

Progressive “Vascular” Corticobasal Syndrome Due to Bilateral Ischemic Hemispheric Lesions

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Abstract

We report a patient that presented with the corticobasal syndrome (CBS), including progressive dementia, asymmetric parkinsonism associated with constructional and ideomotor apraxia, action myoclonus and focal hand dystonia. Magnetic resonance imaging of the brain revealed extensive ischemic lesions in both frontotemporo-parieto-occipital lobes and steno-occlusion of the middle cerebral arteries, bilaterally. This case illustrates that extensive cortical vascular-ischemic lesions may present with symptoms mimicking the corticobasal syndrome.

Key words: corticobasal syndrome, vascular, ischemic

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Introduction

Previous reports on corticobasal degeneration (CBD) have suggested that this disorder is a distinct clinical/pathological entity. However, more recently, considerable heterogeneity between the classic clinical presentation of the corticobasal syndrome (CBS) and the pathological entity CBD has been reported (1). It is well known that CBD pathology may be associated with a variety of clinical presentations including: frontotemporal dementia, speech apraxia, progressive non-fluent aphasia, a progressive supranuclear palsy (PSP)-like syndrome, and a posterior cortical atrophy syndrome.

However, not all patients presenting with classical CBS have CBD as the underlying pathology (1-3). In addition, CBS associated with vascular lesions has been very rarely reported (4). Here, we describe a patient who presented with CBS associated with extensive vascular lesions of the frontotemporo-parieto-occipital lobes bilaterally.

Case Report

A 75-year-old, college-educated, right handed woman was admitted to our hospital with rapid progressive memory impairment and a tendency to fall to the left. The patient had

been well until about two months earlier, when she began to have vague problems with memory. Two weeks before admission, a rapid progression of the cognitive deficits was marked by diurnal fluctuation, with intermittent misidentification of people and disorientation to time and place. Over a period of weeks, the patient began to miss steps and thereafter experienced a tendency to fall to the left during walking, with a loss of coordination. One week before admission, ataxic gait, left hand dystonia and generalized myoclonus developed. The patient had been taking antihypertensive medication, aspirin and a selective serotonin reuptake inhibitor to treat a 4-year history of hypertension, angina pectoris and bipolar disease. There was no family history of parkinsonism or any neurological disorders.

On admission, the patient was alert, but confused and disoriented, with a blood pressure of 120/90 mmHg, a regular heart beat of 82 beats/min, and a temperature of 36.8°C. The physical examination demonstrated no abnormal findings. The evaluation of cognitive function using the Korean mini-mental status examination, showed disorientation to time, immediate and recall impairment, inattention, and visuospatial dysfunction. In addition, the patient showed dressing and ideomotor apraxia. The cranial nerve examinations were normal. The patient had mild left side weakness and bilateral limb ataxia. Spontaneous movements of the arms and

legs were accompanied by myoclonus. No resting tremors were identified. There was a left hand action dystonia, which consisted of flexion of the fingers and wrist. The deep-tendon reflexes in all extremities were symmetric and normoactive and both plantar responses were flexor.

A neuropsychological evaluation showed severe impairment of global cognitive functions. The Korean Mini-Mental State Examination score was 20. On the 12-word list test, from the Hopkins Verbal Learning Test for verbal memory, the numbers for immediate recall were four in the first, three in the second and four in the third trial; the results after a 20-minute delayed recall were three. The results of the Digit Span Test for attention and immediate memory were forward four and backward three. The score for the Korean version of the Boston Naming Test (K-BNT) for language was 37, and the scores for the Word Fluency test (animal, grocery items and three Korean letters) were 3, 5, 1, 1, and 1, respectively. The Go-No-Go, fist-edge-palm, alternating hand movement, alternating square-triangle tasks and the Luria Loop Test for frontal lobe function were abnormal.

