EDITORIAL

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Beyond Patterns: Diagnostic Precision and the Challenge of Neurological Mimics

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Neurology remains a discipline defined by pattern recognition; yet, equally, it requires a constant vigilance against the over-interpretation of patterns. As diagnostic technologies evolve, the risk of premature diagnostic closure has increased. This issue of the Bombay Hospital Journal brings into focus a central challenge in contemporary neurology—the differentiation of disease from its mimics—and reinforces the importance of integrative clinical reasoning.

A unifying theme across this issue is the distinction between descriptive patterns and definitive diagnoses. The original article by Patil et al. on non-immune causes of longitudinally extensive transverse myelitis (LETM) provides a compelling illustration of this principle.[1] Traditionally, LETM—defined as a spinal cord lesion extending across three or more vertebral segments—has been strongly associated with immune-mediated disorders such as neuromyelitis optica spectrum disorder and myelin oligodendrocyte glycoprotein-associated disease.[2,3] However, in their cohort, non-immune etiologies accounted for a substantial proportion of cases, including infectious, vascular, nutritional, neoplastic, and compressive causes.[1]

The clinical implications are significant. The reflex association of LETM with immune-mediated disease often leads to early initiation of immunotherapy, sometimes before alternative etiologies are excluded. As highlighted by Patil et al., such an approach may be detrimental.[1] Corticosteroids can worsen outcomes in vascular conditions such as spinal dural arteriovenous fistulas, while immunosuppression in infectious myelitis may exacerbate disease progression.[4,5] Furthermore, potentially reversible conditions such as vitamin B12 deficiency or compressive myelopathy may be overlooked, resulting in avoidable disability. The high reported rates of misdiagnosis in LETM—ranging from 17% to 74%—underscore the magnitude of this issue.[6]

The strength of the study lies in its emphasis on clinically actionable "red flags." Features such as hyperacute onset, severe pain, progression despite corticosteroid therapy, normal cerebrospinal fluid findings, and characteristic imaging patterns—such as dorsal flow voids in dural arteriovenous fistulas or dorsal column–restricted lesions in nutritional myelopathy—provide a practical framework for clinicians.[1] These observations reinforce a critical concept: LETM is a radiological pattern rather than a diagnosis, and must be interpreted in conjunction with clinical and laboratory data.

A parallel diagnostic challenge is addressed in the original article by Khadilkar et al., which examines the spectrum of amyotrophic lateral sclerosis (ALS) mimics in a tertiary neuromuscular center.[7] ALS remains a clinical diagnosis supported by electrophysiological criteria, yet lacks a definitive biomarker.[8] In this cohort, a substantial proportion of patients referred with suspected ALS were ultimately found to have alternative diagnoses, including Hirayama disease, post-polio syndrome, spinal muscular atrophy, multifocal motor neuropathy, and structural spinal disorders.[7]

The consequences of misdiagnosing ALS are profound. Beyond inappropriate management, such an error carries significant psychological and social implications, including premature prognostication and end-of-life counseling.[9] Importantly, many ALS mimics are treatable or have a more benign course, making early and accurate differentiation essential. Khadilkar et al. identify key predictors of mimic disorders, including younger age at onset, absence of bulbar involvement, presence of conduction block, and structural abnormalities on imaging.[7] These findings provide a clinically useful framework to reduce diagnostic error.

Together, these two original studies converge on a shared principle: diagnostic accuracy in neurology depends on the integration of clinical, radiological, and electrophysiological data. No single modality is sufficient in isolation. Instead, the recognition of discordant features—those that do not fit the expected pattern—often provides the most valuable diagnostic insight.

The review articles in this issue further contextualize these challenges within the rapidly evolving landscape of neurological practice. Mahajan et al., in their review on peripheral neuropathy, highlight advances in diagnostic classification, including the expanding role of genetic testing, antibody profiling, and refined electrophysiological techniques.[10] While these developments enhance diagnostic precision, they also introduce complexity, necessitating careful interpretation to avoid overdiagnosis or misclassification.

Similarly, the review by Singh et al. on acute stroke management reflects the transformation of cerebrovascular care, with a shift toward tissue-based paradigms and expanded therapeutic windows enabled by advanced imaging.[11] These advances have significantly improved outcomes but also place greater emphasis on rapid and accurate diagnostic decision-making, particularly in distinguishing stroke from its mimics.

The case reports in this issue further illustrate the diversity and complexity of neurological disease. Khade et al. describe experiential and autonomic auras in temporal lobe epilepsy, emphasizing the nuanced clinical manifestations of focal epilepsy.[12] Additional reports, including Parry–Romberg syndrome and seronegative autoimmune encephalitis presenting as new-onset refractory status epilepticus (NORSE), highlight the importance of maintaining diagnostic openness, particularly in atypical presentations.[13],[14] These cases underscore the limitations of reliance on biomarkers alone and reinforce the importance of clinical judgment.

A particularly important theme emerging from these reports is the recognition of antibody-negative autoimmune encephalitis. The absence of identifiable antibodies does not exclude an autoimmune etiology, and treatment decisions often need to be guided by clinical probability. This represents a broader shift in neurology toward probabilistic, rather than purely deterministic, diagnostic frameworks.

