Dementia and Neurocognitive Disorders
2004; 3: 55-9

콜린에스터라제 억제제에 반응을 보인 후방피질위축증

김은희 · 이연수 · 이종걸 · 한설희*

충북대학교 의과대학 신경과학교실*
충북대학교 의학연구소

A Case with Cholinesterase Inhibitor Responsive Asymmetric Posterior Cortical Atrophy

Yunhui Kim, M.D., Yeonsu Lee, M.D., Jongkeol Lee, M.D., Seol-Heui Han, M.D.*

Department of Neurology*, Chungbuk National University Hospital and Chungbuk National University Medical Research Center, Cheongju, Korea

A 55-year-old right-handed woman presented initially with mild amnestic and depressive episodes but developed slowly progressive neurobehavioral symptoms indicative of posterior cortical atrophy in ensuing years. A more detailed neurobehavioral test suggested predominant right temporo-parietal dysfunction with executive functional deficits. SPECT and MRI findings revealed right unilateral temporo-parietal involvement. Cholinesterase inhibitor administration for 14 months led to amelioration of cognitive dysfunction on follow-up neuropsychologic evaluation. We suggest that cases of posterior cortical atrophy or visual variant of Alzheimer's disease may be responsive to cholinesterase inhibitor therapy.

Key Words: *Asymmetric posterior cortical atrophy, Visuoconstructional disability, Cholinesterase inhibitor*

Address for correspondence

Seol-Heui Han, M.D.
Department of Neurology, Chungbuk National University Hospital, 62 Gaeshin-dong, Heungduk-gu, Cheongju 361-763, Korea
Tel: +82-43-269-6372
Fax: +82-43-276-8929
E-mail : shhancb@chungbuk.ac.kr

Neurodegenerative disorders progressively destroy the nervous system, resulting in impairments of neuronal function and intercellular communication. The clinical presentation of the disease is determined by the topographic distribution of the responsible neurodegenerative process. Neurodegenerative disorders can present with a remarkably focal clinical presentation related to neuropathological burden, and the term "asymmetric cortical degeneration syndromes"(ASCD) has been used to describe these presentations[1-3]. Many patients with Alzheimer's disease (AD) have visuospatial impairment relatively early in the course of the illness with prominent deficits in judging spatial relations[4] and in visuoconstuctive abilities[5]. Benson coined the term posterior cortical atrophy (PCA) to describe five patients with slowly progressive dementia presenting with visuoconstructive apraxia[6]. Subsequent cases with prominent visuospatial deficits were associated with cerebral gluscose hypometabolism[7] and neuropathological changes[8] of the posterior cortical regions. The neuropathological basis for the marked predominant dysfunction of the posterior parieto-occipital cortex usually is attributed to AD, however non-AD conditions, such as subcortical gliosis, corticobasal degeneration, Pick's disease, dementia with Lewy bodies and Creutzfeldt-Jakob disease, also have been reported[9-11].

We describe a case of progressive early-onset dementia initially presenting with depression and lack of spontaneity who subsequently developed severe visuoconstructive disability, visual agnosia, executive dysfunction and dressing apraxia. This constellation of signs and symptoms was strongly suggestive of right parietal involvement and was supported by functional and structural neuroimaging. Moreover, the patient's cognitive and neurobehavioral impairments were remarkably improved six months after treatment with cholinesterase inhibitor.

CASE PRESENTATION

A 55 year-old, right-handed, high school-educated woman noticed forgetfulness at the age of 54. She became tearful, anxious, and less sociable. Her husband took her to psychiatry clinic, where she was diagnosed with depression and treated with a selective serotonin reuptake inhibitor (SSRI). Her depressive symptom was improved with SSRI medication. Her husband reported she experienced problems in cooking

