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DND Dementia and Neurocognitive Disorder

Letter to the Editor

A Case of Combined Corticobasal Degeneration and Alzheimer's Disease Pathology: Clinical Presentation, and Diagnosis

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Dear Editor,

Corticobasal syndrome (CBS) is a movement disorder characterized by asymmetry.[1] Alzheimer's disease (AD) is a representative neurodegenerative disorder characterized by symmetric pathological accumulation in the brain.[2] With advancements in diagnostic techniques, these 2 diseases once considered to be entirely distinct have been reported to share pathological changes.[3] Various subtypes of CBS have been reported, including CBS-AD.[3] Although cases of AD pathology have been reported in patients clinically diagnosed with CBS, predicting this remains highly challenging.[4] A previous study has reported that when cognitive changes accompany symptoms of CBS, the possibility of AD co-pathology cannot be ruled out.[5] Here, we report a case of CBS-AD with right hemispheric involvement, a relatively rare form of CBS subtype, confirmed through neuroimaging studies.

A 66-year-old male patient visited our memory clinic with progressive cognitive impairment that began 3 years ago. The patient was a right-handed person who had received 12 years of education. The patient reported that he worked in an office job as a manager until 3 years ago when he retired due to cognitive decline and chronic headache. At the onset of symptoms, the patient experienced difficulties with visuo-spatial dysfunction rather than memory impairment. The patient particularly struggled with navigation, frequently taking wrong turns even when driving to familiar locations. Additionally, the patient frequently had trouble perceiving space while parking, often colliding with nearby objects. The patient did not have any difficulties with driving itself or following traffic regulations. No significant issues were reported with remembering daily events or keeping scheduled appointments. He did not report any olfactory disturbance or symptoms suggestive of REM sleep behavioral disorders. At the time, the patient underwent brain imaging and cognitive function test at another hospital, which revealed mild cognitive impairment (MCI) and an atrophic change in the right fronto-temporal area. However, the patient did not receive any specific management thereafter. During the period when the patient did not receive any treatment, his symptoms gradually worsened. About 4 months ago, the patient began to experience memory decline and difficulty recalling names of close acquaintances. Approximately 2 months ago, the caregivers noticed that the patient began exhibiting prominent memory symptoms such as repeating the same phrases and difficulty recalling unwritten information.

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Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Chae SY, Kim JS; Data curation: Chae SY, Kim JS; Formal analysis: Chae SY, Kim JS; Software: Kim HJ; Supervision: Kim HJ; Validation: Kim HJ; Writing - original draft: Baek S, Kim HJ; Writing - review & editing: Kim HJ.

In the neurological examination conducted at the clinic, limb kinetic apraxia, ideomotor apraxia, and higher cortical sensory dysfunction were observed in the left extremity. Akinetic-rigidity and myoclonus were not observed in any extremities. Buccofacial apraxia was not observed. However, hemispatial neglect of the left side of the body along with simultanagnosia was suspected. Ocular movements were intact in all directions without any limitation. Neither optic apraxia nor optic ataxia was observed. Tremor (both resting and action), bradykinesia, and unsteadiness including falling were not observed. Deep tendon reflex was normoactive without any signs of lateralization. No familial history of movement disorder or dementia was identified in the patient. Based on these findings, further evaluations were conducted with a diagnosis of CBS.

Blood test revealed a hemoglobin A1c level of 6.2%, indicating prediabetes. The ApoE genotype was confirmed as ε3/ε3. In the Korean version of the Mini-Mental State Examination, his score was 22. In the Seoul Neuropsychological Screening Battery (SNSB), marked deterioration in visuospatial ability, frontal/executive dysfunction, and visual memory impairment were observed. Specifically, on the Rey Complex Figure Test, the patient's copy performance score had decreased to 16 points (<0.01 percentile). In verbal memory tasks, the encoding performance was impaired, while retention and recognition abilities remained within the lower range of normalcy (**Fig. 1E**). In visual memory tasks, retrieval

