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Short communication

Markedly asymmetric presentation in multiple system atrophy

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ABSTRACT

Background: Multiple system atrophy (MSA) presents with fairly symmetrical, levodopa unresponsive parkinsonism and additional features like autonomic dysfunction, cerebellar and corticospinal tract involvement. Marked asymmetry in atypical parkinsonism suggests alternative diagnosis like Corticobasal syndrome (CBS).
Methods: We describe five unusual cases, who presented initially with markedly asymmetric parkinsonism, rigid dystonic abnormal limb posturing and subsequently developed clinical and/or radiological features consistent with probable MSA-P.
Results: Using the internationally accepted diagnostic criteria, the patients fulfilled the diagnostic criteria for probable MSA-P after 5 years from disease onset. Case 4 and 5 had characteristic MRI features and Case 2 was pathologically confirmed.
Conclusions: We use these cases to highlight that MSA-P MSA-P can present rarely with very marked asymmetry, dystonic limb and myoclonic jerks leading to a diagnosis of CBS at onset.

1. Introduction

Multiple system atrophy (MSA) is an atypical parkinsonian syndrome typically presenting with fairly symmetrical, levodopa unresponsive parkinsonism and additional features like autonomic dysfunction, cerebellar and corticospinal tract involvement [1]. Other characteristic features include a jerky tremor, dysarthria, dysphonia, dysphagia, stridor, inspiratory sighs, orofacial dystonia, anterocollis, camptocormia or Pisa syndrome, and cold extremities [1,2]. Cognition is typically not affected [2].

Corticobasal syndrome (CBS) is characterized by progressive levodopa unresponsive, asymmetric parkinsonism, dystonia and focal cortical signs (e.g. cortical myoclonus, apraxia, cortical sensory loss, alien limb phenomena) [3]. CBS is the typical phenotype in corticobasal degeneration (CBD), but can be also due to other disorders like progressive supranuclear palsy, frontotemporal dementia and others [3]. However, CBS has not been described as a phenotype for MSA. Here we describe five patients who initially presented with markedly asymmetric atypical parkinsonism and were initially diagnosed as CBS. They were subsequently diagnosed as MSA based on pathology in one and Probable MSA based on clinical and radiologic features (in 2 cases) that developed later in disease course. We wish to highlight that amongst atypical parkinsonism, MSA may rarely present as with marked asymmetry and some other features like myoclonus suggesting CBS at onset. Written consent for videos and participation in research was taken from the patients included.

Supplementary video related to this article can be found online at 10.1016/j.parkreldis.2013.05.004.

2. Case 1

This 70-year-old lady first noticed difficulty using her right hand at the age of 64 years, which progressed and the hand became clumsy, useless and slow in performing tasks. Over the next two years, she additionally developed gait difficulty with festination. Levodopa did not improve her symptoms. On examination at that time she had broken smooth pursuit but normal saccades. There

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was a jerky postural tremor of the right arm, which was held rigid and dystonic. There were stimulus sensitive myoclonic jerks of both upper limbs right more than left. She had ideomotor apraxia on right side. There was no cortical sensory loss, and no cognitive dysfunction. There were no cerebellar or pyramidal signs. A diagnosis of CBS was made [4].

Four years after onset she developed marked autonomic dysfunction with postural hypotension and urinary incontinence. She became wheelchair bound within few months, and developed a marked anterocollis. She developed swallowing problems and respiratory difficulties with stridor and inspiratory sighs, later necessitating tracheostomy (Video case 1) (Table 1). Her cognition remained intact despite this progression (verbal IQ 96 and performance IQ was 104). The diagnosis was revised and she was diagnosed as probable MSA-Parkinsonism (MSA-P) [1].

Autonomic tests done at 5 years suggested marked autonomic dysfunction. The MRI suggested nonspecific small vessel disease. Dopamine transporters imaging (DaTSCAN) showed bilaterally, asymmetric reduced dopaminergic uptake left > right. Electrophysiology suggested positive and negative myoclonus of cortical origin.

3. Case 2

This 64 years old lady was first noticed to have difficulty with writing (agramatism and agraphia) the right hand. Over the next two years dystonia and rigidity of right upper and lower limbs developed. On examination at two years she had an asymmetric parkinsonian that did not respond to levodopa. MRI brain was normal. The clinical diagnosis of CBS was made at that visit.

Subsequently over 5 years postural instability, orthostatic hypotension, pyramidal signs and the bladder dysfunction appeared. She developed severe dysphonia, inspiratory stridor and camptocormia. Autonomic testing supported orthostatic hypotension, and the urodynamic study suggested detrusor hyperreflexia. She required tracheostomy and gradually became immobile and bedridden; but her cognition was still fairly good (MMSE score 26). The diagnosis was revised and she was diagnosed as probable MSA-P [1]. Finally, the patient died due to bronchopneumonia after (approximately) 5 years of the disease course.

The neuropathological examination of the brain was done; on macroscopic examination the cerebellar atrophy (Fig. 1a), atrophy of the pons base (Fig. 1b) and atrophy with grayish discoloration of putamen (Fig. 1c) were present which is contrasted with normal coronal section for comparison. On microscopic and immunohistochemical examination, there was a typical alpha-synucleinopathy with argyrophilic oligodendroglial cytoplasmic inclusions in the striatum, cerebellum and oblongata present (Fig. 1d and e), confirming the definite diagnosis of multiple system atrophy Fig. 2.

4. Case 3

This 76-year-old gentleman presented with a postural tremor in the right hand which began at the age of 72 years. This was associated with abnormal posturing of the hand and decline in dexterity for routine activities. On examination two years after onset he had slowing of saccades but normal range of eye movements. He had dystonic posturing of the right hand with postural tremor and some myoclonic jerks in the outstretched arms. At 2 years due to the atypical asymmetric parkinsonism which did not respond to Levodopa he was diagnosed as CBS.

Three years subsequently he developed autonomic disturbance with erectile dysfunction, and a tendency to fall on standing from chair. REM sleep behavior disorder and swallowing difficulty with frequent choking were added on in the fourth year. When seen five years after onset he had urinary problems needing an indwelling catheter. On examination at 5 years his saccades were mildly slow as before (Table 1). There was asymmetric rigidity with bilateral jerky tremor more on right side (video case 3). His cognition was intact. His diagnosis was revised to MSA-P.

In terms of investigations there was evidence of orthostatic hypotension on autonomic tests. His brain MRI had been done twice and was normal. On electrophysiology the jerks were cortical in origin with positive and negative myoclonus.

5. Case 4

A 67-year-old female presented with a 4 year history starting as difficulty with her left leg and could not put her shoe on. She also noticed some dragging of her left foot. On examination one year after onset the left hand was held rigid, mildly flexed and she had a few jerks of her left hand fingers. There was no clear apraxia. At one years due to the atypical asymmetric parkinsonism which did not respond to Levodopa she was diagnosed as CBS.

Two years subsequently, she developed urinary urgency and frequency with orthostatic hypotension suggesting autonomic disturbance. On examination at 5 years there was asymmetric rigidity with jerky tremor on left side (video case 4). Cognition was intact. Clinical diagnosis was revised to MSA-P and MRI brain showed hemosiderin deposition in the lateral aspect of the right putamen, and loss of volume in middle cerebral peduncle.

6. Case 5

This 51 year-old lady first noticed difficulty using the left hand at the age of 45 yrs. This was associated with slowness, rigidity and a postural tremor of the left forearm. She developed dystonic posturing of her arm and difficulty in using it purposefully. 2 years after the onset she had asymmetric parkinsonism and right-sided myoclonus. On examination she had slow saccades and dystonic left limb with multifocal stimulus sensitive myoclonus. She had some difficulty with copying gestures but no clear apraxia. She was diagnosed as CBS at this visit.

Subsequently her gait became slower and she started to fall. She developed bladder dysfunction and other autonomic features. On examination at 5 years she had anterocollis and severe quivery dysarthria. She was still asymmetric at 5 years from onset. Her cognition had still been good though she had been completely bedridden since one year. The diagnosis was revised and she was diagnosed as probable MSA-P [1].

The investigations supported orthostatic hypotension on autonomic tests. MRI brain 5 years into the illness showed mineralization of globi pallidi and dorsal putamina with iron, greater in amount on the left, suggestive of MSA (previous scan at 2 years being normal). DaT scan suggested asymmetric loss of dopaminergic uptake. Myoclonus was electrophysiologically cortical in origin.

7. Discussion

We described here five patients presenting with markedly asymmetric parkinsonism with dystonia initially diagnosed as CBS [4] that later in the disease course (5 years after onset) became less asymmetric and developed autonomic features and respiratory problems that led to a final diagnosis of probable MSA-P [1]. Case 4 and 5 had characteristic MRI features and Case 2 was pathologically confirmed.

The main signs that led to CBS diagnosis initially (asymmetric akinetic–rigid syndrome, limb dystonia, myoclonus and ideomotor