Original article

Epileptic Disord 2019; 21 (5): 437-42

GAD65-Ab encephalitis and subtle focal status epilepticus

Mathilde Goudot¹, Solène Frismand¹, Lucie Hopes¹, Antoine Verger², Bastien Joubert³, Jérôme Honnorat³, Louise Tyvaert^{1,4}

- ¹ Department of Neurology, University Hospital of Nancy
- ² Department of Nuclear medicine, University Hospital of Nancy
- ³ French Reference Center of Paraneoplastic Neurological Syndrome, Hospices Civils de Lyon, Department of Neurology, INSERM U1217/CNRS, UMR5310, Lyon
- ⁴ University of Lorraine, Faculty of Medicine, CRAN CNRS UMR 7039, Nancy, France



Limbic encephalitis

- Clinical subacute onset of:
 - epilepsy
 - cognitive impairment
 - > psychiatric involvement
- Evidence of CNS inflammation
- Positivity of specific antibody
 - Against cell surface membrane antigen
 - Against intracellular antigen
 - → Specific phenotype spectrums are progressively defined for each autoantibody



GAD65-Ab encephalitis

- GAD65-Ab are implicated in:
 - diabetes

stiff man syndrome neurological disorders: - cerebellar ataxia encepahilitis

- Quantitative data from the literature suggest that epilepsy is the most common feature of GAD65-Ab encephalitis.
- To provide qualitative data of epilepsy associated with GAD65-Ab encephalitis, we describe the semiology of three patients followed in our neurological department (CHU Nancy, France).



Case Report

- All three women (33, 30 and 63 yo) presented a recurrent temporal lobe status epilepticus.
- Semiology was subtle and at first difficult to correlate with epilepsy diagnosis (n=2):
 - Prolonged dysmnesic experience (several hours), without clear paroxystic events.
 - Anxiety and mood disorders appeared at the same time.
 - > Initial EEG was normal
- → Only long-term video-EEG showed paroxystic temporal activity during sleep
- The third patient clearly presented with **lateral temporal and frontal seizures** arguing for non-limbic encephalitis. EEG showed direct arguments for epilepsy. Hyperintensity of neocortical and deep grey structures on MRI was in agreement with this **encephalitic pattern**.



Positive diagnosis of anti-GAD encephalitis

- For all, positivity of GAD65-Ab in CSF confirmed the diagnosis.
- Other paraclinical examinations were non-specific:
 - inflammatory brain MRI (n=2)
 - hypermetabolism on ¹⁸F-FDG PET Brain (n=1)
 - inflammatory CSF (n=1)
- All received immunosuppressive therapy, but temporal lobe epilepsy remains pharmacoresistant.
- Specific treatment could improve cognitive and psychiatric prognosis.



Conclusion

Our observation and data from the literature suggest that:

- Limbic or non-limbic encephalitis can be associated with GAD65-Ab.
- Epilepsy is the most frequent feature of GAD65-Ab encephalitis.
- New-onset focal status epilepticus with predominant subjective semiology should suggest this diagnosis
- Careful anamnesis and paraclinical examination with a long-term video-EEG remain essential in cases of subtle epileptic semiology.
- •Even under optimized immunosupressive therapy, **epilepsy remains intractable**

