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Case Study RRJoNS

Late Onset Ataxia: A Case Report

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Abstract

57-year-old man with no prior history of any illness presented with subacute onset of gradually progressive gait ataxia, upper limb incoordination and speech issues. There was history suggestive of orthostatic hypotension and erectile dysfunction. On examination, there was normal cognition with gaze evoked nystagmus, scanning speech and limb incoordination in the form of past pointing, dysdiadochokinesia, and tandem walking abnormality suggestive of pan cerebellar involvement. The patient was evaluated with routine investigations which were normal including liver, thyroid, and renal function tests. MRI Brain showed Hot cross bun sign and cerebellar atrophy. Secondly, secondary causes of subacute ataxia like ANA Profile, Autoimmune and paraneoplastic antibody panel was negative which included anti GAD Antibodies. CT Chest and CT Abdomen as a part of paraneoplastic work up was negative. CSF Study was normal. In view of classical history, examination findings and MRI Brain features with negative autoimmune and paraneoplastic workup a diagnosis of Multisystem Atrophy-C was made, and patient was managed symptomatically and is under follow up.

Keywords: MSA Parkinsons plus ataxia dysautonomia

INTRODUCTION

Multiple system atrophy (MSA) is an uncommon and degenerative neurological condition, characterized by its rarity, progression, and fatality. It manifests in two primary types: MSA-P, resembling Parkinson's disease, and MSA-C, affecting the cerebellum. Typically, the disease manifests with issues such as genitourinary dysfunction, orthostatic hypotension, and rapid eye movement (REM) sleep behavior disorder. As the condition advances, patients swiftly encounter challenges related to balance, speech, and coordination. This disorder poses significant challenges due to its multifaceted impact on various neurological functions, impacting both motor and non-motor aspects of patients' lives. Cerebellar atrophy is due to olivopontocerebellar atrophy degeneration and, to a lesser extent, striatonigral degeneration (SND) [1].

CASE HISTORY

A 57-year-old male came with complaints of difficulty in walking which was gradual in onset and progressive in nature since past 2 years. He also complained of slurring of speech for past 2 years. Patient gives history of giddiness on getting up from sitting position which was gradual in onset and progressive in nature and was diagnosed to have orthostatic hypotension by local physician. Thereof, sexual issues related due to erectile dysfunction. No history of any cognitive decline. He also gave history of difficulty in micturition, he was not able to hold urine well and voided before reaching washroom suggestive of urgency for which he was evaluated by urologist and diagnosed to have neurogenic bladder with a post residual volume was >100 ml. No complaint of any sensory symptoms, tremors, bradykinesia, falls, memory loss, abnormal

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posturing of limbs, swallowing difficulty, choking episodes, abnormal movements in sleep, dream enactments, smell abnormalities or psychiatric symptoms.

On examination: Patient was conscious and oriented. Vitals were within normal limits. Head to toe examination was normal. On neurological examination, higher mental function was normal. MMSE score was 30/30. The speech was scanning type of cerebellar speech. Cranial nerve examination was within normal limits except gaze evoked nystagmus which was present. Under Motor examination showed normal tone and power with no rigidity or spasticity. Deep tendon reflexes in all four limbs were normal, plantar reflex was bilaterally flexor (Figure 1). Cerebellar signs were present as axial and limb ataxia seen by abnormalities during finger-nose test as past pointing, dysmetria and dysdiadochokinesia. Gait ataxia was present with tandem walking. The Rhomberg test was positive. Sensory examination for fine touch and pain was normal in upper and lower limbs along with intact joint position and vibration sensation.

