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CASE REPORT **OPEN ACCESS**

Multiple System Atrophy-Cerebellar Type: A Case Report With Classic Neuroimaging Features

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A B S T R A C T

Background: Multiple system atrophy (MSA) is a rare progressive neurodegenerative disorder characterized by parkinsonism, cerebellar dysfunction, and autonomic failure. The cerebellar variant (MSA-C) presents predominantly with cerebellar ataxia and is often challenging to diagnose in early stages.

Case Presentation: A 60-year-old male presented with a 2-year history of progressive gait instability, starting with difficulty grasping slippers and progressing to proximal muscle weakness requiring walking support. He developed postural hypotension, intentional tremor, and urinary symptoms. Examination revealed gait ataxia, horizontal nystagmus, positive cerebellar signs, and significant postural hypotension (140/90 mmHg supine to 100/60 mmHg standing). MRI brain demonstrated the pathognomonic "hot cross bun" sign in the pons with significant cerebellar atrophy. Based on clinical presentation and neuroimaging findings, a diagnosis of MSA-cerebellar type was established.

Conclusion: This case highlights the importance of recognizing the classic triad of cerebellar dysfunction, autonomic failure, and characteristic neuroimaging findings in diagnosing MSA-C. Early recognition is crucial for appropriate symptomatic management and patient counseling regarding prognosis.

Keywords: Multiple system atrophy, cerebellar ataxia, hot cross bun sign, autonomic dysfunction, neurodegenerative disease

INTRODUCTION

Multiple system atrophy (MSA) is a rare progressive neurodegenerative disorder with an estimated annual incidence of 3.4-4.9 cases per 100,000 people[1]. It belongs to the family of α-synucleinopathies and is characterized by the accumulation of α-synuclein protein in the cytoplasm of oligodendrocytes, forming glial cytoplasmic inclusions[2]. MSA typically presents in adults over 30 years of age, with peak onset in the fifth and sixth decades of life[3].

Clinically, MSA is classified into two main subtypes based on predominant features: MSA-cerebellar (MSA-C) with olivopontocerebellar degeneration and predominant cerebellar symptoms, and MSA-parkinsonian (MSA-P) with striatonigral degeneration and predominant parkinsonian features[4]. Both subtypes commonly present with autonomic dysfunction including orthostatic hypotension, urogenital dysfunction, and sleep disorders[5].

The diagnosis of MSA relies on clinical criteria and supportive neuroimaging findings. Characteristic MRI features include the "hot cross bun" sign in the pons and "bright middle cerebellar peduncle" sign[6]. The prognosis remains poor, with rapid disease progression typically confining patients to wheelchairs within 5 years and median survival of 6-10 years from symptom onset[7].

CASE PRESENTATION

A 60-year-old male presented with a 2-year history of progressive gait instability. The illness began insidiously with difficulty grasping his slippers firmly, which over several months progressed to involve proximal muscles of the lower limbs. He noticed increasing difficulty with sitting and squatting, eventually requiring support while walking.

The patient experienced frequent episodes of lightheadedness when changing postures from sitting or lying down to standing. After 1.5 years of symptom onset, he developed intentional tremor and urinary symptoms including urgency, increased frequency, and urinary retention. Notably, he had no bradykinesia, rigidity, memory loss, or features suggestive of dementia. There was no family history of similar neurological conditions or dementia.

Physical examination revealed gait ataxia with short-stepping gait pattern, reduced arm swing, and episodes of freezing. Horizontal nystagmus and intentional tremors were present. Cerebellar function testing showed positive finger-nose test, dysdiadochokinesia, and abnormal heel-shin test. Significantly, there was no resting tremor, bradykinesia, or rigidity. Deep tendon reflexes were normal with negative Babinski sign. Mental status examination was within normal limits.

Autonomic assessment revealed significant postural hypotension with supine blood pressure of 140/90 mmHg dropping to 100/60 mmHg upon standing. Ultrasound abdomen demonstrated significant post-void residual urine, confirming urinary retention.

MRI brain study was performed, revealing hyperintense cruciform signal in the pons on T2 FLAIR imaging, consistent with the pathognomonic "hot cross bun" sign. There was significant cerebellar atrophy with no changes in the putamen or significant cerebral cortical atrophy.

Based on the clinical presentation of progressive cerebellar ataxia, autonomic dysfunction, and characteristic neuroimaging findings, a diagnosis of multiple system atrophy-cerebellar type (MSA-C) was established.

