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The spectrum of corticosbasal syndromes

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ABSTRACT

Cortical-basal degeneration (CBD) is a neurodegenerative disorder characterised by a combination of symptoms and signs of cognitive dysfunction, extrapyramidal features and myoclonus. CBD can only be diagnosed with certainty at autopsy as there are several mimics that can have a similar clinical phenotype. On the other hand, corticobasal syndrome (CBS), as the name suggests, is a syndromic diagnosis that can be made in the clinical setting and does not mandate a histopathological diagnosis. Several different pathologies can present with the clinical phenotype of CBS including CBD, progressive supranuclear palsy (PSP), Alzheimer's disease (AD) and frontotemporal lobar degeneration (FTLD). Although the clinical syndromes and neuroimaging features of typical cases of PSP, AD, FTLD and CBD are distinct; however, atypical cases are described that have overlapping clinical features. For example, patients with PSP may present with severe unilateral apraxia and supranuclear gaze palsy can occur in CBD. Pathological overlap also occurs and histopathologically "mixed" cases have been reported. The anatomical substrate of lesions in the nigrostriatal pathways and contralateral cerebral cortex, due to several diverse pathologies can cause the motor disturbances seen in CBS [1].

Contents

1. Introduction

Cortical-basal degeneration (CBD) is a clinicopathologic entity characterised clinically by features of cortical and basal ganglionic involvement such as cognitive problems, behavioural changes and extrapyramidal signs. The neuropathology of CBD is characterised by ballooned neurons that are frequent and a sine qua non for its diagnosis. The minimal pathological features required for the diagnosis of CBD are tau-positive neuronal and glial lesions, including astrocytic plaques and extensive thread pathology in both grey and white matter of the cerebral cortex and striatum along with focal neuronal loss in cortical regions and in the substantia nigra [2]. A definitive diagnosis can only be made at autopsy. Corticobasal syndrome (CBS), on the other hand, is a syndromic diagnosis that can be made in the clinic based on a constellation of cortical signs such as limb apraxia, cognitive impairment, higher sensory function deficits (2-point discrimination, graphesthesia and stereognosis) and signs of basal ganglionic involvement such as parkinsonism and dystonia. The neuropathological findings of CBD can be associated with several distinct clinical phenotypes (Fig. 1), and the clinical phenotype of CBS has been linked with a number of diverse brain pathologies from

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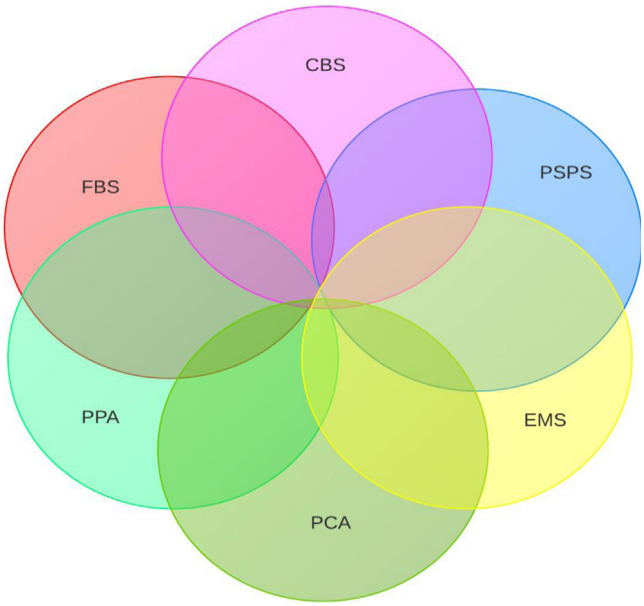

Fig. 1. Various clinical phenotypes of cortical-basal degeneration. CBS, Corticobasal syndrome; FBS, frontal behavioural syndrome; PSPS, progressive supranuclear palsy syndrome; PPA, non fluent variant of primary progressive aphasia; EMS, executive motor syndrome; PCA, posterior cortical atrophy syndrome.

Table 1
Differential diagnosis of a corticobasal syndrome.

Syndrome	Aetiologies
Corticobasal syndrome	Cortical basal degeneration (CBD) Alzheimer's dementia (AD) Progressive supranuclear palsy (PSP) Frontotemporal lobar degeneration (FTLD) Cerebrotendinousxanthomatosis (CTX) Multiple system atrophy (MSA)

progressive supranuclear palsy (PSP), Alzheimer's disease (AD) and frontotemporal lobar degeneration (FTLD) (Table 1) [3–5].

