Anti-titin antibody encephalitis mimicking a cerebrovascular disorder

Uncini Chiara[1], Terraciano Chiara[2], Vollaro Stefano[2], Marchesi Elena[2], Cillerai Marta[2],Bazzurri Veronica[2], Parrino Liborio[1], Immovilli Paolo[2]

1. Department of Medicine and Surgery, Unit of Neurology, University of Parma, Parma, Italy.
2. Neurology Unit, Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy.

Case report

Patient: 82 years-old man

PMH: hypertension, dyslipidemia and benign prostatic hyperplasia

HPI

- Came to ER for a 1-hr episode of non-fluent aphasia. CT scan was unremarkable.
- He was diagnosed with TIA and dual antiplatelet therapy had been prescribed.
- After 5 days he was re-admitted to the hospital for another transient episode of aphasia; an EKG showed atrial fibrillation, therefore he was switched to novel anticoagulant therapy.
- The day after he came back to the ER for a persistent confusional state, slowed thinking, compromised comprehension, visuo-spatial and executive function impairment and shuffling gait. A new CT scan turned out negative for new lesions.

Diagnostic workup

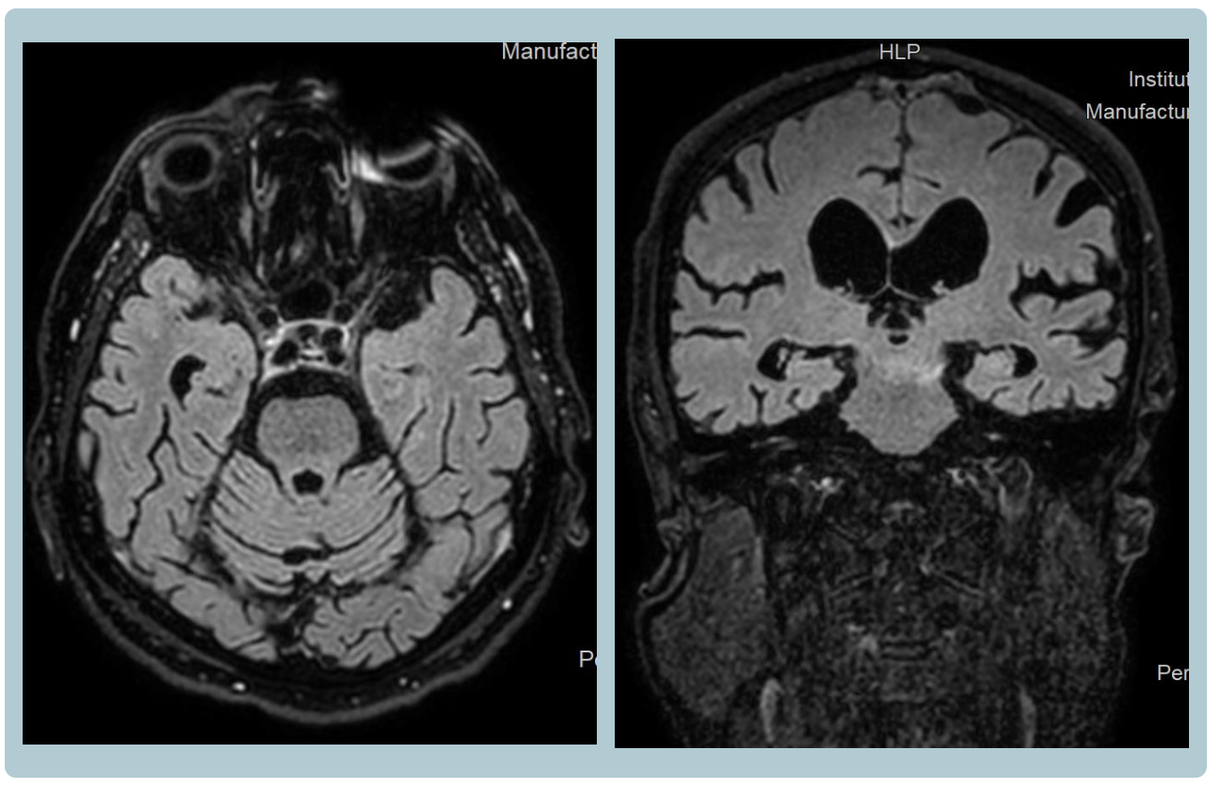
Imaging

- **Brain MRI**: cortical-subcortical atrophy and mild microvascular changes
- **CT NCAP**: unremarkable, no thymic hyperplasia or thymoma
- **FDG PET**: unremarkable

EEG: diffuse slow activity, slow spike and wave paroxysmal activity

Lab

- **CSF**: Clear, colorless; protein 46 mg/dL; WBC 12/mm³ (66% mononuclear); CRP = 0
- **CSF Virology & Cultures**: Negative
- **Paraneoplastic panel**: Negative
- **Autoimmune encephalitis panel**: Positive for anti-titin antibodies (positivity also in the serum)
- **Serum anti-AchR**: Low titer positivity
- **Markers for neurodegeneration**: Normal Tau, slight reduction of Amyloid-beta



Discussion

- Anti-titin antibodies are typically associated with thymoma, particularly in myasthenia gravis.
- Very few cases of anti-titin autoimmune encephalitis have been reported.
- This patient had positive anti-titin antibodies without any evidence of thymoma.

Outcome

Progressive improvement without complete resolution of symptoms.

Treatment

- **First line**: Steroid therapy with 1 gr IV Methylprednisolone for 5 days followed by slow tapering
- **Second line**: 5 sessions of plasma exchange followed by 5 days of IVIG
- **Anti-seizure medication**: Lacosamide 100 mg BID, Levetiracetam 1500 mg BID, Perampanel 8 mg 1/die, Phenytoin 250 mg 3/die

Conclusion

- Once excluded the commonest causes of encephalitis associated NORSE, a complete autoimmune panel, including anti-titin antibodies might be advisable even in the absence of thymoma.
- Further studies to assess the cause-effect relationship of anti-titin Abs and encephalitis are warranted.

References

1. Vargas-Cañas A et al -Anti-Titin antibodies and Autoimmune Encephalitis: Casuality or Causality? About a clinical case. Journal of Neuropsychiatry - Chile (digital version online) vol 61(3), 2023 https://www.journalofneuropsychiatry.cl/docs/18/149.pdf - accessed 08-june-2025
2. Berger B et al. Screening for anti-titin antibodies in patients with various paraneoplastic neurological syndromes. J Neuroimmunol. 2016 Jun 15;295-296:18-20. doi: 10.1016/j.jneuroim.2016.04.004. Epub 2016 Apr 13. PMID: 27235344.