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Can multiple system atrophy clinically be misdiagnosed as corticobasal syndrome in the early stages?

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Multiple System Atrophy; Corticobasal Degeneration; Corticobasal Syndrome; Atypical Parkinsonism; Asymmetric Parkinsonism; Hand Dystonia

Multiple system atrophy (MSA), an atypical parkinsonian syndrome (APS) and synucleinopathy, usually presents with early autonomic dysfunction, symmetrical levodopa-unresponsive parkinsonism, and cerebellar symptoms. Myoclonus, speech disturbance, rapid-eye-movement sleep behavior disorder (RBD), stridor and dystonia are other features. Cognition is not impaired in majority.[1]

Corticobasal degeneration (CBD), another APS, is characterized by cognitive and asymmetrical motor symptoms. Prominent unilateral akinetic-rigid parkinsonism, limb dystonia, myoclonus, corticospinal tract involvement, and cortical sensory loss are the cardinal manifestations.[2] CBD is a pathologic diagnosis (tauopathy) while the term corticobasal syndrome (CBS) describes the clinical syndrome without pathologic confirmation.

Diagnosis of APSs (including MSA and CBD) is challenging, especially at early stages when the manifestations overlap. We report three probable MSA cases, with unusual presentation (asymmetric parkinsonism, severe limb dystonia, and prominent myoclonus) initially diagnosed as CBS.

Case 1: This was a 57-year-old woman; her problems started 10 years ago with jerky tremor of left hand. Her movements gradually got slower without response to levodopa. During the last 2 years, she had not been able to walk independently and been suffering from a fixed posture in the left hand, making it immobile and useless. She had a history of RBD and nocturnal stridor for years and urinary incontinence since the last year. Her family history was negative. Examination revealed normal cognition, anarthria, slow saccadic eye movements, severe jaw-closing dystonia, dystonic posture of hands (fixed-posture in left), hypokinesia, and rigidity, more severe in the left side (video 1).

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She was not able to walk without aid. With bilateral support the gait was not wide based. As far as it was possible to examine there was no apraxia or ataxia in the limbs. Brain magnetic resonance imaging (MRI) revealed pallidal hypointensity on fluid-attenuated inversion recovery (FLAIR) with putaminal slit/rim sign (Figure 1, a-b).

Case 2: This 62-year-old man came with slowness of movements, progressive clumsiness, and slowing of left hand, which began 9 years earlier. He had been wheelchair-bound since the last year. He had a history of RBD and urinary incontinence for a couple of years. Progressive parkinsonism, gait disturbance, and limb posturing along with urinary incontinence had been the major clinical picture in the last several years. Levodopa therapy (up to 600 mg levodopa per day) had no significant benefit neither on parkinsonism nor dystonia. His family history was negative. Examination revealed hypophonic speech, slow saccades, rigidity and hypokinesia of limbs more severe on the left side, severe dystonic posture in the left hand, and myoclonic jerks of the fingers (video 2). There was no cognitive dysfunction, apraxia, or cortical sensory loss. Brain MRI betrayed a typical hot-cross-bun sign in the pons, atrophic putaminal slit sign (Figure 1, c-e).

Case 3: A 61-year-old woman visited our clinic with a history of gait disturbance, imbalance, and recurrent falls beginning four years earlier. She mentioned RBD but no urinary disorder or orthostatic dizziness. Her family history was negative. Increasing the dose of levodopa (up to 600 mg per day) did not improve parkinsonism, gait, or dystonia. Urinary incontinence developed after three years of disease onset. She had hypophonic speech with slow saccades. There was severe dystonic posture with finger poly-mini-myoclonus in the left hand and severe rigidity and hypokinesia in the left limbs. There was no cortical dysfunction. She had severely asymmetric parkinsonian gait with postural instability two year after symptom onset and was not able to walk independently after four years (video 3). Brain MRI showed hot-cross-bun sign in the pons and bilateral atrophic putamina with slit sign (Figure 1, f-i).

