DO MANY CRYPTOGENIC EPILEPSIES EVENTUALLY TURN OUT TO BE IMMUNE-MEDIATED? - YES

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Very recently, antibodies to neural surface antigens have been detected a diagnostic tool for autoimmune encephalitides, which often present with epileptic seizures. For patients with a prominent epilepsy phenotype, the term “autoimmune epilepsies” has been proposed. It has been suggested to include this group as one of the etiological categories in the upcoming revision of the “Organization of the epilepsies” by the Classification Taskforce of the International League against Epilepsy. Key for the “success” of this novel field of neurology and epileptology was the development of techniques that allow determining specific antineural antibodies by routine laboratory methods. These are mainly antibodies to the NMDA receptor, to elements of the voltage-gated potassium channel complex (i.e., LGI1, CASPR2 and others), and to the GABA(B) receptor (and some others, which are less frequently found).

Since then, it has frequently been asked which relevance these autoantibody diagnostics may have in daily clinical life. This includes the question if “many” so far etiologically unexplained (“cryptogenic”) epilepsies will turn out to be immune-mediated. The answer to this question will – of course – very much depend on what is conceived as “many” in this context.

Data for this discussion come from recent peer-reviewed studies. In two adult cohorts (one with newly diagnosed epilepsies and one with chronic epilepsies), a British group found 11% of antibody-positive patients in each of the two groups (Brenner et al., Epilepsia 2013; 54:1028-35). In a pediatric cohort of patients with new-onset seizures, an Australian-British group found 10% of positives (Suleiman et al., Epilepsia 2013;54:2091-100). In both studies, the number of positives was particularly high in those patients who otherwise had been classified as having “epilepsy of unknown cause” or “cryptogenic epilepsy”: 15% in the adult study and 21% in the pediatric series.

Does this mean that “many cryptogenic patients turn out to be antibody-positive”? One may tentatively compare these figures with the frequency of positive findings in another epileptological diagnostic tool. This tool that is widely agreed on as providing “many” relevant diagnostic results: brain MRI. In a population based study in Conneticut/USA, 16% of pediatric epilepsy patients had a potentially epileptogenic brain lesion (Berg et al., Brain 2009:132;2785–97). Thus, by means of this comparison, antibody diagnostic would provide a good yield of positive results.

However, one may ask if the mere frequency of antibody positives is what the clinician would like to know. It is probably more important to define the yield if antibody diagnostics are coupled with an immunological therapeutic intervention and the number of improved patients (ideally: in comparison to conventional treatment) is determined. In other words, the next question would be: For how many epilepsy patients does the demonstration of antineural antibodies blaze a novel, more effective treatment trail? Going back to Berg’s brain MRI study, such “final outcome data” were presented: They found that 19/518 patients (3%) of those with technically adequate images finally came to respective or disconnective surgery with a seizure-free outcome of 11/19 patients, i.e. 2% of the imaged cohort.

In conclusion, an estimate of the efficacy of a diagnostic tool – including autoantibodies – will eventually require outcome data that may finally lead to figures like “number needed to test to achieve a seizure free outcome”. Such studies are (not only for antibodies) a pending challenge in epileptology.