

# A Guideline for Early Diagnosis of Autoimmune Epilepsy Based on Clinical Manifestations and Common Para-Clinical Tests

Man Amanat<sup>1,2</sup>, Mona Salehi<sup>1,2</sup>, Nima Rezaei<sup>2,3,4</sup>

<sup>1</sup> NeuroImmunology Research Association (NIRA), Universal Scientific Education and Research Network (USERN), Tehran, Iran

<sup>2</sup> Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup> Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

<sup>4</sup> Network of Immunity in Infection, Malignancy and Autoimmunity (NIIMA), Universal Scientific Education and Research Network (USERN), Tehran, Iran

Received: 13 Oct. 2017; Accepted: 19 Dec. 2017

We read with great interest the article of *Dubey D et al.*, (1), demonstrating the validation of their predictive models in the diagnosis and treatment of autoimmune epilepsy, known as “antibody prevalence in epilepsy of unknown etiology score” (APE-score) and “response to immunotherapy in epilepsy score” (RITE score) (2). They reported that APE and RITE scores have approximately 99.7% and 87.5% sensitivity and 77.9% and 83.8% specificity, respectively.

This study had various strength points, including its large number of patients as well as its statistical methods. Moreover, the introduced models included components, which can be achieved by history, physical exams, and some cost-effective para-clinical tests; therefore, they can be assumed as introductions to a pathway, which can guide us to earlier diagnosis and better treatment modalities of autoimmune epilepsy with lower cost.

*Suleiman J* in 2013 (3) also introduced criteria, which could facilitate the diagnosis of autoimmune epilepsy. The first step of diagnosis in that criteria was the presence of acute or subacute onset seizure and excluding other causes of seizures such as previous diseases of the central nervous system (CNS), trauma, tumor, toxic, metabolic disorders, and CNS infection. In the next step, the existence of each of these parts demonstrated the high possibility of autoimmune epilepsy: 1) well defined

clinical syndromes, such as limbic encephalitis; 2) presence of CNS inflammation; 3) history of autoimmune disorders in patients, and 4) response to immunotherapy.

With the combination of *Suleiman J* criteria and APE-score, new criteria could be introduced, which can navigate us to a better and easier approach for diagnosis and treatment of autoimmune epilepsy. To predict the possibility of the presence of autoimmune epilepsy, we suggest that 3 steps should be passed: 1) Provoked seizures should be excluded and the onset of seizures should be asked; 2) Different clinical manifestations associated with autoimmune epilepsy should be tracked; and 3) Routine para-clinical tests, including electroencephalography (EEG), magnetic resonance imaging (MRI), and cerebrospinal fluid (CSF) analysis should be performed (Figure 1). After assessing cases with the above-mentioned criteria, high, intermediate, or low possibility of autoimmune epilepsy can be recognized (Table 1). In epileptic patients, whom autoimmunity is highly suspected as the etiology of seizures, immunotherapy and anti-epileptic drugs can be started even if autoantibodies were not measured; while in individuals with the intermediate possibility of autoimmune epilepsy, identification of anti-neuronal surface antibodies is essential for definite diagnosis.

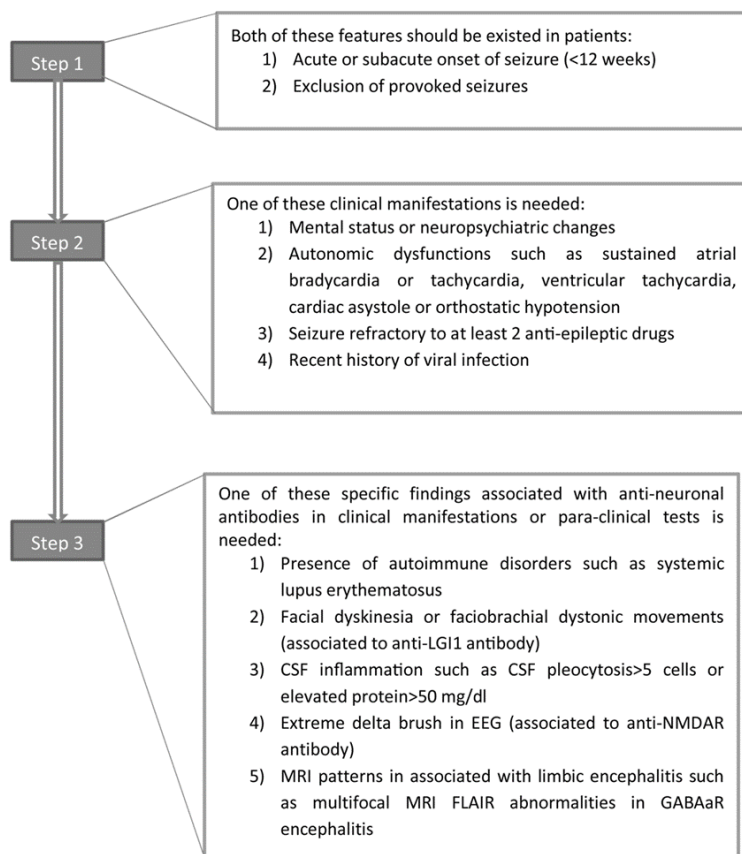
**Table 1. Recognition of possibility of autoimmune epilepsy in patients with seizures**

<b>High possibility</b>	- Fulfill the criteria of all 3 steps - Fulfill the criteria of step 1 and 3, but not 2 (when at least 2 of mentioned findings in step 3 were observed)
<b>Intermediate possibility</b>	- Fulfill the criteria of step 1 and 2, but not 3 (when at least 3 of mentioned findings in step 2 were observed) - Fulfill the criteria of step 1 and 3, but not 2 (when only 1 of the mentioned findings in step 3 was observed)
<b>Low possibility</b>	None of above

**Corresponding Author:** N. Rezaei

Research Center for Immunodeficiencies, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran  
Tel: +98 21 66929234, Fax: +98 21 66929235, E-mail address: rezaei\_nima@tums.ac.ir

## Early diagnosis of autoimmune epilepsy



**Figure 1.** The criteria for prediction of autoimmune epilepsy; based on clinical manifestations and routine para-clinical tests  
 LGI1: leucine-rich glutamate inactivated 1; NMDAR: N-methyl-D-aspartate receptor; MRI: magnetic resonance imaging; FLAIR: fluid attenuated inverse recovery; GABAaR: gamma-aminobutyric acid receptor

## References

- Dubey D, Singh J, Britton JW, Pittock SJ, Flanagan EP, Lennon VA, et al. Predictive models in the diagnosis and treatment of autoimmune epilepsy. *Epilepsia* 2017;58:1181-9.
- Dubey D, Alqallaf A, Hays R, Freeman M, Chen K, Ding K, et al. Neurological autoantibody prevalence in epilepsy of unknown etiology. *JAMA Neurol* 2017;74:397-402.
- Suleiman J, Brilot F, Lang B, Vincent A, Dale RC. Autoimmune epilepsy in children: case series and proposed guidelines for identification. *Epilepsia* 2013;54:1036-45.