Chapter 10

Corticobasal Degeneration

History

In 1968, Rebeiz et al. reported corticobasal degeneration (CBD) as a clinicopathologically independent disease. Pathologically, CBD manifests strong asymmetric cerebral cortical atrophy in the frontoparietal lobe, together with degeneration in the basal ganglia and substantia nigra. Histologically, accumulation of abnormal phosphorylated tau is observed in neurons and glial cells. CBD is characterized by astrocytic plaque, and is classified as 4-repeat tauopathy (4RT), like progressive supranuclear palsy (PSP).

The typical clinical features of CBD are cerebral cortical signs including progressive and asymmetric apraxia, as well as extrapyramidal signs including muscle stiffness. Currently, these signs are referred to as corticobasal syndrome (CBS). Recently, CBD is used when the disease is pathologically diagnosed, and CBS is used when the disease is clinically diagnosed.

Diagnosis

In the diagnostic criteria of Armstrong et al. (2013), clinical symptoms of CBD were extracted from brain banks and published articles reporting at least 5 pathologically proven cases, and four clinical phenotypes associated with CBD pathology were proposed (CQ10-1). Furthermore, the four clinical phenotypes and other features were combined to create clinical research criteria for "probable sporadic CBD" that corresponds to pure CBD, and clinical criteria for "possible CBD" that includes tauopathy other than CBD (CQ10-1). However, subsequent validation study shows that the sensitivity of the new classification is not different from the conventional diagnostic criteria. Furthermore, the specificity is not high. Therefore, search for clinical diagnostic criteria with higher sensitivity and specificity or biomarkers will be a challenge for future research. The definitive diagnosis of CBD is pathological diagnosis.

CQ 10-1

What are the features of cognitive impairment in corticobasal degeneration (CBD), and what are the test methods?

Answer

In CBD, cognitive impairment often appears, and impaired executive function, behavioral and personality changes such as disinhibition, visuospatial disorder, and non-fluent aphasia are observed. A useful test for differentiating CBD from other diseases has not been established. D

Comments and evidence

1. Features of cognitive impairment in CBD

The clinical phenotypes of CBD proposed in the clinical diagnostic criteria of CBD by Armstrong et al. [1] in 2013 consist of the following: (1) corticobasal syndrome (CBS), (2) frontal behavioral-spatial syndrome (FBS), (3) non-fluent/agrammatic variant of primary progressive aphasia (naPPA), and (4) progressive supranuclear palsy syndrome (PSPS). Apart from these types, cases with a clinical picture resembling Alzheimer's disease dementia have also been reported. Among the clinical symptoms of pathologically confirmed CBD cases, general cognitive impairment is the most frequently seen cerebral cortical symptom, and is found in 52% of the patients at onset and in 70% during the course of disease [1]. Among the four CBD phenotypes, FBS manifests impaired executive function, behavioral/personality changes such as disinhibition, and visuospatial deficit. Moreover, naPPA manifests effortful, non-fluent speech, and apraxia of speech with distorted speech production and agrammatism. These symptoms appear before onset of dementia [1].

Lee et al. [2] studied 18 patients with histopathologically confirmed CBD, and found 4 clinical syndromes: progressive non-fluent aphasia (5 patients), behavioral variant frontotemporal dementia (5 patients), executive-motor (7 patients), and posterior cortical atrophy (1 patient). They reported that behavioral or cognitive problems were the initial symptoms in 15 of 18 patients.

2. Methods for assessing cognitive impairment in CBD

Scales used to assess cognitive impairment in CBD include Mini Mental State Examination (MMSE), Addenbrooke's Cognitive Examination (ACE) [3], Dementia Rating Scale (DRS), Frontal Assessment Battery (FAB) [4], and Neuropsychiatric Inventory (NPI). A meta-analysis examined whether several higher brain function tests were useful in differentiating parkinsonian disorders, but evaluation of these tests was difficult due to inadequate sample size [5].