The positive predictive value for CBD in those with a clinical diagnosis of CBS was less than 25% in a clinic–pathologic study of 21 cases from the Queen Square brain bank for neurological disorders. In 6 of these 21 cases the neuropathologic diagnosis was PSP, 5 had AD and the remaining 5 had other non-tau pathologies [2].

2. Clinical phenotype

The classic textbook description of CBD is the initial presentation of a patient to the clinician with clumsiness and loss of dexterity of one hand due to a combination of frontoparietal involvement (apraxia) and basal ganglionic dysfunction (dystonia and rigidity). It is this combination of cortical involvement (cognitive deficits (executive dysfunction, behavioural changes and dementia), higher modality sensory loss (two point discrimination, astereognosis, graphesthesia) and apraxia) and basal ganglia affliction (asymmetric parkinsonism, dystonia and jerky tremor) that makes this disorder sit at the borderlands of cognitive neurology and movement disorders. The classic features described here were first recognised about 50 years ago by Rebeiz et al. who described three patients with progressive, clumsy, slow, awkward movements of one limb [6] and labelled the condition cortico–dentato–nigral degeneration with neuronal achromasia and swollen cortical cells based on their neuropathological findings. Other features may include mirror movements, poor response of the parkinsonian features to levodopa, delayed horizontal saccades (reflecting parietal lobe involvement), frontal release signs, pyramidal signs and alien limb phenomenon (Table 2).

Alien limb phenomenon (more commonly an alien hand) refers to involuntary motor activity of a limb, not just levitation, in conjunction with the feeling of estrangement from that limb. It has also been characterised as an apraxia. This clinical sign has an anatomic substrate i.e a contralateral lesion in a particular brain location (corpus callosum or medial frontal cortex) can cause it and the underlying pathology can be diverse (Table 3). Alien limb therefore could theoretically be found in any cause of a CBS and is neither a pathognomonic clinical sign of CBD nor present in all cases [7]. Further, the alien limb seen in CBS tends to be subtle, unlike the gross alien limb phenomena seen in the acute stroke setting.

The extrapyramidal features representing basal ganglionic involvement are also asymmetrical with one limb involved initially, that is held in a rigid dystonic posture [2]. The asymmetric motor features, therefore, represent lateralised cortical and basal ganglionic involvement, contralateral to the motor disturbances, which can be confirmed at autopsy studies [1]. However, contrary to common belief, very rarely, a symmetric presentation of CBD is possible and should not put the clinician off, from thinking about this condition when other diagnostic features point towards it [8].

Some CBD cases in the past had been diagnosed as Parkinson's disease (PD) and treated with levodopa. However, in contrast to PD, these cases have a poor levodopa response, short duration of disease (time from onset to death, average 5 years), early onset of falls and early wheelchair dependency. The hand tremor is coarse, jerky and more obvious on movement that is different from the characteristic pill-rolling resting tremor of PD [2]. The dystonic hand, limb apraxia and myoclonus in a CBD case also serve as red flags distinguishing it from typical PD. It is worth noting though, that limb dystonia considered to be one of the classical features of CBD is reported in up to 83% of cases in CBS but only 37.5% of pathologically confirmed cases of CBD [9].

The limb apraxia is usually asymmetrical, affecting one limb at onset, but there may be bilateral involvement later and patients can also show evidence of orobuccal or orofacial apraxia [2]. These deficits, by definition, should not be explained by any motor, sensory or proprioceptive deficit. Ideomotor apraxia is the most commonly described apraxia in CBD [3] and can be tested by commanding a patient to use a tool such as a screwdriver, for its

Table 2
Clinical features of cortical-basal degeneration.

Cognitive dysfunction	Extrapyramidal signs	Cortical signs	Other features
Executive problems	Tremor	Sensory loss	Alien limb
Behavioural changes	Rigidity	Apraxia	Mirror movements
Dementia	Bradykinesia	Myoclonus	Pyramidal signs
		Aphasia	Falls
			VSGP, AEO

VSGP, vertical supranuclear gaze palsy; AEO, apraxia of eyelid opening.