Laboratory testing included a complete blood count, blood chemistry, thyroid function testing, prothrombin and partial thromboplastin time, antithrombin III-protein C and protein S activity, venereal disease research laboratory testing, vasculitis markers, HIV antibodies, vitamin B12, pyruvate, lactate and folate levels; all were within normal limits. A spinal tap was performed; the cerebro-spinal fluid had a normal opening pressure with a leukocyte count of 0/mm³, a protein level of 44.4 mg/dL and a glucose level of 62 mg/dL. The Western blot test for the 14-3-3 protein, in the cerebrospinal fluid, was negative. Magnetic resonance imaging (MRI) of the brain showed diffuse cortical high signal intensities with intravascular enhancement at the frontal, parietal, occipital and temporal lobes, bilaterally, but predominantly in the right hemisphere. On the diffusion-weighted images, the lesions had high signal intensity with low signal intensity on the ADC map (Fig. 1). MR angiography of the brain revealed steno-occlusions of the right distal internal carotid artery (ICA) and middle cerebral artery (MCA) and severe stenosis of the left MCA. An electroencephalographic (EEG) examination showed generalized theta activity at a frequency of 5-8 Hz bilaterally, but no periodic epileptiform discharge was observed. The patient was diagnosed as both ICA infarction, and 100 mg aspirin was prescribed.

Over the subsequent two weeks, the general cognitive functions, the generalized myoclonus and focal hand dystonia improved spontaneously. The patient was discharged for conservative care at home.

One month after discharge, the patient presented to the emergency room with a generalized seizure and unresponsiveness. Akinetic mutism, lethargy and withdrawal were observed. No other lateralizing signs were not observed. The follow-up imaging showed some aggravation of the high signal intensities at the frontal and temporal regions. The EEG demonstrated patterns of periodic lateralized epileptiform discharges (PLEDS) in both hemispheres. The patient

was treated with 1,000 mg sodium valproate in addition to 100 mg aspirin, and did not have additional seizures during the following three months. The cognitive and motor functions gradually resolved over six months.

Discussion

We treated a patient with bilateral ischemic hemispheric lesions presenting with the clinical features consistent with CBS, including progressive cognitive decline, action myoclonus, dystonia, gait disturbance, and limb apraxia.

As in the present case, a T2-weighted MRI generally shows high signal areas selectively at the fronto-parietal lobes. However, the lesion locations in our patient were unusual in comparison with typical ischemic infarct seen in large vessel disease. These lesions likely represent cytotoxic edema, reflecting a diffuse ischemic change due to vasospasm. In addition, lesions were involved which have severe steno-occlusions. Accordingly, the lesions in brain MRI were thought to be typical of progressive ischemia due to large vessel steno-occlusion, although mechanism is unclear.

Classically, CBD presenting with CBS usually begins during the sixth, seventh or eighth decade of life with the initial symptoms affecting either one arm or, less frequently, a leg. The symptoms include varying combinations of stiffness, clumsiness, jerking, or sensory impairment, mild to severe limb rigidity, bradykinesia and apraxia, often with or without significant dysphasia or dementia (5). A pathology series of patients with the clinical presentation of classical CBS demonstrated a wide variety of different pathologies: CBD accounts for more than 55% of the cases, other tau pathologies including PSP and Pick's disease are seen in 28%, and the remaining cases include a wide variety of non-tau related pathologies (3). However, the large number of different pathologies associated with CBS makes ante mortem prediction of the pathology extremely difficult.

Therefore, clinical information such as a positive family history and the course of disease can help with the determination of the etiology of the disease (e.g., a very short course may indicate Creutzfeldt-Jakob disease, and less than 3 years of disease duration can differentiate neurofilament inclusion body disease) (3). Neuroimaging studies are unable to differentiate cases of CBS with CBD pathology from those without this pathology (6). Similar patterns of regional atrophy and subcortical and periventricular white matter signal changes have been seen in patients with CBS with or without underlying CBD pathology (7). However, reports of vascular lesions, such as a large artery stroke or multiple cerebral infarctions presenting as CBS, are extremely rare. Several cases associated with multi-infarct pathology have been reported to masquerade as CBS, and alter the clinical diagnosis of the disease (4).

In the present patient, the wide-spread cortical-subcortical panhemispheric involvement bilaterally was thought to be due to a wide range of possible causes; because the etiology remains unclear and the lesion location was uncommon. The