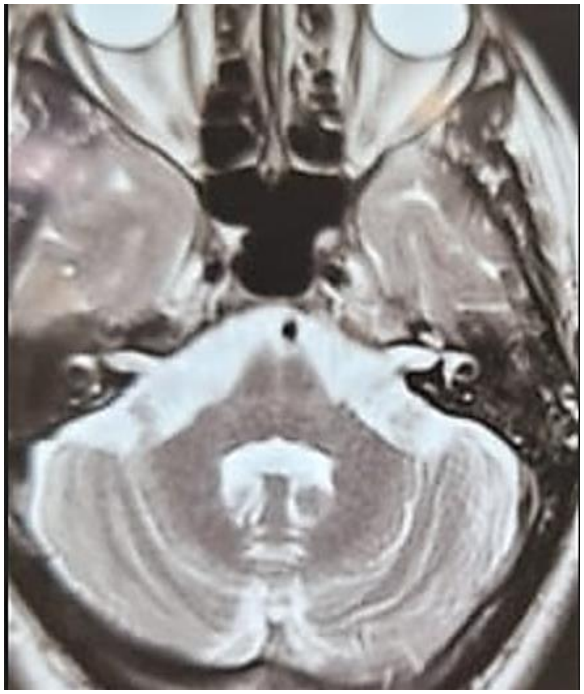

Figure 1. MRI Flair Axial view showing hot cross bun sign and cerebellar atrophy.

The patient underwent a comprehensive evaluation, encompassing routine investigations that yielded normal results, inclusive of liver, thyroid, and renal function tests. Magnetic Resonance Imaging (MRI) of the brain revealed the distinctive Hot Cross Bun sign and cerebellar atrophy. Subsequent investigations for secondary causes of subacute ataxia, such as the Anti-Nuclear Antibody (ANA) profile and autoimmune and paraneoplastic antibody panel, proved negative, encompassing anti-glutamic acid decarboxylase (GAD) antibodies. Computed Tomography (CT) scans of the chest and abdomen, conducted as part of the paraneoplastic workup, also returned negative results. Cerebrospinal fluid (CSF) analysis demonstrated normal findings.

Given the classical clinical history, examination findings, and the specific MRI brain features combined with the absence of abnormalities in the autoimmune and paraneoplastic workup, a conclusive diagnosis of Multisystem Atrophy-Cerebellar (MSA-C) was established. The patient was currently undergoing symptomatic management and remained under regular follow-up to address and monitor the progression of the condition. This thorough diagnostic process underscores the complexity of neurological disorders and the importance of a meticulous approach to ensure accurate diagnosis and appropriate management.

DISCUSSION

Multiple system atrophy-cerebellar type is uncommon disorder (Table 1). Differentiation of MSA-C from MSA-P, Idiopathic late-onset cerebellar ataxia (ILOCA) is very difficult [2].

Cerebellar symptoms are seen in 100% of patients with MSA-C compared to 54% of MSA-P patients [3]. In MSA-C, cerebellar dysfunction manifests as acquired gait ataxia, limb ataxia, ataxic dysarthria, and eye movement abnormalities such as dysmetria, saccadic intrusion, and ocular dysmetria [4].

The average age of diagnosis is between 55 and 60 years, and the average survival from the onset of motor symptoms is 8 to 9 years [5]. Autonomic dysfunctions are very common in MSA which is mainly due to secondary damage and loss of neurons in the intermediolateral part of the spinal cord and loss of catecholaminergic neurons in the ventrolateral medulla [6].

At present, the management of Multisystem Atrophy (MSA) primarily revolves around symptomatic treatments, encompassing both pharmacologic and nonpharmacologic interventions. In the pharmacological realm, Riluzole, functioning as a glutamate receptor antagonist, is commonly employed. This medication aims to mitigate the toxicity of glutamate on neurons. However, despite a clinical trial indicating the tolerability of a 200 mg dose, it did not demonstrate efficacy in alleviating extrapyramidal symptoms in individuals with MSA. The search for effective therapeutic interventions continues, emphasizing the need for ongoing research to address the complex challenges posed by MSA and improve patient outcomes [7].

