequent features during the course of the disease. Parietal and frontotemporal cortical atrophy are recognized components of the entity. In some neuropathologically diagnosed CBD series, all patients developed cognitive deficits.

CBD is suffering from similar dichotomy as PiD in that the pathological and clinical descriptions do not fully match. There are some case reports describing patients presented clinically as CBD as defined by unilateral rigidity, apraxia and alien hand syndrome but have the pathological findings of PSP or PiD with Pick bodies. Other cases pathologically typical of CBD have FTD or PPA without the extrapyramidal features.⁴⁶ We suggested that clinical syndrome of prominent apraxia, unilateral extra-pyramidal syndrome and alien hand phenomenon should be designated as corticobasal degeneration syndrome (CBDS) and CBD should be used for the pathological picture. s. Primary progressive aphasia (PPA) is also a component of PiD/FTD and CBD. A great deal of clinical and pathological overlap is prompted us to suggest the use of "Pick Complex" to indicate their relationship.

Patients with axial dystonia, bradykinesia, falls, dysphagia, and vertical gaze palsy are considered typical of PSP, but the overlap with CBDS has been increasingly recognized. Many CBDS patients also have vertical gaze palsy extended posture and symmetrical extrapyramidal syndrome, dysarthria and dysphagia.

PSP patients often develop asymmetrical rigidity. Some studies comparing the neuropsychological features of PSP and CBD found no significant difference between them. The pathological features are also considered to be overlapping to a great extent. Glial changes, tufted astrocytes, globose neurofibrillary tangles are prominent in both and stain with the same histochemical markers and antibodies. Biochemical and genetic evidence also support the relationship. They have predominantly 64 and 69Kd bands on western blotting. They are both considered to be predominantly 4 repeat tauopathies. Certain tau mutations are common to both of them. They also have common tau haplotypes

There is continuing controversy to what extent PSP and CBD can be differentiated, but most experts in the field consider the extent of the overlap significant. PSP was, of course, one of the examples where subcortical dementia was described. The frontal features have been emphasized in the neuropsychological investigations leading to the terms striatofrontal dysfunction and frontosubcortical dementia. Although there are large advocacy groups for PSP as a distinct entity, the PSP groups have recently adopted CBD admitting that the differentiation can be difficult. The clinical, biochemical, pathological, and genetic overlap with CBD and CBDS is acknowledged by both movement disorder clinicians and neuropathologists.

We had eight cases that were considered to have overlapping clinical features of CBDS/PSP. Five of the eight had CBD pathology at autopsy. One of these was considered to have pathological features of both CBD and PSP. The other three had non-CBD pathology of Pick's disease (n = 1) and FTD with motor neurone disease type inclusions (MNDI, n = 2). . Among motor onset CBDS patients CBD pathology was confirmed in two cases at autopsy. A third case had pathology consistent with progressive supranuclear palsy (PSP) with some features of CBD and a fourth was considered typical of PSP. Pathology was available for 15 patients with cognitive onset CBDS and CBD pathology was confirmed in nine. Alternative pathologies were Pick's disease (n = 3), FTD with motor neuron disease type inclusions (MNDI, n = 1), Gerstmann-Straussler-Scheinker disease (n = 1) and Alzheimer's disease (n = 1).

New technologies provide discoveries leading to changing concepts and classifications. However, undue reliance on any single field, such as genetics or histochemistry to solve the nosological issues is fraught with hazards. As new technologies develop even "gold standards," such as pathology change. The same mutation can be associated with divergent clinical phenotypes. None of the current levels of description is able to provide all the questions, let alone the answers to neurodegenerative disease. Therefore, integration of all levels of description becomes crucial and the clinical approach remains as important as the others on which this has to be based.

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