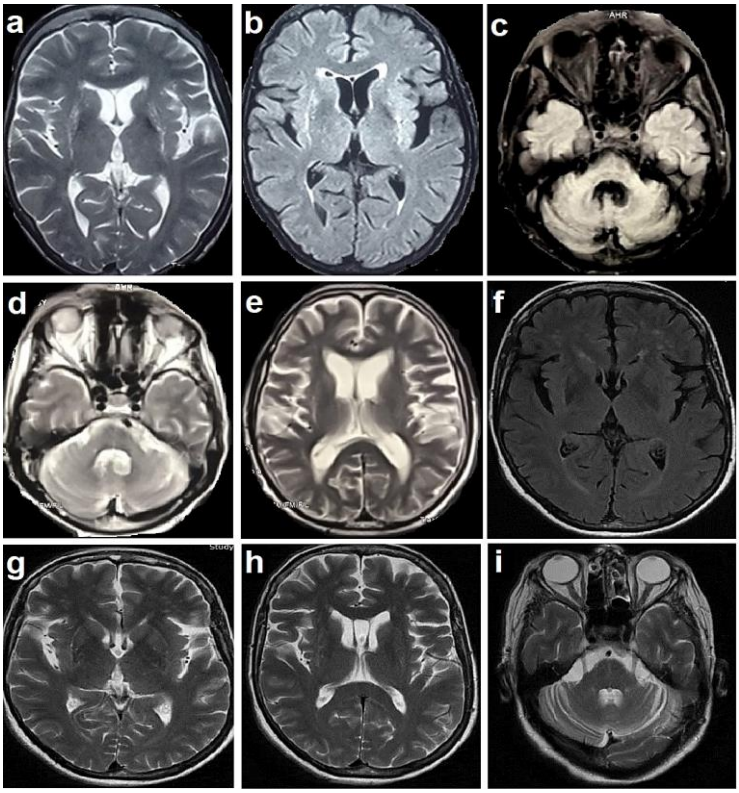

Figure 1. a, b, e, f, g, and h) T2 and fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI) of patients showing bilateral putaminal atrophy and putaminal slit sign; c, d, and i) FLAIR and T2 MRI showing hot-cross-bun sign; planes a and b related to case 1, c-e to case 2, and f-i to case 3

Autonomic dysfunctions, symmetrical parkinsonism, and cerebellar and corticospinal involvements are the main clinical manifestations of MSA. In contrast, significant motor asymmetry associated with higher-cortical malfunctions is the main feature of CBS. Although dystonia is more typical of CBS, different types of dystonia such as camptocormia, blepharospasm, oromandibular and cervical dystonia (retrocollis and antecollis) may be observed in MSA. However, limb dystonia particularly restricted to one side is more characteristic for CBD.[3,4] Antecollis is the most common form of dystonia in MSA.[5] Prominent myoclonic jerks of fingers, combined with dystonic hand in the second and third cases made CBS even more probable. Mini-myoclonus of fingers is observed in MSA, but it is common in CBS too. Nevertheless, in CBS, myoclonus is asymmetric and limited to the dystonic limb.[1-5]

Autonomic dysfunction, an essential feature of MSA, can present as orthostatic hypotension, sphincter dysfunction, or impotency. However, it is rare in CBD.[1-5] All three patients had incontinence in the course of their illness, even though, orthostatic hypotension was not detected. Cognition remained normal even in the advanced stages, which is in accordance with the diagnosis of MSA.[1] In contrast, multiple cognitive domains are usually impaired in CBD and it can be the first presentation.[5-10] Our patients had prominent RBD, a characteristic finding in synucleinopathies including MSA, but it is rare in CBD.[4] In addition, stridor in the first case is highly suggestive for MSA. The previously reported five patients with similar asymmetric parkinsonism had many common features with our patients. Similar to our cases, they were dominated by asymmetric parkinsonism with limb dystonia without prominent ataxia or apraxia and with normal cognition.[10] This may highlight the notion for this phenotype of MSA when cortical signs are absent or minimal and the advantage of using additional diagnostic tests such as brain MRI which can be revealing in APS. Hot-cross-bun in the pons, pontine and/or cerebellar atrophy, and putaminal rim sign are suggestive of MSA, whereas brain MRI in CBS typically shows asymmetrical and focal cortical atrophy.[9]

In conclusion, despite the usual symmetric findings, MSA can present with asymmetrical dystonia, myoclonus, and parkinsonism leading to CBS misdiagnosis. Normal cognition, RBD, stridor, and autonomic dysfunction are clues for the correct diagnosis of MSA, as are typical brain MRI findings.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

This study was approved by the ethics committee of Iran University of Medical Sciences, Tehran, Iran and performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki (DoH) and its later amendments or comparable ethical standards.

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