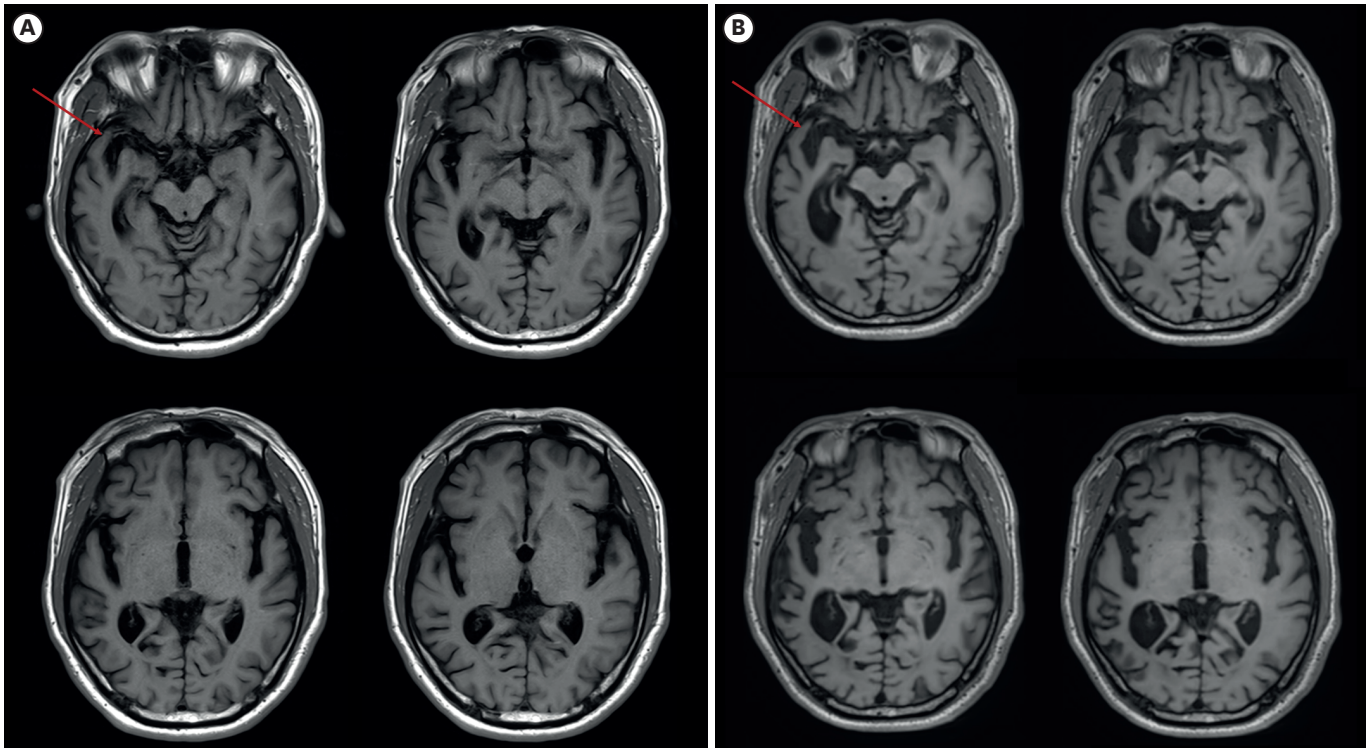

Fig. 1. (A, B) Brain MRI of the patient. Compared to the previous study (A), transaxial MRI after 3 years show atrophic changes in right frontal and temporal cortices around the sylvian fissure (red arrow, B). (C) Transaxial amyloid PET images show asymmetrical amyloid deposition patterns. A greater amyloid deposition is observed in the left frontal cortex (dashed arrows). (D) Transaxial ^{18}F-fluorodeoxyglucose PET images exhibit a decrease in metabolism in the right fronto-parieto-temporal occipital lobe, right caudate nucleus, right basal ganglia, left parietal, and bilateral posterior cingulate gyrus (more severe in the right side). (E) Results of SNSB performed at the patient's initial visit. (F) Results of SNSB performed at 1-year follow-up.