DISCUSSION

This case exemplifies the classic presentation of MSA-cerebellar type, demonstrating the characteristic triad of cerebellar dysfunction, autonomic failure, and supportive neuroimaging findings. MSA belongs to the spectrum of atypical parkinsonian disorders, also known as Parkinson-plus syndromes, and is distinguished from idiopathic Parkinson's disease by its more rapid progression and poor response to levodopa therapy[8].

Pathophysiology and Classification

The pathophysiology of MSA involves widespread glial cell degeneration, particularly affecting oligodendrocytes. The accumulation of α-synuclein in glial cytoplasmic inclusions leads to progressive neurodegeneration affecting the basal ganglia, cerebellum, and autonomic centers[9]. This patient's presentation with predominant cerebellar features classifies the condition as MSA-C, which accounts for a significant proportion of MSA cases, particularly in Asian populations[10].
The α-synuclein pathology in MSA differs fundamentally from that seen in Parkinson's disease, where α-synuclein accumulates in neuronal cytoplasm (Lewy bodies) rather than in glial cells[11]. This distinction has important implications for disease progression and potential therapeutic targets[12].

Diagnostic Challenges and Neuroimaging

The diagnostic challenge in MSA often lies in its early stages when it may be misdiagnosed as isolated cerebellar ataxia, spinocerebellar ataxia, or even idiopathic Parkinson's disease. The overlapping features with other neurodegenerative diseases necessitate the use of advanced imaging techniques and careful clinical assessment for accurate diagnosis[13].
In this case, the presence of the "hot cross bun" sign on MRI was crucial for diagnosis. This finding is highly specific for MSA and results from selective loss of myelinated transverse pontocerebellar fibers with preservation of corticospinal tracts[14]. The sign appears as a hyperintense cruciform pattern on T2-weighted images in the pons and is observed in approximately 50-70% of MSA patients[15]. Additional MRI findings that support MSA diagnosis include the "bright middle cerebellar peduncle" sign, putaminal atrophy with T2 hyperintensity, and cerebellar atrophy[16].

Autonomic Dysfunction

The autonomic dysfunction observed in this patient represents a cardinal feature of MSA that significantly impacts quality of life and often serves as an early indicator of the disease. Orthostatic hypotension, defined as a drop in systolic blood pressure of at least 20 mmHg or diastolic blood pressure of at least 10 mmHg within 3 minutes of standing, occurs in over 90% of MSA patients[17]. The severity of orthostatic hypotension in this case (40 mmHg systolic drop) is consistent with the profound autonomic dysfunction characteristic of MSA.
Urogenital dysfunction, including urinary urgency, frequency, and retention as observed in this patient, affects approximately 80-90% of MSA patients and often precedes motor symptoms[18]. These symptoms result from involvement of the pontine micturition center and sacral parasympathetic neurons[19].

Clinical Course and Prognosis

The clinical course in this patient, with initial distal motor symptoms progressing to proximal involvement over 2 years, is typical of MSA-C. The disease typically follows a relentless progressive course, with patients developing wheelchair

dependency within 5-8 years and death occurring within 6-10 years of symptom onset[20]. The presence of early autonomic dysfunction, as seen in this case, is often associated with a more rapid disease progression[21].

Management Considerations

Currently, no disease-modifying treatments are available for MSA. Management remains primarily symptomatic, focusing on addressing motor symptoms, autonomic dysfunction, and providing supportive care[22]. Physical therapy is crucial for maintaining mobility and preventing contractures, while occupational therapy helps adapt daily activities to the patient's functional capacity[23].

For orthostatic hypotension management, non-pharmacological measures include increased fluid and salt intake, compression garments, and postural maneuvers. Pharmacological options include fludrocortisone, midodrine, and droxidopa[24]. Urological symptoms may require intermittent catheterization or anticholinergic medications[25].

While levodopa may provide modest benefit in some patients with MSA-P, the response is typically poor and diminishes over time. In MSA-C patients like this case, levodopa therapy is generally ineffective for cerebellar symptoms[26].

Differential Diagnosis

The differential diagnosis for this patient included other causes of progressive cerebellar ataxia such as spinocerebellar ataxias, cerebellar stroke, or paraneoplastic cerebellar degeneration. However, the combination of cerebellar signs, autonomic dysfunction, and characteristic neuroimaging findings strongly supported the diagnosis of MSA-C[27]. The absence of family history and the adult onset helped exclude hereditary ataxias[28].