Neuroimaging, a recurring element across multiple articles in this issue, exemplifies both the strengths and limitations of modern diagnostics. While advanced imaging techniques have greatly enhanced disease detection and characterization, they also carry the risk of over-reliance on pattern recognition. As demonstrated in LETM and ALS mimics, similar imaging findings may arise from fundamentally different pathologies. The integration of imaging with clinical context remains essential.

This issue also highlights the importance of regional epidemiology in shaping diagnostic reasoning. The spectrum of neurological disease in India differs from that in Western populations, with a higher prevalence of infectious, nutritional, and structural disorders.[15] Consequently, diagnostic frameworks derived from Western cohorts may not always be directly applicable. The data presented in this issue provide valuable region-specific insights that are highly relevant to clinical practice.

Cognitive biases in clinical decision-making represent an underrecognized contributor to diagnostic error. Anchoring bias, premature closure, and availability bias can all influence clinical reasoning. The reflex association of LETM with immune-mediated disease or progressive weakness with ALS exemplifies such biases. Awareness of these cognitive processes, combined with systematic approaches to differential diagnosis, can mitigate their impact.

From an educational perspective, this issue underscores the importance of teaching neurology as a method of thinking rather than merely a body of knowledge. The concept of "red flags," as emphasized in both original articles, provides a practical framework for trainees to identify diagnostic inconsistencies and avoid common pitfalls.

Despite rapid technological advances, the importance of bedside neurology remains undiminished. Careful history-taking and examination continue to provide critical insights that cannot be replaced by investigations alone. The tempo of progression, distribution of deficits, associated systemic features, and response to prior therapies often provide the most reliable clues to diagnosis.

In conclusion, this issue of the Bombay Hospital Journal reinforces a fundamental principle: patterns are essential, but they are not definitive. The clinician must balance recognition with skepticism, remaining alert to alternative possibilities when features do not align with expected diagnoses. In conditions such as LETM and ALS, where diagnostic labels carry significant therapeutic and prognostic implications, this balance becomes particularly critical.

As neurology continues to evolve, the integration of technological advances with thoughtful clinical reasoning will remain central to effective practice. The contributions in this issue serve as a timely reminder that while knowledge informs diagnosis, it is judgment—grounded in experience, context, and critical reflection—that ultimately ensures optimal patient care.

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REFERENCES

1. Patil VA, Phulsunge SD, Khadilkar SV, Kumar S, Jaggi ST, Lalkaka J, et al. Non-immune causes of longitudinally extensive transverse myelitis: Lessons learnt from a tertiary care cohort. Bombay Hosp J. 2026;68(1):1–7.
2. Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitis optica. Neurology. 2006;66(10):1485–9.
3. Jarius S, Paul F, Weinshenker BG, Levy M, Kim HJ, Wildemann B. Neuromyelitis optica. Nat Rev Dis Primers. 2020;6(1):85.
4. Brinjikji W, Nasr DM, Morris JM, et al. Clinical and imaging features of spinal dural arteriovenous fistulas. AJNR Am J Neuroradiol. 2017;38(4):766–72.
5. Kelley BJ, Erickson BJ, Weinshenker BG. Compressive myelopathy mimicking transverse myelitis. Neurologist. 2010;16(2):120–2.
6. Abbas SA, et al. Misdiagnosis of LETM as immune-mediated myelitis: a systematic review. Neuroimmunol Rep. 2025;5:100178.

7. Khadilkar S, Mahajan J, Khade S, Bhoot A. Not all that looks like ALS is ALS: Spectrum of amyotrophic lateral sclerosis mimics at a tertiary neuromuscular center. Bombay Hosp J. 2026;68(1):8–15.
8. Shefner JM, Al-Chalabi A, Baker MR, et al. A proposal for new diagnostic criteria for ALS. Lancet Neurol. 2020;19(5):383–94.
9. Turner MR, Talbot K. Mimics and chameleons in motor neurone disease. Pract Neurol. 2013;13(3):153–64.
10. Mahajan J, Khadilkar S, Khade S, Bhoot A. What is new in peripheral neuropathy? Bombay Hosp J. 2026;68(1):16–25.
11. Singh R, Joshi R, Phulsunge S, Kumar S. Contemporary advances in acute stroke management: A fully integrated review. Bombay Hosp J. 2026;68(1):26–32.
12. Khade S, Khadilkar S, Mahajan J. Echoes of the present: Experiential and autonomic auras in temporal lobe epilepsy. Bombay Hosp J. 2026;68(1):33–34.
13. Khade S, Mahajan J, Khadilkar SV. The case of a melting face: Parry–Romberg syndrome. Bombay Hosp J. 2026;68(1):35–36.
14. Khade S, Pardasani V, Phulsunge S. Antibody-negative but not immune-negative: Seronegative autoimmune encephalitis presenting as NORSE. Bombay Hosp J. 2026;68(1):37–39.
15. Kanikannan MA, et al. Etiological profile of LETM in South India. Neurology Asia. 2018;23(1):23–30.