MRI: magnetic resonance imaging, PET: positron emission tomography, SNSB: Seoul Neuropsychological Screening Battery, DST:F: Digit Span Test in the Forward Condition, K-BNT: Korean Version of Boston Naming Test, RCFT:Copy: Rey Complex Figure Test: Copy, SVLT:DR: Seoul Verbal Learning Test: Delayed Recall, RCFT:DR: Rey Complex Figure Test: Delayed Recall, DSC: Digit Symbol Coding, COWAT: Controlled Oral Word Association Test, K-TMT-E:B: Korean Trail Making Test for the Elderly: B, K-CWST:CR: Korean-Color Word Stroop Test: Color Reading.
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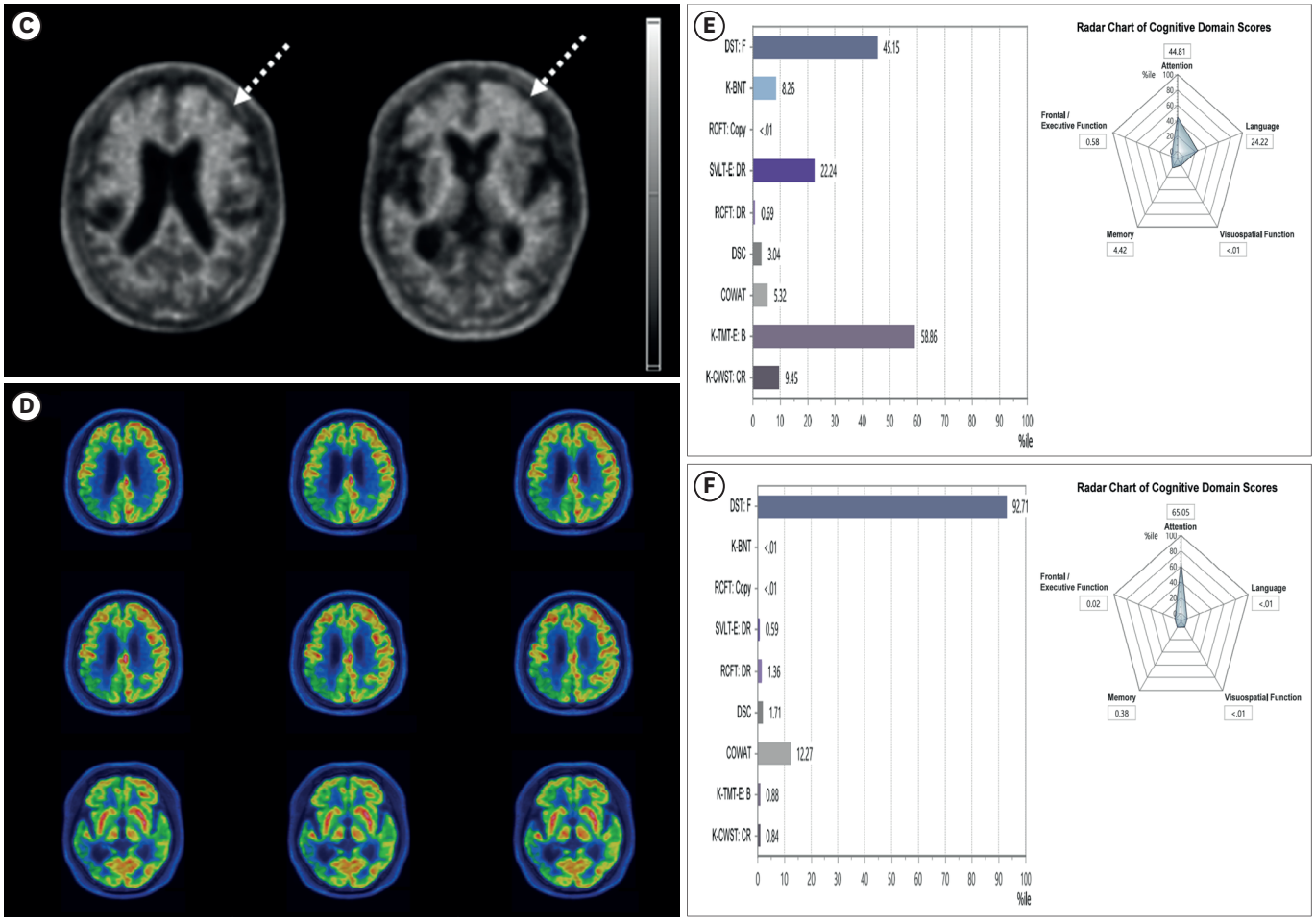

