Autoimmune encephalitis

Autoimmune encephalitis refers to a group of conditions that occur when the body's immune system mistakenly attacks healthy brain cells , leading to inflammation of the brain. People with autoimmune encephalitis may have various neurologic and/or psychiatric symptoms.

The clinical criteria for autoimmune encephalitis (AE) were proposed by Graus et al. in 2016. In this study, the AE criteria were validated in the real world, and common AE mimics were described. In addition, criteria for probable anti-LGI1 encephalitis were proposed and validated.

Methods: In this retrospective cohort study, patients referred to our national referral center with suspicion of AE and specific neuroinflammatory disorders with similar clinical presentations were included from July 2016 to December 2019. Exclusion criteria were pure cerebellar or peripheral nerve system disorders. All patients were evaluated according to the AE criteria.

Results: In total, 239 patients were included (56% female; median age 42 years, range 1-85). AE was diagnosed in 104 patients (44%) and AE mimics in 109 patients (46%). The most common AE mimics and misdiagnoses were neuroinflammatory CNS disorders (26%), psychiatric disorders (19%), epilepsy with a noninflammatory cause (13%), CNS infections (7%), neurodegenerative diseases (7%), and CNS neoplasms (6%). Common confounding factors were mesiotemporal lesions on brain MRI (17%) and false-positive antibodies in serum (12%). Additional mesiotemporal features (involvement extralimbic structures, enhancement, diffusion restriction) were observed more frequently in AE mimics compared with AE (61% vs 24%; p = 0.005). AE criteria showed the following sensitivity and specificity: possible AE, 83% (95% CI 74-89) and 27% (95% CI 20-36); definite autoimmune limbic encephalitis (LE), 10% (95% CI 5-17) and 98% (95% CI 94-100); and probable anti-NMDAR encephalitis, 50% (95% CI 26-74) and 96% (95% CI 92-98), respectively. Specificity of the criteria for probable seronegative AE was 99% (95% CI 96-100). The newly proposed criteria for probable anti-LGI1 encephalitis showed a sensitivity of 66% (95% CI 47-81) and specificity of 96% (95% CI 93-98).

Discussion: AE mimics occur frequently. Common pitfalls in AE misdiagnosis are mesiotemporal lesions (predominantly with atypical features) and false-positive serum antibodies. As expected, the specificity of the criteria for possible AE is low because these criteria represent the minimal requirements for entry in the diagnostic algorithm for AE. Criteria for probable AE (-LGI1, -NMDAR, seronegative) and definite autoimmune LE are applicable for decisions on immunotherapy in early disease stage, as specificity is high [1)]

Strik H, Keber U, Hammoud WA, Riera-Knorrenschild J, Carl B, Dodel R, Pagenstecher A, Neubauer A. Immune checkpoint inhibitor-associated CNS autoimmune disorder (ICICAD) following nivolumab treatment: A new entity of drug-induced autoimmune encephalitis? Eur J Cancer. 2017 Dec;87:205-208. doi: 10.1016/j.ejca.2017.09.026. Epub 2017 Oct 16. PubMed PMID: 29050806.

Recognition of clinical syndromes, reliable methods of diagnosis, and early targeted immunotherapy can lead to a favourable outcome in acute and subacute neurological disorders that may be associated with significant morbidity and mortality if left untreated. This review focuses on the rapidly

expanding field of autoimmune encephalitis. We describe the differences between limbic encephalitis associated with antibodies targeting intracellular antigens, and neuronal surface antibody syndromes (NSAS) where the antigens are primarily receptors or synaptic proteins located on the neuronal cell surface. We chronologically highlight important developments in NSAS by focusing on voltage gated potassium channel complex-associated antibody mediated encephalitis, anti-N-methyl-d-aspartate receptor (anti-NMDAR) encephalitis, and anti-dopamine 2 receptor antibody-associated basal ganglia encephalitis. Contentious issues such as the complexities of using serum antibodies as biomarkers, the initiation of central nervous system autoimmunity, and possible pathogenic mechanisms of these antibodies will be reviewed. The therapeutic challenges that clinicians face such as the timing of therapy and the role of second-line therapy will be discussed, with crucial concepts highlighted in the form of clinical vignettes. Future directions will involve the identification of novel antigens and methods to establish their pathogenicity, as well as evaluation of the most efficacious therapeutic strategies in patients with established NSAS [2)].

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2)
Ramanathan S, Mohammad SS, Brilot F, Dale RC. Autoimmune encephalitis: recent updates and emerging challenges. J Clin Neurosci. 2014 May;21(5):722-30. doi: 10.1016/j.jocn.2013.07.017. Epub 2013 Sep 15. Review. PubMed PMID: 24246947.