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The Diagnostic Challenges in Patient with Multiple System Atrophy: A Case Report

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Abstract:

Introduction

Multiple system atrophy (MSA) is a rare, severe adult onset, sporadic, progressive neurodegenerative movement disorders that are still poorly understood. It is characterized by cerebellar ataxia, autonomic disorders, and parkinsonism syndrome in various combinations. The incidence rate is 0.6 cases per 100,000 people per year. Prevalence is 4-5 cases per 100,000 people. Despite of the presence of well-established clinical criteria for multiple system atrophy, ante-mortem diagnosis is difficult.

Case

We present a case of 44-year-old, male who with unsteady, wide based gait and rigidity which had developed gradually for 2 years. One year after the appearance of the first symptoms, he developed dysarthria, difficulty in swallowing, dizziness when changing position, and bladder incontinence. From neurologic examination we found orthostatic hypotension, dysmetria and dysdiadochokinesia on the both side. He met all the major criteria for possible rapid progression of MSA. In addition, brain Magnetic Resonance Imaging (MRI) showed prominent solids left and right cerebellum hemispheres and slight atrophy pons.

Conclusion

Our case can be classified as MSA according to the diagnostic criteria because the definitive diagnosis of MSA is only based on post-mortem pathological analysis. From this case we can learn that diagnosing MSA is quite challenging especially in early years of disease. The importance of good MRI interpretation and early finding of brain MRI abnormality can improve the accuracy of MSA diagnosis.

Keywords: cerebellar ataxia, Multiple System Atrophy, movement disorder, neurodegenerative disease, parkinsonism

1. INTRODUCTION

Multiple system atrophy (MSA) is an idiopathic, rare, adult-onset, progressive, sporadic, fatal neurodegenerative disease.[1] MSA is one of Parkinson's plus syndromes, with an annual incidence rate of 0.6 per 100,000 population.[2,3] The main clinical features are autonomic dysfunction, parkinsonism, cerebellar ataxia and pyramidal symptoms. Two types

of MSA can be distinguished clinically; parkinsonian (MSA-P) and cerebellar type (MSA-C). The latest diagnostic criteria suggest three categories for improving diagnostic accuracy: probable, possible and definite. The definitive diagnosis is confirmed by neuropathological examination.[4] A definitive diagnosis is made by the presence positive cytoplasmic α -synuclein inclusion in the central nervous system in relation to neurodegenerative changes, even without a clinical history of MSA. According to the revised diagnostic criteria for the diagnosis of MSA, it has included Magnetic Resonance Imaging (MRI) images as supporting evidence for the diagnosis of possible MSA.[5] We present a case of male patient with manifestation of clinical symptoms and the course of the disease in accordance with MSA, where the lack of specific imaging features in the course of the disease presents a challenge in excluding the differential diagnosis with the disease similar neurodegenerative.

2. CASE HISTORY

A 44-year-old male, truck driver admitted to the neurological clinic of Dr. Soetomo Hospital Surabaya with staggering and unstable gait for 2 years which was felt increasingly burdensome. One year after the first symptoms, he complained of difficulty in swallowing, choking when eating and drinking accompanied by frequent bedwetting. The patient also complained of dizziness when changing positions. History of tremor and cognitive deficit was denied by the patient. There were no similar symptoms among family members.

From neurological examination revealed dysarthria, dysphagia, rigidity and bradykinesia. There was no visible tremor at rest and eyeballs could move in all directions. There were no motor weakness or sensory abnormalities found in the patient. However, physiological reflexes were increased on both sides and the Romberg test was positive when the patient opened and closed eyes. Dysmetria and dysdiadokokinesia were positive on both sides, and wide based gait was seen. Postural hypotension and urinary incontinence were also present.

Brain MRI revealed prominent solid folia on the left cerebellum and right hemispheres, slight atrophy on pons horizontal view (Figure 1). The patient underwent physiotherapy, and received Levodopa, betahistine dihydrochloride and neurotropic for treatment. After 3 weeks of treatment, spinning dizziness were improved, but gait ataxia still remained.

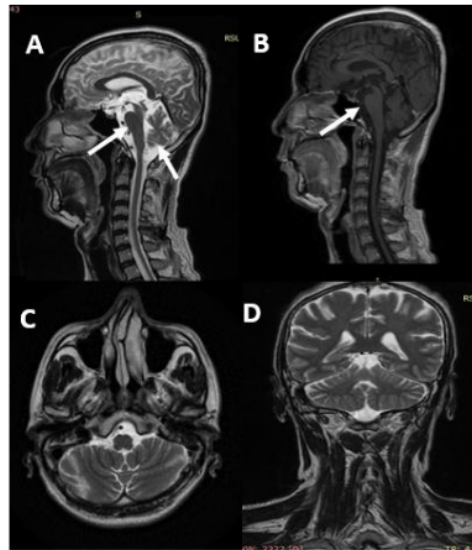


Figure 1. MRI of the Head (1.5 Tesla) (A) Sagittal T2 weighted (B) Sagittal T1 with contrast showing slight pons and cerebellar atrophy (white arrow) (C) Axial T2-weighted (D) Coronal T2-weighted shows folia cerebellum which is prominent

3. DISCUSSION

Although a definitive diagnosis of MSA can only be made in neuropathological evidence, the diagnosis of MSA can be based on the course of clinical symptoms and imaging. Based on the patient's chief complaint that ataxia gait, will be very difficult for clinicians to diagnose MSA because there are many variations of symptoms in this disease, especially if the clinician meets the patient early in the course of the disease. Therefore, the diagnosis of MSA can only be established years after the progression of symptoms appears.

