Anti-GAD limbic encephalitis in a hospitalized 79-year-old woman after COVID 19 pneumonia: a case report

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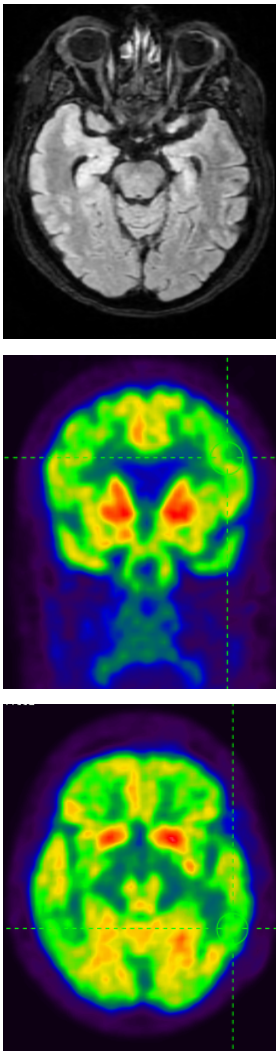
Introduction: Anti-glutamic acid decarboxylase (GAD) antibodies are associated with a spectrum of neurological syndromes, including stiff-person syndrome, cerebellar ataxia, autoimmune epilepsy, and limbic encephalitis. Anti-GAD limbic encephalitis antibodies typically presents with subacute onset of memory impairment, psychiatric symptoms, and seizures, reflecting GABAergic dysfunction. Diagnostic evaluation typically reveals high-titer anti-GAD antibodies in serum and, in many cases, intrathecal synthesis confirmed by cerebrospinal fluid (CSF) analysis. Brain MRI may show medial temporal lobe hyperintensities and EEG commonly demonstrates temporal lobe epileptiform activity.
During COVID-19 era emerged evidence of an increased incidence of autoimmune encephalitis (AE). Among these, limbic encephalitis appears as one of the most frequent subtypes, and anti-GAD an anti-VGKC the most frequently detected antibodies. Systematic Reviews of the literature showed an association between the SARS-CoV-2 infection and the AE, suggesting a parainfective etiology to explain the increased number of cases.

Case report: A 79-year-old woman, with many cardiovascular risk factors and a remote history of ovarian cancer, presented to the Emergency Department of Cittadella due to chest pain, palpitations and fever. After examinations, she was hospitalized in Medicine Department for highly responsive atrial fibrillation and COVID-19 pneumonia.

Five days later she developed progressive weakness in all four limbs. Neurological examination revealed marked proximal weakness without sensory involvement and the absence of all deep tendon reflexes. She was transferred to Neurology Department with a suspected diagnosis of parainfective polyradiculoneuropathy. CSF examination showed an increased protein content (180 mg/dl) and 18 leukocytes. Isoelectrofocusing showed a Mirror Pattern. Electromyography documented no signs of peripheral damage and spinal MRI showed a mild cervical stenosis, not consistent with the clinical presentation.
She rapidly developed disorientation, short term amnesia, apathy and depressed mood tone. The EEG showed evidence of epileptic discharges. Brain MRI T2/Flair sequences showed bilateral asymmetric hyperintensity of hippocampus suggestive of limbic encephalitis. Brain PET/RM reveled hypermetabolic pattern in both medial temporal lobes. Autoimmune screening detected high level anti-GAD antibodies in both plasma and CSF (respectively >2800.0 kUI/L, 160.7 kUI/L) detected by ELISA.
Clinical, radiological and biohumoral data were suggestive for anti-GAD limbic encephalitis with proximal tetraparesis of unknown origin.
Despite a rare association between anti-GAD neurological syndromes and tumors, given the patient's clinical history, a diagnostic-work up was performed to rule out an underlying malignancy. The only significant finding was FDG lung uptake at the total body PET/CT, but it was localized in the area of the pneumonia, suggesting a parainfective etiology.

She was treated with high dose steroids followed by a slow oral tapering and intravenous immunoglobulin, resulting in mild improvement of limbic symptoms and EEG pattern. However, immunotherapy and physical therapy had minimal benefit on the muscle weakness.

Conclusion: Autoimmune encephalitis should be considered in the differential diagnosis of subacute confusional state, especially in the context of a recent infection, even if advanced age and in-hospital onset might initially suggest a diagnosis of delirium.



Neuroimaging:
Figure a. Brain MRI FLAIR showing bilateral asymmetric hyperintensity of hippocampus.
Figure b,c. Brain PER/RMI showing hypermetabolism in both medial temporal lobes

References

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