“The Double-Negative Paradox: Unveiling Hyperekplexia and Neuromyotonia in VGKC Encephalitis”

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Aims

VGKC-complex antibody encephalitis presents with a heterogeneous spectrum including limbic encephalitis, neuromyotonia, Morvan syndrome, and progressive encephalomyelitis with rigidity and myoclonus (PERM). Antibodies to LGI1 and CASPR2 are typically implicated; however, rare cases are double-negative with atypical features. We report two such cases with unusual phenotypes and therapeutic response to immunotherapy.

Material & Methodology

- We retrospectively evaluated the clinical profile, neuroimaging, electrophysiological findings, serology, treatment, and outcomes of two patients with suspected VGKC-complex encephalitis who tested negative for both LGI1 and CASPR2 antibodies.

Results

Case 1: 48-year-old male presented

- progressive generalized stiffness,
- exaggerated startle response (hyperekplexia), and action-induced myoclonus ----- three months.
- Brain MRI ----- normal
- EEG------diffuse slowing.
- LGI1, CASPR2, and glycine receptor antibodies ------ negative.


ULTIMATE
Freedom

Case 2

22-year-old male

- Focal seizures, painful spasms, generalized rigidity
- Insomnia, hallucinations
- Features mimicking Morvan syndrome and tetanus.
- LGI1, CASPR2, autoimmune/paraneoplastic panels negative.

- Treatment- intravenous methylprednisolone pulses (1 g/day for 5 days)
- significant clinical improvement, with reduction in myoclonus, rigidity, and neuropsychiatric symptoms.

Discussion

These cases expand the clinical spectrum of double-negative VGKC-complex encephalitis. Hyperekplexia is classically linked with glycine receptor antibody syndromes but was observed here in the absence of such antibodies. The combination of PERM-like symptoms with neuromyotonia and encephalopathy in antibody-negative cases presents diagnostic challenges. Notably, both cases responded well to corticosteroid therapy.

Conclusion

- Double-negative VGKC-complex encephalitis can manifest with atypical features including hyperekplexia and tetanus-like rigidity. Despite negative LGI1, CASPR2, and glycine receptor serologies, immunotherapy with methylprednisolone may yield favorable outcomes. High clinical suspicion remains critical for early diagnosis and treatment