



Commentary: Epidemiology of Antibody-Positive Autoimmune Encephalitis in Southwest China: A Multicenter Study

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A Commentary on

Epidemiology of Antibody-Positive Autoimmune Encephalitis in Southwest China: A Multicenter Study

by Gu, Y., Zhong, M., He, L., Li, W., