Diagnostic Clues in Multiple System Atrophy: A Case Report and Literature Review

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**Summary**

Multiple system atrophy (MSA) is an adult-onset, sporadic, progressive neurodegenerative disease. Based on the consensus criteria, patients with MSA are clinically classified into cerebellar (MSA-C) and parkinsonian (MSA-P) subtypes. In addition to major diagnostic criteria including poor response to levodopa, and presence of pyramidal or cerebellar signs (ataxia) or autonomic failure, certain clinical features or “red flags” may raise the clinical suspicion for MSA. In our case report we present a 67-year-old female patient admitted to our hospital due to inability to walk, with poor response to levodopa therapy, whose neurological examination revealed severe Parkinsonism, and who fulfilled all criteria for MSA, as rarely seen in clinical practice. (Turkish Journal of Neurology 2013; 19:28-30)

**Key Words:** Multiple system atrophy, autonomic failure, diagnostic criteria

**Introduction**

Multiple system atrophy (MSA) is an adult-onset, progressive, idiopathic neurodegenerative disease. Clinical pictures previously known as striatoniigral degeneration, olivopontocerebellar atrophy, and Shy-Drager syndrome are now all named as “multiple system atrophy”. MSA is one of the Parkinson plus syndromes, with an annual incidence of 0.6/100,000 (1,2). Differential diagnosis from idiopathic Parkinson’s disease (PD) can be difficult, due to its rare nature. Main clinical features are autonomous failure, parkinsonism, cerebellar ataxia and pyramidal symptoms. We are presenting this case that fulfills all the rare diagnostic criteria of MSA, to remind the very significant clues in the differential diagnosis of MSA, with a literature review.

**Case Report**

Sixty-seven year old, right-handed woman presented at our outpatient clinic with complaint of inability to walk. Her history showed that her complaints started two years ago with slowing of walking and tremor at rest in the right hand; although she was diagnosed with Parkinson’s disease at that time and dopaminergic treatment was initiated, she did not benefit from that treatment. Swelling in the feet, dizziness, ataxia were added to these complaints one year ago, and she had been experiencing urinary and fecal incontinence for the last 4-5 months. The patient could not walk without assistance for the last one month. There was nothing special in the patient’s medical history and family history.
Her neurological history showed clear bilateral bradykinesis on the left side, hypokinesis and dysphonia and cerebellar tests were impaired on the left side. Romberg sign was positive both when eyes were open and closed, masked facies was present, and glabella reflex was positive. She could walk with assistance at anteflexion posture and her gait was ataxic.

Her routine laboratory investigations did not show any pathology. As she did not respond to levodopa treatment, and considering the present clinical picture, idiopathic Parkinson’s disease was excluded and Parkinson plus syndrome was suspected.

The cerebral MRI showed brain stem and cerebellar atrophy, symmetric cerebral atrophy, as well as the cross sigh in the axial sections of the brain stem (Figure 1). Neuropsychology tests showed median SEP to be within normal range and tibial SEP elongated on the left (right: 41 msec, left: 44.2 msec). Investigations performed to evaluate autonomous impairment showed that although sympathetic skin response in upper extremities was normal, there was no sympathetic skin response in lower extremities (Figure 2). R-R interval work-up (Figure 3) and tilt test were consistent with autonomous dysfunction. Mini mental status test results were normal.

**Discussion**

Multiple system atrophy (MSA) is a rare neurodegenerative disease characterized with glial cytoplasmic inclusion bodies containing alpha synuclein. Clinical features can be manifested as a combination of cerebellar,自主性和parkinsonian symptoms (Table 1). It has two subtypes: cerebellar (MSA-C) and parkinsonian (MSA-P). There are very few pathognomonic signs to differentiate MSA-P from Parkinson’s disease in the early stage. In a study conducted by the European MSA Study Group (EMSA-SG) statistically significant red flags for the differential diagnosis of MSA were noted. The presence of at least 2 of six red flags (early instability, rapid progression, abnormal posture, bulbar dysfunction, respiratory dysfunction, and emotional incontinence) was reported to be 98.3% specific and 82.4% sensitive for the diagnosis of MSA (3). Early instability developing with recurring falls is frequently seen in progressive supranuclear palsy (PSP) cases (4,5,6). Among the various clinical conditions resulting in Parkinsonism, falling is seen in the very early stages in PSP patients, mid-stages in MSA patients, and late stages in Parkinson’s patients (6). Although early instability is not diagnostic of MSA, it is a sign of atypical parkinsonian disorders.

