Indian Journal of
Neurology

Open Science Publications

Volume 7, Issue 1 - 2026

www.opensciencepublications.com

Multiple System Atrophy Type C and Its Neuropsychiatric Manifestations: Challenges in Diagnosis and Management-A Case Report

Case Report

Kothekar M*, Parkar S, Ghodke J, Desai S, Dhar A and Purohit S

Department of Psychiatry, Vedantaa Institute of Medical Sciences, Dahanu, Palghar

***Corresponding author:** Dr. Mansi Kothekar, Vedantaa Institute of Medical Sciences, Dahanu, Palghar. E-mail Id: dr.mansikothekar16@gmail.com

Article Information: **Submission:** 02/04/2026; **Accepted:** 16/04/2026; **Published:** 20/04/2026

Abstract

Background: Psychotic symptoms in Multiple System Atrophy (MSA) are uncommon, affecting approximately 5–10% of patients, and are frequently attributed to dopaminergic therapy or advanced disease. Early-onset psychosis intrinsic to MSA–C remains underrecognized and may result in misdiagnosis as a primary psychiatric disorder, delaying appropriate management.

Case Summary: A 54-year-old man with no prior psychiatric history presented with a one-week history of persecutory delusions and multimodal hallucinations. The psychosis was accompanied by executive dysfunction (MMSE 23/30; impaired Trail Making Test) and had emerged in the setting of progressive cerebellar ataxia, parkinsonism, and autonomic dysfunction (constipation, bladder dysfunction) — all antedating dopaminergic exposure. MRI demonstrated periventricular T2/FLAIR hyperintensities without the pathognomonic 'hot cross bun' sign. Based on consensus diagnostic criteria, a diagnosis of probable MSA–C was established. Olanzapine 5 mg nightly led to gradual resolution of psychosis without extrapyramidal worsening over two weeks.

Conclusion: This case illustrates that psychosis may be an early, intrinsic manifestation of MSA–C, preceding dopaminergic therapy and motor symptom dominance. Late-onset psychosis co-occurring with executive dysfunction and autonomic features should prompt systematic evaluation for neurodegenerative synucleinopathies. Recognition of underlying MSA has critical implications for antipsychotic selection and prognostication.

Keywords: Multiple System Atrophy-C; Parkinsonism; Psychosis; Neurodegeneration; Late-onset psychosis; Synucleinopathy; Antipsychotic selection

Introduction

Late-onset psychosis presents a significant diagnostic challenge in neuropsychiatric practice. While primary psychotic disorders can emerge in midlife, secondary causes – particularly neurodegenerative disorders - must be systematically excluded before a primary psychiatric diagnosis is assigned.

Among synucleinopathies, psychosis is well characterised in Parkinson's disease (PD) and dementia with Lewy bodies (DLB). In contrast, psychotic manifestations in Multiple System Atrophy (MSA) are less frequently emphasised in the literature and are often attributed to dopaminergic therapy or advanced disease stages. [9,10]

MSA is a progressive α-synucleinopathy characterised by variable combinations of autonomic failure, parkinsonism, and cerebellar ataxia.[1,9] It arises from oligodendroglial cytoplasmic inclusions containing misfolded α-synuclein, leading to multisystem neurodegeneration.[1] Consensus criteria classify MSA into MSA-P (parkinsonian predominant) and MSA-C (cerebellar predominant) subtypes.[11] The prevalence is estimated at 3-5 per 100,000

individuals, with onset typically in the fifth to seventh decades of life. [9]

Although motor and autonomic symptoms predominate, neuropsychiatric manifestations including depression, cognitive impairment, sleep disturbances, and - less commonly - psychosis are increasingly recognised.[6,12] Neuropathological studies have demonstrated that α-synuclein pathology in MSA may extend beyond classical motor circuits to involve limbic and associative cortical regions, [2,3] providing a plausible substrate for early psychiatric manifestations.

We report a case in which psychosis emerged as an early and clinically dominant feature of probable MSA-C, preceding both dopaminergic therapy and full motor syndrome characterisation. We discuss the neurobiological mechanisms, differential diagnostic considerations, and pharmacological implications of this presentation.

Case Presentation

A 54-year-old man with no prior psychiatric history presented with a one-week history of persecutory delusions and multimodal hallucinations. He expressed a fixed belief that unknown persons intended to cause him harm, was observed muttering to himself, and was noted to gesture toward unseen stimuli. Sleep was markedly reduced and appetite had declined.

Over the preceding year, he had developed progressive imbalance, frequent falls, and difficulty with postural stability. Two weeks prior to psychiatric presentation, he experienced constipation, abdominal distension, and incomplete bladder emptying – autonomic disturbances consistent with MSA. [6,9] There was no history of substance use, head trauma, seizures, or family history of psychiatric illness. No fluctuating sensorium was recorded on any assessment.

Mental Status Examination

On assessment, the patient was dishevelled with a stooped posture. Psychomotor slowing and limited eye contact were noted. Spontaneous speech was decreased with increased latency. Mood was anxious ("I feel unsafe"); affect was restricted and congruent. Thought process was goal-directed but slowed. Thought content revealed systematised persecutory delusions. Perceptual abnormalities included second- and third-person auditory hallucinations and intermittent visual hallucinations.