As mentioned previously the clinical picture of MSA is a combination of cerebellar, autonomic, and parkinsonian symptoms. [6] MSA has two subtypes, the cerebellar type (MSA-C) and the parkinsonian type (MSA-P). MSA itself based on the latest consensus criteria is divided into three categories for improving diagnostic accuracy: probable, possible, and definite (Table 1). [8]

Table 1. Diagnostic Criteria for Multiple-System Atrophy[8,12]

<p>Definite MSA</p> <p>Autopsy-confirmed case with neuropathologic evidence of widespread and abundant CNS a-synuclein-positive glial cytoplasmic inclusions in association with striatonigral and/or olivopontocerebellar neurodegeneration</p>
<p>Probable MSA</p> <p>Sporadic, progressive, adult-onset (age >30 years) disease characterized by</p> <ul style="list-style-type: none"> • Autonomic failure involving -Urinary incontinence (with erectile dysfunction in males); OR -Orthostatic blood pressure drop of at least 30 points systolic or 15 points diastolic within 3 minutes after standing from a recumbent position

AND one of the following predominant motor features

- Poorly levodopa-responsive parkinsonism (defined as bradykinesia with rigidity, tremor, or postural instability); OR
- A cerebellar syndrome consisting of gait ataxia with cerebellar dysarthria, limb ataxia, or cerebellar oculomotor dysfunction

Possible MSA

Sporadic, progressive, adult-onset (age >30 years) disease characterized by

- Parkinsonism (defined as bradykinesia with rigidity, tremor, or postural instability); OR

- A cerebellar syndrome consisting of gait ataxia with cerebellar dysarthria, limb ataxia, or cerebellar oculomotor dysfunction

AND at least one of the following symptoms that suggest autonomic dysfunction, including otherwise unexplained

- Urinary urgency
- Urinary frequency or incomplete bladder emptying
- Erectile dysfunction in males
- Significant orthostatic blood pressure drop not meeting the criteria for probable MSA

AND at least one of the following additional features for MSA-P or MSA-C

- MSA-P or MSA-C
 - Babinski sign with hyper-reflexia
 - Stridor
- MSA-P
 - Rapidly progressive parkinsonism
 - Poor response to levodopa
 - Postural instability within 3 years of motor onset
 - Gait ataxia, cerebellar dysarthria, limb ataxia, or cerebellar oculomotor dysfunction
 - Dysphagia within 5 years of motor onset
 - Atrophy on MRI of putamen, middle cerebellar peduncle, pons, or cerebellum
 - Hypometabolism on FDG-PET in putamen, brainstem, or cerebellum
- MSA-C
 - Parkinsonism (bradykinesia and rigidity)
 - Atrophy on MRI of putamen, middle cerebellar peduncle, or pons
 - Hypometabolism on FDG-PET in putamen
 - Presynaptic nigrostriatal dopaminergic denervation on SPECT or PETFDG-PET

With various clinical presentations, MSA presents a diagnostic challenge to clinicians. Despite having more rapid progression of motor symptoms, MSA can mimic Parkinson's disease or idiopathic disease of slow onset cerebellar ataxia with additional symptoms of autonomic dysfunction. In addition, other diseases that can manifest symptoms as cerebellar ataxia are caused by toxins (alcohol, chemotherapy drugs, lead, lithium, and toluene) or due to vitamin B1 deficiency and ataxia due to genetic abnormalities such as

fragile X-associated tremor or ataxia syndrome, spinocerebellar ataxia (especially type 6), or Friedreich ataxia which occurs slowly.[10]

In a study conducted by the European MSA Study Group (EMSA-SG) it was noted that there were red flags that were of particular concern to MSAs that were statistically significant to rule out the differential diagnosis of other MSAs. The appearance of at least 2 of the 6 red flags (instability arises early, rapid development, abnormal posture, bulbar dysfunction, respiratory dysfunction, and emotional incontinence) were reported 98.3% specific and 82.4% sensitive for the diagnosis of an MSA.[10]

MRI is an important tool not only for diagnosis but also for evaluating the clinical symptoms of MSA and the changes in T2 signals in the cerebellum, basal ganglia, and brainstem that appear on MRI 1.5 Tesla are diagnostically significant even though the typical hot cross bun sign was not yet visible in our patient's Brain MRI.[11] This may occur because the patient's disease course was still in its early stages but from the diagnostic criteria supporting the diagnosis of Multiple System Atrophy.

4. CONCLUSION

The diagnosis of MSA is mainly based on clinical criteria, although some diagnostic studies might help to support the diagnosis or to rule out other disease. Brain imaging, such as MRI, is often used and can be helpful, especially in cases with atypical symptoms. Consensus-based diagnostic criteria for MSA are only validated retrospectively. Symptoms and disease progression are still the most important in the diagnostic process and to rule out a differential diagnosis due to the absence of a reliable and widely available ante-mortem biomarker. Thus, future clinical research should develop to define early MSA diagnosis through a combination of clinical, imaging and molecular criteria.

Disclosure

Conflicts of interest: None.

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