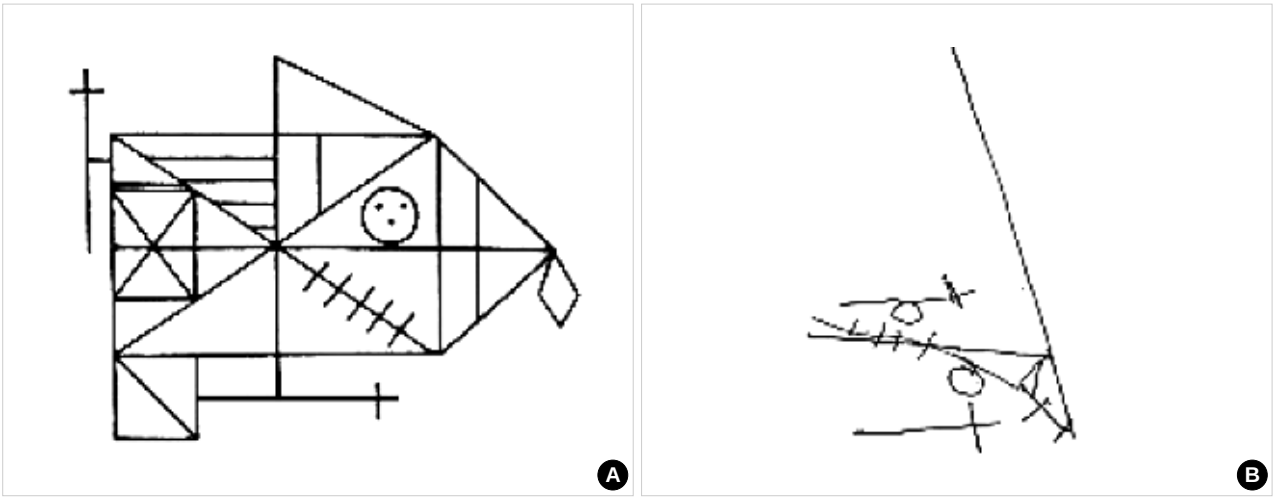

Fig. 1. Copy of (A) the Rey-Osterreith Complex Figure by the patient (B) Overall shape and gestalt are lacking.

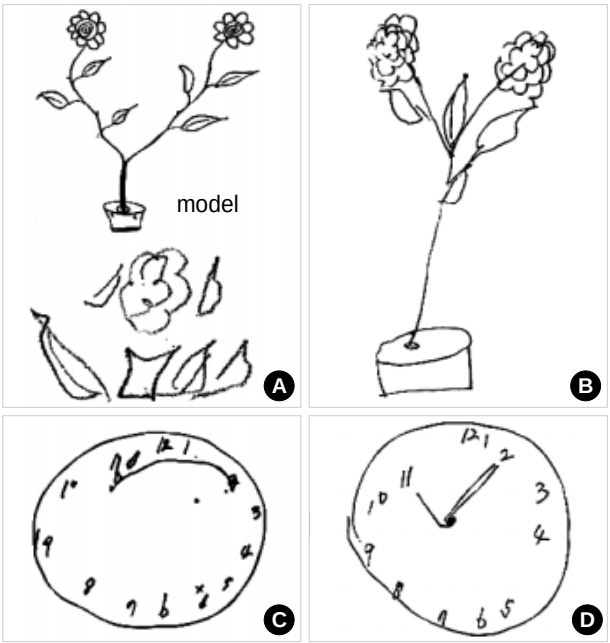

Fig. 2. Copying of double daisy and drawing the face of clock. Initial (A, C) and 6 months later (B, D). Note the improvements both in double daisy copying and clock face drawing.

and dressing herself. She had difficulty with numbers, was unable to use the automatic teller machine. She had trouble finding her way home from a nearby supermarket.

She was seen at memory disorder clinic three months after first behavioral problems noted. General physical examination was normal. On neurologic examination, no motor or primary sensory deficits were present but combined sensations such as stereognosis and graphesthesia were mildly disturbed in the left hand. The deep tendon reflexes were generally brisk with flexor plantar responses. Cerebellar signs were absent. Gait, stance and posture were normal. During neurobehavioral testing, she was apprehensive and lacked confidence in her test-taking. The head turning sign was positive.