■ References

1) Armstrong MJ, Litvan I, Lang AE, et al. Criteria for the diagnosis of corticobasal degeneration. Neurology. 2013; 80(5): 496-503.
2) Lee SE, Rabinovici GD, Mayo MC, Clinicopathological correlations in corticobasal degeneration. Ann Neurol. 2011; 70(2): 327-340.
3) Rittman T, Ghosh BC, McColgan P, et al. e Addenbrooke's Cognitive Examination for the differential diagnosis and longitudinal assessment of patients with parkinsonian disorders. J Neurol Neurosurg Psychiatry. 2013; 84(5): 544-551.
4) Marconi R, Antonini A, Barone P, et al. Frontal assessment battery scores and non-motor symptoms in parkinsonian disorders. Neurol Sci. 2012; 33(3): 585-593.
5) Lee W, Williams DR, Storey E. Cognitive testing in the diagnosis of parkinsonian disorders: a critical appraisal of the literature. Mov Disord. 2012; 27(10): 1243-1254.

■ Search formula

PubMed search: June 23, 2015 (Tuesday), July 7, 2015 (Tuesday), July 13, 2015 (Monday), August 12, 2015 (Monday)
#1 (("Dementia/diagnosis" [Mesh] OR (dementia [TI] AND (diagnosis [TI] OR diagnostic [TI])) OR "Cognition Disorders/diagnosis" [Mesh] OR ("cognition disorder*" [TI] AND (diagnosis [TI] OR diagnostic [TI]))) AND "corticobasal degeneration") OR ((corticobasal [TI] OR ("Basal Ganglia/pathology" [Mesh] AND "Cerebral Cortex/ pathology" [Mesh] AND "Neurodegenerative Diseases/pathology" [Mesh]) OR "Primary Progressive Nonfluent Aphasia" [Majr] OR "progressive nonfluent aphasia" [TI]) AND ("Cognition Disorders/etiology" [Majr] OR "Cognition" [Majr] OR cognition [TI] OR cognitive feature* OR behavioral feature* OR cognitive mechanism* OR "emotion processing" OR "Emotions" [Majr]))

Ichushi search: June 23, 2015 (Tuesday)
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CQ 10-2

Are there effective pharmacological and non-pharmacological therapies for cognitive impairment in corticobasal degeneration (CBD)?

Recommendation

No pharmacological and no non-pharmacological therapies have been confirmed to be effective for treating cognitive impairment in CBD. When Alzheimer's disease is considered to be the underlying pathology for CBS, cholinesterase inhibitor or N-methyl-D-aspartate (NMDA) receptor antagonist may be tried. Rehabilitation is recommended for language disorders, behavioral disorders, and visuospatial deficits. 2D

Comments and evidence

1. Pharmacotherapy for cognitive impairment

Regarding pharmacotherapy for cognitive impairment in CBD, no effective drugs with an adequate level of evidence have been reported. For CBS, cholinesterase inhibitors have been tried based on the personal opinions of experts [1, 2]. The effect of NMDA receptor antagonist is unknown.

2. Pharmacotherapy for behavioral and psychological disorders

There is little evidence of pharmacotherapy for behavioral and psychological symptoms in CBD. Sertraline hydrochloride, which is a selective serotonin reuptake inhibitor (SSRI) may be effective for depression [1]. Cholinesterase inhibitors are used for apathy and anxiety, but these symptoms are difficult to treat [1].

3. Non-pharmacological therapies

Although evidence of a certain level is lacking, physiotherapy, occupational therapy, and speech therapy may be effective for cognitive impairment in CBD [1, 2]. Cognitive behavioral therapy may be effective in some cases of depression in CBD, according to expert opinion [2].

■ References

1) Armstrong MJ. Diagnosis and treatment of corticobasal degeneration. Curr Treat Options Neurol. 2014; 16(3): 282.
2) Boeve BF, Josephs KA, Drubach DA. Current and future management of the corticobasal syndrome and corticobasal degeneration. Handb Clin Neurol 2008; 89: 533-548.

■ Search formula

Pharmacotherapy

PubMed search: June 23, 2015 (Tuesday), August 12, 2015 (Monday)

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Non-pharmacological therapies

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