Future Perspectives

Research efforts are currently focused on developing disease-modifying therapies targeting α-synuclein aggregation, neuroinflammation, and mitochondrial dysfunction. Clinical trials investigating immunotherapies, autophagy enhancers, and neuroprotective agents are ongoing[29]. Early and accurate diagnosis, as demonstrated in this case, will be crucial for enrollment in future therapeutic trials[30].

CONCLUSION

This case demonstrates the classic presentation of multiple system atrophy-cerebellar type with characteristic clinical features and pathognomonic neuroimaging findings. The combination of progressive cerebellar ataxia, profound autonomic dysfunction manifesting as orthostatic hypotension and urinary symptoms, and the presence of the "hot cross bun" sign on MRI established the diagnosis of MSA-C.

Early recognition of MSA-C is essential for several reasons: appropriate symptomatic management can improve quality of life, patient and family counseling regarding prognosis allows for advance care planning, and accurate diagnosis prevents unnecessary investigations and inappropriate treatments. While no curative treatment exists, multidisciplinary symptomatic management involving neurology, urology, physical therapy, and occupational therapy can help maintain functional independence and quality of life for as long as possible. This case underscores the importance of recognizing the characteristic clinical and radiological features of MSA-C to ensure timely diagnosis and optimal patient care.

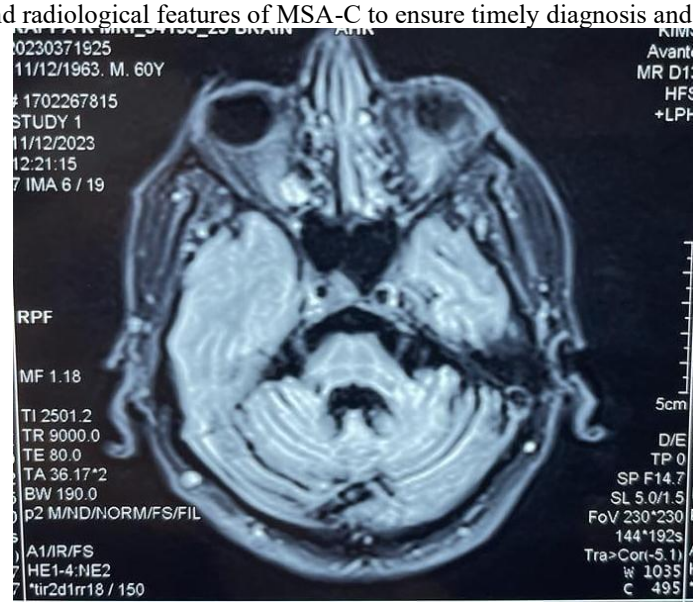

Figure 1: T1 MRI with hot cross bun sign of pons

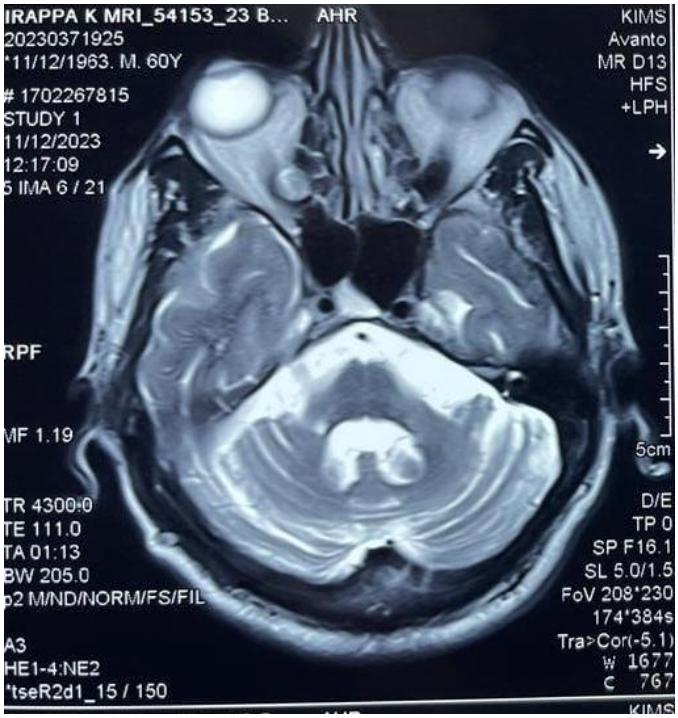

Figure 2: T2 MRI with bright MCP sign

Declarations

Patient Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of Interest: The authors declare no conflicts of interest.

Ethical Approval: Not applicable for this case report.

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