Severe neurogenic orthostatic hypotension is a presenting symptom that manifests with postural light-headedness, dizziness, sensation of blacking out, and falls with or without syncope [8]. Drugs such as midodrine have been shown to worsen supine hypertension [9]. Treatment options for neurogenic orthostatic hypotension are Alpha/beta agonist Droxidopa shows excellent result in increasing standing systolic pressure [10].

Alpha agonist and acetylcholinesterase inhibitor can be used. Erectile dysfunction is usually an early manifestation of MSA and a symptom of autonomic failure. Clinical study showed the ED prevalence of 96% in male MSA patients and as the first symptom in 37% [11]. Sildenafil acts as an inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase (PDE)-5 which is used in erectile dysfunction [12].

Table 1. Elaborates the diagnostic criteria of the types of Multisystem atrophy.

Clinically Established MSA	**Clinically Probable MSA**
1. Autonomic dysfunction defined as (at least one is required) • Unexplained voiding difficulties with post-void urinary residual volume ≥100 ml • Unexplained urinary urge incontinence • Neurogenic OH (≥20/10 mmHg blood pressure drop) within 3 min of standing or head-up tilt test and at least one of	At least two of: 1. Autonomic dysfunction defined as (at least one is required): • Unexplained voiding difficulties with post-void urinary residual volume • Unexplained urinary urge incontinence • Neurogenic OH (≥20/10 mmHg blood pressure drop) within 10 min of standing or head-up tilt test
2. Poorly L-dopa-responsive parkinsonism	2. Parkinsonism
3. Cerebellar syndrome (at least two of gait ataxia, limb ataxia, cerebellar dysarthria, or oculomotor features)	3. Cerebellar syndrome (at least one of gait ataxia, limb ataxia, cerebellar dysarthria, or oculomotor features)
At least two At least one Absence	At least one At least one Absence

Supportive clinical features

Supportive motor features	Rapid progression within 3 years of motor onset Moderate to severe postural instability within 3 years of motor onset Moderate to severe postural instability within 3 years of motor onset Severe speech impairment within 3 years of motor onset Severe dysphagia within 3 years of motor onset Unexplained Babinski sign Jerky myoclonic postural or kinetic tremor Postural deformities	**Supportive non-motor features**	Stridor Inspiratory sighs Erectile dysfunction (below age of 60 years for clinically probable MSA) Pathologic laughter or crying

MRI Markers of Clinically Established MSA
Each Affected Brain Region as Evidenced by Either Atrophy or Increased Diffusivity Counts as one MRI Marker

For MSA-P	For MSA-C
Atrophy of: • Putamen (and signal decrease on iron-sensitive sequences) • Middle cerebellar peduncle • Pons • Cerebellum Hot cross bun" sign Increased diffusivity of: • Putamen • Middle cerebellar peduncle	*Atrophy of:* • Putamen (and signal decrease on iron-sensitive sequences) • Infratentorial structures (pons and middle cerebellar peduncle) • "Hot cross bun" sign • Increased diffusivity of: ○ Putamen

Exclusion Criteria

Substantial and persistent beneficial response to dopaminergic medications.

Unexplained anosmia on olfactory testing.

Fluctuating cognition with pronounced variation in attention and alertness and early decline in visuoperceptual abilities.

Recurrent visual hallucinations not induced by drugs within 3 years of disease onset.

Dementia according to DSM-V within 3 years of disease onset.

Downgaze supranuclear palsy or slowing of vertical saccades.

Brain MRI findings suggest an alternative diagnosis (e.g., PSP, multiple sclerosis, vascular parkinsonism, symptomatic cerebellar disease, etc.).

Documentation of an alternative condition (MSA look-alike, including genetic or symptomatic ataxia and parkinsonism) known to produce autonomic failure, ataxia, or parkinsonism and plausibly connected to the patient's symptoms.

CONCLUSION

Multisystem atrophy-C (MSA-C) is a common cause of late onset ataxia with dysautonomia. A hot cross bun sign in MRI Brain may be crucial in the diagnosis along with the clinical history and the examination findings.

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