Neuropsychologic assessment (Seoul Neuropsychological Screening Battery, SNSB) indicated poor memory (K-MMSE, 20/30), spatiotemporal disorientation, marked ideomotor and constructional apraxia, severe impairment of the abstraction capacity, associative thinking and language, especially in naming (K-BNT, less than 1 percentile). Visuospatial and constructive abilities assessed by copying of Rey-Osterreith Complex Figure (Fig. 1), Clock Drawing Test (Fig. 2) and imitation of finger configuration were severely impaired. She could not imitate examiner's meaningless (non-symbolic) finger postures, although she was aware of her mistakes but was unable to correct them. She could read and write normally. She performed poorly on executive tasks; Stroop test, contrasting paradigm and go-no-go test. Other neurobehavioral abnormalities included a left homonymous hemianopia, left-sided partial neglect, tactile extinction, simultagnosia, poor attention and concentration, dyscalculia, and dressing apraxia. She dressed herself most of the time but slowly and often improperly. For instance, she became confused and unable to dress when one sleeve was turned inside-out. Alien limb phenomenon was not present. Magnetic resonance imaging (MRI) of the brain showed generalized mild brain atrophy with suspicious right posterior preponderance (Fig. 3M). 99m-Tc SPECT revealed profound perfusion defects in right temporal and temporo-parietal regions with decreased perfusion in right frontal area (Fig. 3A, B). Electroencephalogram (EEG) showed no remarkable