Cognitive assessment demonstrated

Orientation to time, place, and person intact; impaired recent memory; MMSE score of 23/30; and impaired Trail Making Test performance indicative of executive dysfunction. Insight was absent and judgment impaired. Executive dysfunction of this nature is consistent with prior neuropsychological studies demonstrating frontal-subcortical deficits in MSA, reflecting disruption of dorsolateral prefrontal–striatal circuitry. [4,5,12]

Neurological Examination and Neuroimaging

Neurological examination revealed coarse tremors, reduced arm swing, short-stepped gait, cerebellar incoordination, and impaired proprioception — a mixed cerebellar and parkinsonian phenotype consistent with MSA-C. [1,11]

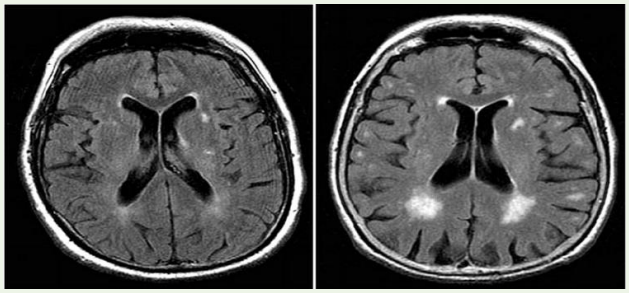

Figure 1: MRI Findings T2/ Flair-periventricular hyperintensities unremarkable for cerebello-pontine T2 hyperintensities. (likely due to the disease's rapid progression)

Brain MRI demonstrated periventricular T2/FLAIR hyperintensities. The pathognomonic 'hot cross bun' sign of pontine degeneration was absent; however, absence of this finding does not exclude MSA, particularly in early stages. [1,9] Blood investigations including complete blood count, metabolic panel, thyroid function, serum B12, VDRL, and HIV serology were within normal limits, excluding common metabolic and infective causes of psychosis. An electroencephalogram showed no epileptiform activity.

Based on the Second Consensus Statement on the Diagnosis of Multiple System Atrophy,[11] the combination of cerebellar dysfunction, parkinsonism, and autonomic failure supported a diagnosis of probable MSA-C.

Differential Diagnosis

The differential diagnosis considered included:

- Late-onset schizophrenia: No prior psychiatric history; motor and autonomic features atypical for primary psychosis.
- Psychotic disorder due to neurocognitive disorder: Cognitive impairment was mild and executive-predominant without frank dementia at presentation.
- Dementia with Lewy bodies (DLB): Absence of characteristic cognitive fluctuations and predominant cerebellar features argued against this diagnosis.
- Parkinson's disease psychosis: Cerebellar-predominant phenotype and absence of prior dopaminergic therapy argued against a PD-related aetiology.
- Delirium: No fluctuating consciousness or identifiable acute precipitant; investigations excluded metabolic and infective causes.

Critically, psychosis antedated dopaminergic therapy in this patient, implicating intrinsic neuropathological mechanisms rather than medication-induced phenomena. [10,12]

Management and Outcome

Olanzapine 5 mg nightly was initiated following a risk-benefit

Citation: Kothekar M, Parkar S, Ghodke J, Desai S, Dhar A, et al. Multiple System Atrophy Type C and Its Neuropsychiatric Manifestations: Challenges in Diagnosis and Management-A Case Report. Indian J Neurol. 2026;7(1): 166.

discussion. Gradual resolution of psychotic symptoms was observed over two weeks, with no worsening of extrapyramidal or cerebellar features on serial examination.

Typical (first-generation) antipsychotics were avoided given the risk of exacerbating parkinsonian features in the context of nigrostriatal degeneration.[8] In parkinsonian disorders, antipsychotic selection requires careful consideration of D2-receptor blockade and associated motor vulnerability. Although clozapine and pimavanserin have the strongest evidence base in PD-related psychosis, cautious low-dose use of selected second-generation antipsychotics may be considered when closely monitored - particularly when clozapine prescribing infrastructure is unavailable.[8]

The patient was counselled regarding the progressive nature of MSA and referred for multidisciplinary input including neurology, physiotherapy, and speech therapy. Family members received caregiver education.

Discussion

Neurobiological Basis of Psychosis In MSA–C MSA is characterised by oligodendroglial α-synuclein inclusions producing degeneration of the striatonigral and olivopontocerebellar pathways. [1,9] Neuropathological studies have demonstrated convergence of α-synuclein pathology into limbic structures, including the amygdala and anterior cingulate cortex, [2,3] regions critically implicated in emotional salience, threat appraisal, and the pathogenesis of delusions.

Executive dysfunction in this patient implicates additional disruption of dorsolateral prefrontal–striatal circuitry. [4,5] Impaired top-down regulatory control over limbic salience networks may predispose to delusional ideation and aberrant threat perception. Furthermore, cerebellar degeneration in MSA–C disrupts cerebello-thalamo-cortical circuits, and the cerebellum has been increasingly implicated in psychosis through mechanisms of cognitive dysmetria and predictive processing failure.[7] The convergent degeneration of frontostriatal and cerebellar networks in MSA–C may thus synergistically increase vulnerability to psychotic experiences.