Fig. 1. (Continued) (A, B) Brain MRI of the patient. Compared to the previous study (A), transaxial MRI after 3 years show atrophic changes in right frontal and temporal cortices around the sylvian fissure (red arrow, B). (C) Transaxial amyloid PET images show asymmetrical amyloid deposition patterns. A greater amyloid deposition is observed in the left frontal cortex (dashed arrows). (D) Transaxial ^{18}F-fluorodeoxyglucose PET images exhibit a decrease in metabolism in the right fronto-parieto-temporal occipital lobe, right caudate nucleus, right basal ganglia, left parietal, and bilateral posterior cingulate gyrus (more severe in the right side). (E) Results of SNSB performed at the patient's initial visit. (F) Results of SNSB performed at 1-year follow-up.
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deficit was observed. The score of the global deterioration scale was 3. His score for Korean-Instrumental activities of daily living was 0.22. For a definitive diagnosis, brain magnetic resonance imaging, ^{18}F-florbetaben amyloid positron emission tomography (amyloid PET), and ^{18}F-fluorodeoxyglucose PET (FDG PET) study were conducted. First, compared to the prior study conducted 3 years ago (**Fig. 1A**), more atrophic changes were observed in right frontal and temporal cortices around the sylvian fissure (**Fig. 1B**). Second, the amyloid PET revealed positive amyloid deposits with a global standardized uptake value ratio (SUVR) of 1.46 (centiloid scale 39.4, Neurophet Scale PET) (**Fig. 1C**, **Supplementary Table 1**). The pattern of amyloid deposition appeared asymmetrical, with a greater amount of amyloid deposition observed on the left side (left side SUVR 1.51, right side SUVR 1.41). The greatest amount of amyloid deposition was observed in the left frontal cortex (SUVR 1.77). Third, the FDG PET scan observed a decrease in metabolism across the entirety of the right hemisphere including the supplementary motor area and the posterior cingulate cortex (**Fig. 1D**). At the time of diagnosis, the patient was initiated a treatment with memantine 10 mg/day. After 3 months

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of follow-up period, the patient continued to report progressive memory decline. Thus, rivastigmine 3.0 mg/day was added to the treatment regimen. A follow-up SNSB assessment was performed 12 months after the initial diagnosis. Cognitive decline was observed in all domains except attention, with a particularly pronounced decline in verbal retention function (**Fig. 1F**). Results indicated progression from MCI to dementia.

This case was a relatively young patient who presented with prominent visuospatial dysfunction and progressive memory impairment. It was significant in 3 aspects. First, amyloid PET confirmed amyloid pathology even in CBS, a rare neurodegenerative disorder. Second, it was intriguing that cognitive changes and characteristics of both right hemispheric CBS (rhCBS) and AD were observed. Third, despite asymmetric patterns of amyloid deposition, patterns of cognitive decline were notable characterized by worsening retention, which was an interesting finding. In this case, it was presumed that due to the patient being right-handed, motor symptoms associated with rhCBS were not prominently manifested. According to previous studies, while motor symptoms could also manifest in rhCBS, it had been reported that significant visuospatial dysfunction could be prominently evident,[6] as observed in our case. Considering these findings, the cognitive decline observed in our patient is more likely attributable to CBS rather than amyloid pathology in early stages of symptoms such as visuospatial dusfunction.[7] While the global SUVR suggests amyloid positivity, the deposition pattern of amyloid appears asymmetric and focal rather than diffuse. Nevertheless, patterns of cognitive decline in this case implied a mixed form with AD, suggesting that AD pathogenesis might be involved. There is an ongoing debate regarding the certainty of using this focal amyloid deposition pattern for confirming AD continuum.[2,8] However, given the patient's ongoing complaints of memory decline and observed changes in memory domain of cognitive function test, consideration for progression to AD might be warranted. Finally, the lack of autopsy results, which limits the ability to establish a precise pathological diagnosis, could be considered a limitation.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

Quantitative amyloid deposition (standardized uptake value ratio)

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