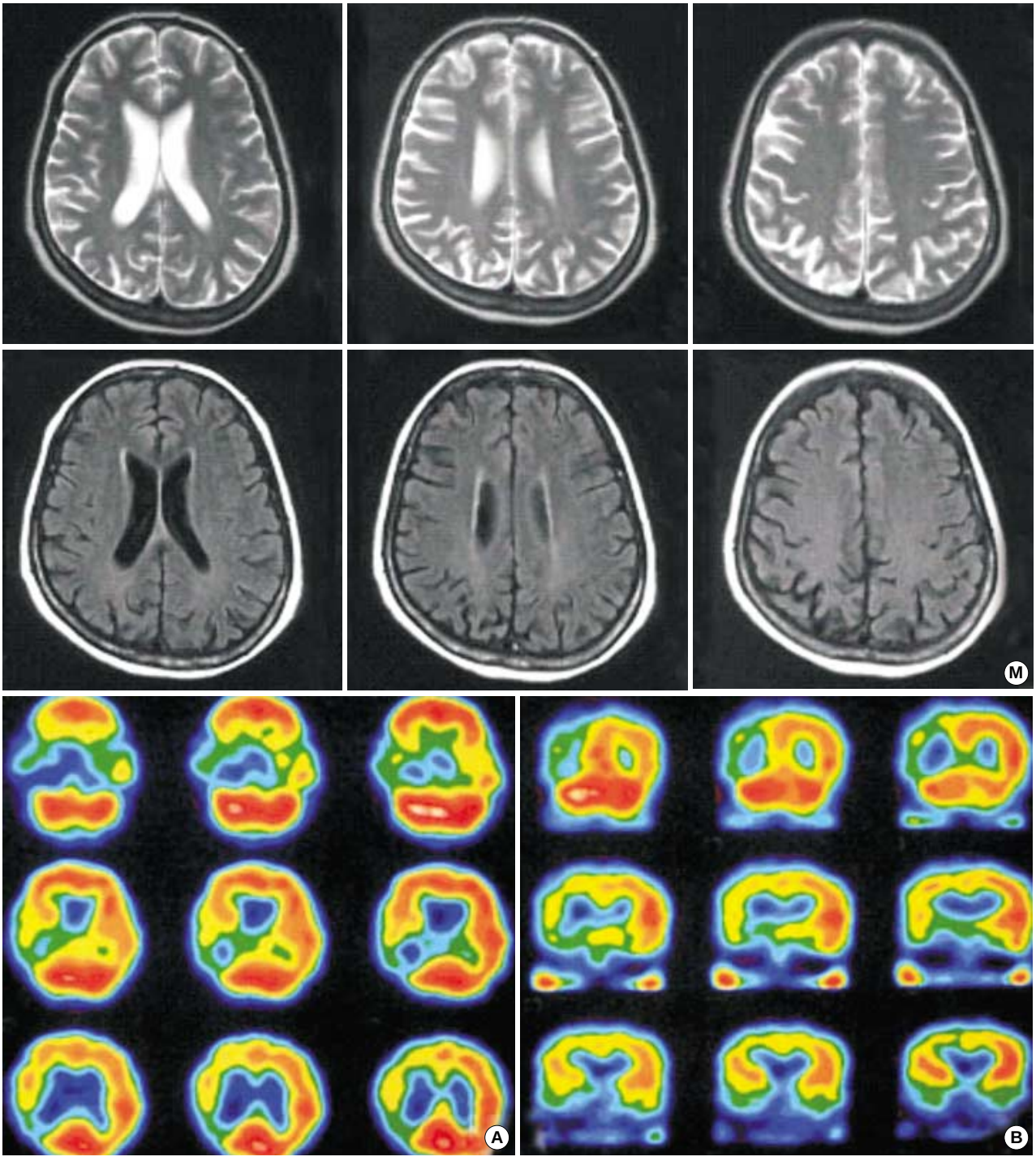

Fig. 3. (M) MRI of the brain showed generalized mild brain atrophy with suspicious right posterior preponderance. No evidence of vascular or mass lesion is noted. Upper panel, T2-weighted axial images; Lower panel, FLAIR axial images (M). (A, B) 99m-Tc SPECT revealed profound perfusion defects in right temporal, and temporoparietal regions. A. axial; B. coronal view.

findings. All routine blood work was normal. She started on a cholinesterase inhibitor drug, galantamine and maintained at 12 mg/day. She showed moderate improvements in visuoconstructive function assessed by the clock drawing test, double daisy copying (Fig. 2) and simultagnosia and attention six months after initiation of the cholinesterase inhibitor. Dressing apraxia and frontal executive function remained unchanged. MMSE score done 14 months after initial evaluation re-

mained stable at 21 (initial score, 20).

DISCUSSION

Patients with PCA are easily recognized when the full blown clinical characteristics are present due to bilateral posterior cortical dysfunction i.e., early onset of visual agnosia progressing to Balint's syndrome, environmental agnosia, alexia, Gerstmann's syndrome, and transcortical sensory aphasia. Predominant unilateral posterior cortical dysfunction unrelated to other etiologies (e.g., stroke, tumor or other structural lesion) should be considered an early stage of PCA when the patient presents with focal symptoms referable to parieto-occipital regions. For example, our case study presented initially with mild memory complaints and depressive symptoms, she progressively developed executive dysfunction and right parietal lobe syndrome. The patient's poor performance on the Rey-Osterreith Complex copying was characteristic of right parietotemporal injury (Fig. 1).

The right hemisphere mediates visuospatial perception and interpretation of gestalt figures, while the left hemisphere is concerned with detail, graphic formulas, and executive motor functions of praxis[12]. Visual symptoms in such patients are broadly divisible into dorsal and ventral visual syndromes that result from dysfunction in occipito-parietal and occipito-temporal visual association cortices, respectively. The dorsal visual syndrome includes simultagnosia and Balint's syndrome. The ventral visual syndrome includes alexia and visual agnosia (prosopagnosia). Less often, hemineglect or visual field defects result[13]. Our patient showed simultagnosia as evidenced by overlapping figure test, however she did not demonstrate optic ataxia or gaze apraxia. The patient revealed left homonymous hemianopia on perimetric examination (Fig. 3). She could not imitate finger configuration offered by the examiner although she recognized her mistakes in imitating finger posture. Imitation of finger figures probably entails a combination of limb apraxia, optic praxis, visuospatial, and visuoconstructional skills[14]. Goldenberg proposes that the left hemisphere contributes mainly to body-part coding and the right hemisphere to perceptual analysis of hand and finger postures[15]. Attig reported a case with progressive disturbances initially localized in the right parieto-occipital region followed by posterior bilobar degeneration (pronounced on the right side) without dementia until late in the course[16]. A case with left unilateral parieto-occipital degeneration demonstrated by SPECT and MRI also has been reported[17].