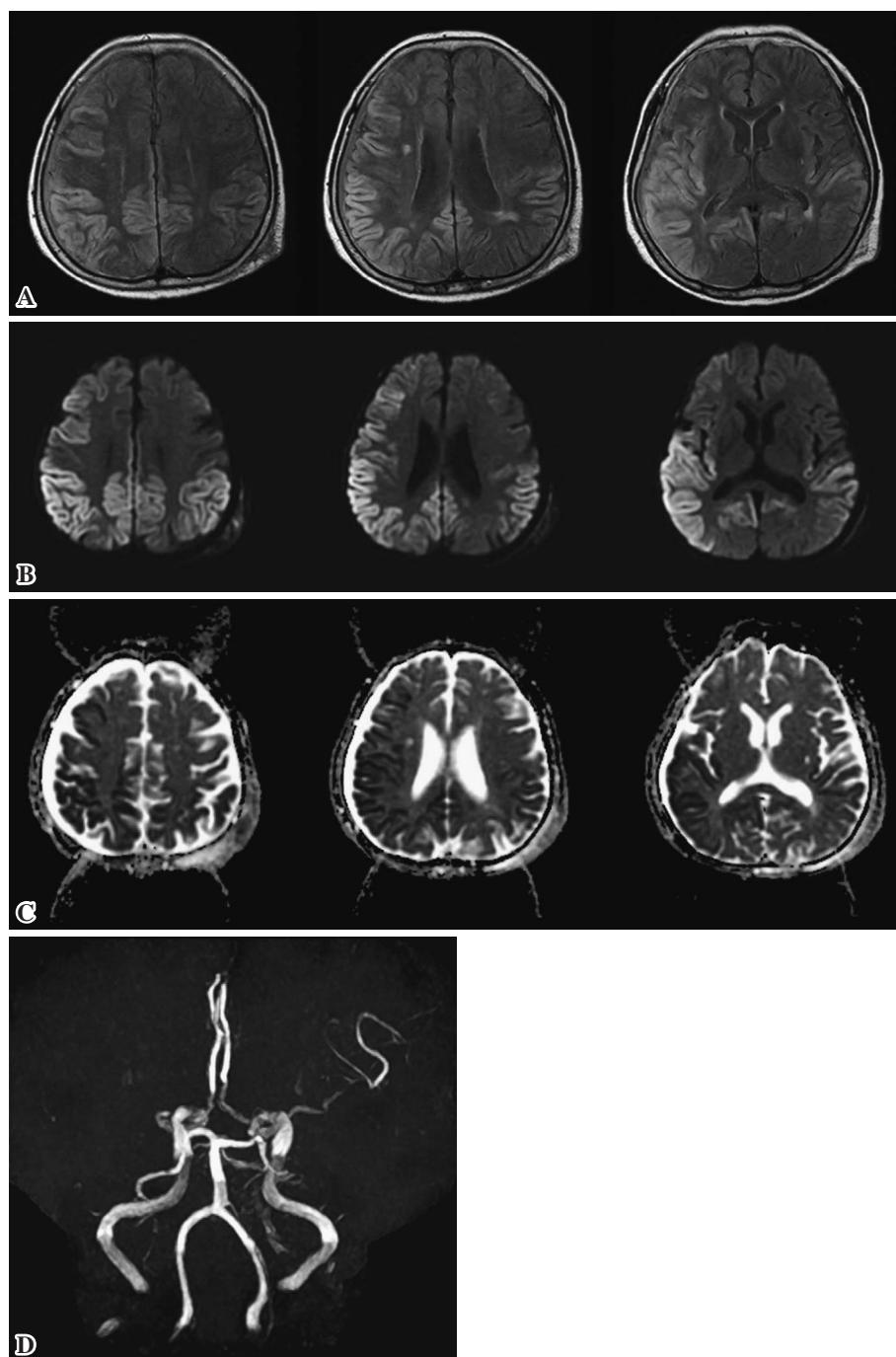


Figure 1. A fluid-attenuated inversion-recovery magnetic resonance imaging (MRI) of the brain on admission showed diffuse cortical high signal intensities with intravascular enhancement at the frontal, parietal, occipital and temporal lobes, bilaterally, and predominantly in the right hemisphere (A). On the diffusion-weighted images (B), the lesion had high signal intensity with low signal intensity on the ADC map (C). MR angiography of the brain revealed steno-occlusions of the right distal internal carotid artery and middle cerebral artery (MCA) and severe stenosis of the left MCA (D).

differential diagnosis included Creutzfeldt-Jakob disease, Moyamoya disease, venous sinus thrombosis, vasculitides, mitochondrial encephalopathy and hypertensive encephalopathy. However, in the present case, these diseases can be excluded due to the improved clinical course, normal laboratory findings and absence of typical radiological signs such as an empty delta.

Although we could not exclude underlying CBD or CJD pathology by brain biopsy, the clinical and laboratory evidence of vascular ischemic lesions support the fact that extensive cortical vascular-ischemic lesions may be the cause of symptoms that mimic CBS.

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