Expanding the Spectrum: Isolated Acute Diencephalitis as the Initial Manifestation of Neuromyelitis Optica Spectrum Disorder

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Received: 01 November 2025; *Accepted:* 24 November 2025

Journal of The Association of Physicians of India (2026): 10.59556/japi.74.1510

Diencephalic syndrome is a rare clinical variant of neuromyelitis optica spectrum disorder (NMOSD), observed in approximately 3.4% of presentations. Its hallmark features include endocrine and sleep-wake disturbances such as syndrome of inappropriate antidiuretic hormone secretion (SIADH), hypothermia, narcolepsy, daytime somnolence, and appetite dysregulation.[1] We report a case of NMOSD presenting as an isolated acute diencephalic syndrome, a rare and diagnostically challenging initial manifestation. This case underscores the importance of considering NMOSD even in the absence of typical optic neuritis or longitudinally extensive transverse myelitis.

A 27-year-old woman presented with a 3-week history of neuropsychiatric symptoms. Her illness began 1 month prior with a self-limited febrile episode. She subsequently developed right upper limb pain and paresthesia, followed by a complex diencephalic syndrome characterized by visual hallucinations, confabulation, significant recent memory deficits, excessive daytime sleepiness (10–14 hours/day), hyperphagia, hypothermia, and urinary frequency. She had no hiccups, vomiting, pruritus, blurred vision, pain on moving the eyes, painful tonic spasms, sensory loss, and urinary retention. Examination revealed a drowsy but arousable patient with cognitive deficits [mini-mental state examination (MMSE) 24/30, frontal assessment battery (FAB) 14/18]. Cranial nerve, motor, sensory, and cerebellar examinations were normal. Basic hemogram and renal, liver, and thyroid function tests were normal. Viral markers were negative. Laboratory investigation identified profound hyponatremia (112 mEq/L) consistent with SIADH. She was treated at an outside hospital for SIADH, and sodium was corrected over 2 days. Magnetic resonance imaging (MRI) of the brain revealed striking T2/fluid-attenuated inversion recovery (FLAIR) hyperintensities within the diencephalon, involving mammillary bodies, septum pellucidum, medial thalami, fornices, hypothalamus, and striatum (Figs 1A to C). Cerebrospinal fluid (CSF) analysis was unremarkable. Broad differentials included Wernicke encephalopathy, autoimmune encephalitis (anti-Ma2, IgLON5), neurosarcoidosis, neuro-Behçet's disease, infiltrative disorders, and central nervous system (CNS) neoplasms. Antinuclear antibody (ANA), antineutrophil cytoplasmic antibody (ANCA), autoimmune, and paraneoplastic panel were negative. Visual evoked potentials were normal. Serum MOG and CSF oligoclonal bands were negative. Serum NMO tested strongly positive. The patient was treated with intravenous (IV) methylprednisolone (1 gm/day for 5 days), followed by five sessions of plasma exchange and an oral steroid taper. She was initiated on rituximab for relapse prevention. Her clinical course showed marked improvement in mentation, sleepiness, and hypothermia. A follow-up MRI 1 month later demonstrated significant resolution of the signal abnormalities.

Our patient, with exclusive symptomatic diencephalic involvement and positive anti-AQP4 antibodies, meets the 2015 NMOSD diagnostic criteria given by Wingerchuk et al.[2] While NMOSD is classically defined

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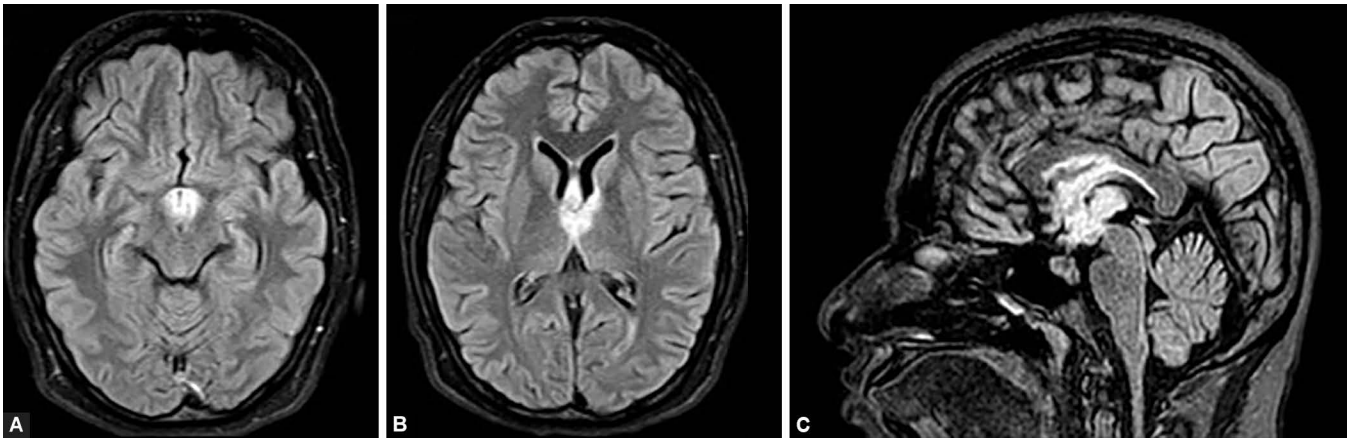
How to cite this article: Saibaba J, Pazhani P, Iyer VV. Expanding the Spectrum: Isolated Acute Diencephalitis as the Initial Manifestation of Neuromyelitis Optica Spectrum Disorder. J Assoc Physicians India 2026;74(7):86–87.



Figs 1A to C: Magnetic resonance imaging of the brain, FLAIR sequence, axial sections (A and B), and sagittal section (C) showing hyperintensities in mammillary bodies, hypothalamus, septum pellucidum, and thalami

by opticospinal involvement, atypical presentations are increasingly recognized. The diencephalic structures, rich in AQP4 channels, are a known target. Narcolepsy or hypersomnia from diencephalic periependymal lesions is a well-recognized, and sometimes presenting, feature of NMOSD.[3] In our patient, the profound hypersomnia suggests hypothalamic involvement, and CSF orexin level measurement, though not performed, would have been of interest to investigate this association. Similarly, the observed SIADH with hyponatremia has also been documented as an initial manifestation of the disease.

Similarly, Suzuki et al. reported a case with hypothermia, hypersomnia, and hyponatremia from a hypothalamic lesion as the initial sign of NMOSD.[4] It is important to distinguish NMOSD from other mimics like Wernicke encephalopathy, which also affects mammillary bodies but is typically associated with different clinical and radiological contexts. Peethambar et al. highlighted a similar case of a 19-year-old female with SIADH, narcolepsy, bradycardia, and somnolence who presented as a diencephalic syndrome of NMOSD and improved with steroids.[5]

This case illustrates that an isolated acute diencephalic syndrome, especially with accompanying SIADH, can be the heralding presentation of NMOSD. Early serological testing for AQP4-IgG is crucial in such scenarios to enable prompt immunotherapy, which can significantly improve outcomes as demonstrated here.

Authors' Contributions

Jayaram Saibaba, Pushkar Pazhani, and Vivek Venkataraman Iyer contributed equally to this work. All three authors were involved in the conception, organization, and execution of the research project, as well as the writing of the first draft of the manuscript and its subsequent review and critique.

Funding

This study was not funded.

Conflict of Interest

None.

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