Although the functional imaging study (SPECT) and visual field examination in our case suggest focal dysfunction of right parieto-occipital lesion, bilateral dysfunction was also demonstrated on neuropsychological testing. Thus, the case with right hemispheric predominance appears to represent an early clinical manifestation of posterior cortical atrophy. With progression of the underlying neurodegenerative diseases, wider extension of involved cerebral cortex and other brain regions eventually occurs. Although most of the reported cases demonstrated lack of clinical improvement on cholinesterase inhibitors, our case showed improvement in aspects of neurocognitive function. Non-pharmacological intervention such as behavioral rehabilitation reduce the errors in functional tasks by 50% in patients with PCA[18]. Patients presenting with atypical neurocognitive symptoms presumed to be degenerative origin may benefit from empirical treatment with best potential therapeutic measures. Although the definite nosological entity of our patient cannot be made without neuropathological investigation, modest improvement with cholinesterase inhibitor favors the diagnosis of a visual variant of AD. Further clinical study and neuropathological pursuit of atypical cases may contribute to our current understanding of these unusual syndromes.

ACKNOWLEDGEMENTS

We would like to thank Professor John C. Morris, Washington University School of Medicine, St. Louis, MO, USA for invaluable comments and critical reading for the manuscript. This report was supported by 2003 Chungbuk National University Hospital Clinical Research Fund.

REFERENCES

1. Caselli RJ. *Focal and asymmetric cortical degenerative syndromes. Focal and asymmetric cortical degenerative syndromes. Adv Neurol 2000; 82: 35-51.*
2. Caselli RJ. *Asymmetric cortical degeneration syndromes. Curr Opin Neurol 1996; 9: 276-80.*
3. Caselli RJ, Jack CR Jr. *Asymmetric cortical degeneration syndromes. A proposed clinical classification. Arch Neurol 1992; 49: 770-80.*
4. Cogan DG. *Visual disturbances with focal progressive dementing disease. Am J Ophthalmol 1985; 100: 68-72.*

5. Henderson VW, Mack W, Williams BW. *Spatial disorientation in Alzheimer's disease. Arch Neurol 1989; 46: 391-4.*
6. Benson DF, Davis RJ, Snyder BD. *Posterior cortical atrophy. Arch Neurol 1988; 45: 789-93.*
7. Pietrini P, Furey ML, Graff-Radford N, Freo U, Alexander GE, Grady CL, *et al. Preferential metabolic involvement of visual cortical areas in a subtype of Alzheimer's disease: clinical implications. Am J Psychiatry 1996; 153: 1261-8.*
8. Hof PR, Bouras C, Constantinidis J, Morrison JH. *Balint's syndrome in Alzheimer's disease: specific disruption of the occipito-parietal visual pathway. Brain Res 1989; 493: 368-75.*
9. Victoroff J, Ross GW, Benson DF, Verity MA, Vinters HV. Posterior cortical atrophy. *Neuropathologic correlations. Arch Neurol 1994; 51: 269-74.*
10. Zakzanis KK, Boulos MI. *Posterior cortical atrophy. Neurologist 2001; 7: 341-9.*
11. Renner JA, Hou CE, Burns JM, McKeel DW, Storandt M, Morris JC. *submitted*
12. Devinsky O, D'Esposito. *The right hemisphere, interhemispheric communication and consciousness. In; Neurology of cognitive and behavioral disorders. Oxford University Press, Inc., New York, New York, 2004; 68-102.*
13. Caselli RJ. *Visual syndromes as the presenting feature of degenerative brain disease. Semin Neurol 2000; 20: 139-44.*
14. Moo LR, Slotnick SD, Tesoro MA, Zee DS, Hart J. *Interlocking finger test: a bedside screen for parietal lobe dysfunction. J Neurol Neurosurg Psychiatry 2003; 74: 530-2.*
15. Goldenberg G. *Imitation and matching of hand and finger postures. Neuroimage 2001; 14: S132-6.*
16. Attig E, Jacquy J, Uytdenhoef P, Roland H. *Progressive focal degenerative disease of the posterior associative cortex. Can J Neurol Sci 1993; 20: 154-7.*
17. Mizuno M, Sartori G, Liccione D, Battelli L, Campo R. *Progressive visual agnosia with posterior cortical atrophy. Clin Neurol Neurosurg 1996; 98: 176-8.*
18. Perez FM, Tunkel RS, Lachmann EA, Nagler W. *Balint's syndrome arising from bilateral posterior cortical atrophy or infarction: rehabilitation strategies and their limitation. Disability Rhabili 1996; 18: 300-4.*