Psychiatric manifestations in MSA — including hallucinations and delusions — have been documented in both clinical and clinicopathological studies, [12,13] though they remain less common than affective or sleep-related symptoms and are under emphasised in clinical guidance.

Clinical Implications

This case highlights several clinically important points:

- Late-onset psychosis warrants systematic neurological evaluation, including assessment of motor and autonomic function.
- The combination of executive dysfunction and autonomic symptoms in a patient with new-onset psychosis should function as a red flag for underlying neurodegenerative disease. [4-6]
- Psychosis in MSA may occur independently of dopaminergic therapy, indicating intrinsic neuropathological mechanisms. [10,12]
- Antipsychotic selection in this context must carefully consider motor vulnerability: D2-blocking agents carry risk of extrapyramidal exacerbation, and second-generation agents should be used at the lowest effective dose with close monitoring.[8]
- Early and accurate diagnosis prevents prolonged misclassification as primary psychosis, enables family counselling, and guides prognosis.

Conclusion

Psychosis may represent an early, intrinsic manifestation of MSA–C rather than a treatment-related epiphenomenon. The co-occurrence of executive dysfunction, autonomic features, and late-onset psychosis should prompt evaluation for underlying synucleinopathies. Integration of psychiatric and neurological assessment is essential for diagnostic accuracy and for guiding safer antipsychotic management in this vulnerable patient population.

Declarations

Declaration of Patient Consent

The authors declare that written informed consent was obtained from the patient for publication of this case report. The patient has consented to the publication of clinical information. His name will not be published, and due efforts have been made to conceal identifying information, although complete anonymity cannot be guaranteed.

References

1. Watanabe H, Hara K, Kato M, Ueda A, Ito M (2023) Multiple system atrophy: advances in diagnosis and therapy. J Mov Disord 16: 1-19.
2. Brettschneider J, Del Tredici K, Irwin DJ, Fang L,Lee EB et al. (2018) Converging patterns of α-synuclein pathology in multiple system atrophy. J Neuropathol Exp Neurol 77: 1005-1020.
3. Brettschneider J, Irwin DJ,Boluda S, Byrne MD, Fang L, et al. (2016) Progression of α-synuclein pathology in multiple system atrophy of the cerebellar type. Acta Neuropathol Commun 43: 315-329.
4. Lazzeri G, Difonzo T, Francesconi D, Carandina A, Gramegana C, Vergari M et al. (2022) Cognitive and autonomic dysfunction in multiple system atrophy: a comparative neuropsychological study. Front Neurol. 13: 912820.
5. Eschlböck S, Delazer M, Krismer F, Bodner T, Fanciulli A, et al. (2020) Cognition in multiple system atrophy: a single-center cohort study. Ann Clin Transl Neurol 7: 219-228.
6. Hu WZ, Cao LX, Yin JH, Zhao XS, Piao YS, et al. (2023) non-motor symptoms in multiple system atrophy: a comparative study with Parkinson's disease and progressive supranuclear palsy. Front. Neurol.13.
7. Argyropoulos GPD, Dun KV, Adamaszek M, Leggio M, Masciullo M (2019) The Cerebellar Cognitive Affective/Schmahmann Syndrome: a Task Force Paper Cerebellar 19: 102-125.
8. Rose O, Huber S,Trinka E, Pachmayr J, Clemens S (2024) Treatment of Parkinson's disease psychosis: systematic review and multi-methods synthesis. Biomedicines 12: 2317.
9. Fanciulli A, Wenning GK (2015) Multiple-system atrophy. N Engl J Med. 372: 249-263.

Citation: Kothekar M, Parkar S, Ghodke J, Desai S, Dhar A, et al. Multiple System Atrophy Type C and Its Neuropsychiatric Manifestations: Challenges in Diagnosis and Management-A Case Report. Indian J Neurol. 2026;7(1): 166.

10. Stankovic I, Krismer F, Jesic A, Antonini A, Benke T, et al. (2014) Cognitive impairment in multiple system atrop. Mov Disord. 29; 857-867.

11. Gilman S, Wenning GK, Low PA, Brooks DJ, Mathias JQ, et al. (2008) Second consensus statement on the diagnosis of multiple system atrophy. Neurology 71: 670-676.

12. Duranti E, Villa C (2024) Insights into Dysregulated Neurological Biomarkers in Cancer 16: 2680.

13. Hu WZ, Cao LX, Yin JH, Zhao XS, Piao YS, et al. (2023) non-motor symptoms in multiple system atrophy: A comparative study with Parkinson's disease and progressive supranuclear palsy Front Neurol 13:1081219.

Citation: Kothekar M, Parkar S, Ghodke J, Desai S, Dhar A, et al. Multiple System Atrophy Type C and Its Neuropsychiatric Manifestations: Challenges in Diagnosis and Management-A Case Report. Indian J Neurol. 2026;7(1): 166.