Familial Corticobasal Syndrome Associated with Basal Ganglia Hypointensities

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ABSTRACT

OBJECTIVE: We aim to characterize the clinical and imaging features of two cases of rapidly progressive familial corticobasal syndrome (CBS).

BACKGROUND: Corticobasal syndrome usually results from abnormal deposits of tau protein in the brain (i.e. corticobasal degeneration) and is considered a sporadic disorder; however imaging findings resembling neurodegeneration with iron accumulation (NBIA) have been described in these patients.

METHODS: We describe two first cousins with CBS associated with abnormal MRI findings.

RESULTS: Extensive bilateral T1-W hypointensities and T2-W hypointensities in the basal ganglia and thalamus were observed in the female patient. Postmortem examination of the brain in the 79 year old woman showed scattered tau positive inclusions in neurons and glia in the basal ganglia and thalamus. Marked diffuse gliosis was also noted in these areas.

CONCLUSIONS: Corticobasal syndrome may be a presentation of a rare, unknown form of NBIA.

INTRODUCTION

Corticobasal degeneration (CBD) was initially identified by Rebez as the clinical syndrome of progressive asymmetric rigidity and apraxia with possible alien limb phenomenon myoclonus, or dystonia with pathology consisting of cortical ballooned neurons, frontoparietal neuronal loss and gliosis, and nigral and basal ganglia degeneration (Mathew 2012). This clinical syndrome may be due to classical (CBD) pathology, but the term corticobasal syndrome (CBS) is used for the clinical entity (Mathew 2012). Other pathologies including Alzheimer’s disease, fronto-temporal dementia, progressive supranuclear palsy, and Creutzfeld-Jakob disease have been implicated (Mathew 2012). Alternatively, NBIA pathology may yield other clinical syndromes such as FTD or primary progressive aphasia (Maselis 2006).

Further mutations leading to CBS have been identified. Mutations in microtubule-associated protein tau (MAPT) have been reported to cause CBS. Familial cases of CBS associated with PGRN mutation in a Chinese kindred have been identified (Maselis 2006) as well as CBS from G2019S LRRK2 mutation (Chen-Pplotkin 2008).

RESULTS

72 year old right handed Caucasian male who presented for evaluation of tremor, apraxia and balance difficulty.

Onset of the disorder was at age 68 in the right arm with mild slowness, tremor, and apraxia. One and a half years later, the left side became involved. At age 68, he also noticed difficulty with balance, requiring him to hold the banister while using the stairs.

During our interview, the patient stated that he "doesn't like his thumbs, because sometimes they feel like they are not a part of his body."

The patient received a score of 17/30 on the Montreal Cognitive Examination (MOCA). There was impairment of vertical opto-kinetic nystagmus and moderate slowing of horizontal and vertical saccades. There was moderate right sided and mild left sided upper and lower extremity bradykinesia and rigidity. He had mild bilateral myoclonic rest and action tremor and upper motor neuron signs with 3/4 knee reflexes bilaterally, 2 beats of ankle clonus bilaterally, and extensor plantar reflexes bilaterally. There was bilateral ideomotor apraxia and finger agnosia, complete agraphia, and difficulty with serial seven subtraction beyond 93 in addition to mild bilateral proprioceptive loss. Gait was ataxic with a wide base.

This is a 79-year-old right-handed Native American woman who was sent to our center for evaluation of atypical Parkinson’s disease. The neurological manifestation started in at age 74 with postural and kinetic tremor in the left arm and hand. A few weeks later, the patient and family noted generalized slowness with shuffling gait. At age 75, she has noticed deterioration of the left arm tremor. She developed progressive multiple contractions on the left hand, elbow, and shoulder lead to complete loss of function of her left upper limb by age 77. At that time, postural and kinetic tremor appeared in the right arm.

Her gait has progressively deteriorated with severe balance impairment associated with falls. As a result of this imbalance and severe gait disturbance, she has been confined to a wheelchair for approximately six months at her initial visit.

CONCLUSIONS

Corticobasal syndrome may be a presentation of a rare, unknown form of NBIA.