Rapid progression is one of the very important warning signs for MSA patients. In a study conducted by Köllensperger et al. rapid progression was seen in 2/3 of MSA-P patients and only 2.6% of Parkinson’s patients (3). Hoehn and Yahr progression rate was
found to be significantly high in atypical Parkisonian disorders (3). Abnormal postures including Pisa syndrome, antecollis, and contractures in hands and feet are common in MSA. The pathophysiology underlying this unusual dystonic appearance was reported to be the progressive striatal degeneration in MSA (7).

Although bulbar involvement, severe dysarthria, dysphagia, and dysphonia occur in many of MSA patients, only 5% of Parkinson’s patients experience these symptoms (4). Speech is also impaired in most of MSA patients (8). While speech disorder develops within 24 months in MSA patients, this period may take up to 84 months in Parkinson’s patients (9). Development of dysphagia within 1 year of the onset of disease symptoms is reported to be specific (100%) for atypical parkinsonian disorders. Respiratory dysfunction such as inspiratory stridor or sighing is frequent in MSA and rare in PD. On the other hand, severe snoring and sleep apnea syndrome are not specific for MSA (3).

Table 1. Clinical diagnostic criteria

<table>
<thead>
<tr>
<th>Category</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Autonomic and urinary dysfunction</td>
<td>Orthostatic hypotension*</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>Urinary incontinence / incomplete voiding of the bladder, impotence</td>
</tr>
<tr>
<td>Cerebellar dysfunction</td>
<td>Bradiakinesia*</td>
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<tr>
<td>Corticospinal tract dysfunction</td>
<td>Rigidity</td>
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<td></td>
<td>Postural ataxia</td>
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<td>Tremor</td>
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<tr>
<td></td>
<td>Gait ataxia*</td>
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<tr>
<td></td>
<td>Ataxic dysarthria</td>
</tr>
<tr>
<td></td>
<td>Extremity ataxia</td>
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<tr>
<td></td>
<td>Hyperreflexia, extensor plantar response</td>
</tr>
</tbody>
</table>

*Signs that must be present

Table 2. Clinical warning signs – red flags – for MSA (3)

1- Early instability with recurring falling attacks
2- Rapid progression
3- Abnormal posture (camptocormia, antecollis)
4- Bulbar dysfunction (severe dysphonia, dysarthria, dysphagia)
5- Respiratory dysfunction (sleep apnea syndrome)
6- Emotional incontinence (crying and laughing without reason)
7- No response to dopaminergic treatment
8- Cerebellar signs
9- Autonomic signs
10- Jerk tremor – myoclonus

Table 3. MRI findings in multiple system atrophy (10)

1) Significant atrophy in ventral medulla, pons and cerebellum
2) Clear signal decrease in the putamen compared to globus pallidus in axial T2 (putaminal iron accumulation)
3) Hot cross bun sign in pons

Although Parkinson plus syndromes are very similar clinically, they can be easily distinguished by a few distinct features which may be very important in early diagnosis of MSA. Therefore, all clinicians should be aware of the early stage symptoms listed in Table 2, investigate these symptoms in patients presenting with a parkinsonism picture and assess the development of these symptoms in the follow-up of these patients.

Magnetic resonance imaging (MRI) is an important tool not only for diagnosis but also for evaluating the clinical features of MSA and the T2-signal changes in the basal ganglia and brain stem on 1.5 tesla MRI are diagnostically significant. Hyperintense lateral putaminal ring and the hot cross bun sign are considered typical for MSA. In addition, posterior putaminal hypointensity and mid-cerebellar peduncular hyperintensity support MSA diagnosis (11).

Our patient had early instability, rapid progression, autonomic signs, abnormal posture, bulbar dysfunction, cerebellar dysfunction, and a parkinsonism picture that did not respond to dopaminergic treatment; she fulfilled all the diagnostic criteria. In addition, cranial MRI fiundings were typical for MSA. This article aims to present this rare case to assist clinicians by reviewing literature on MSA, and summarizing important features of the condition.

References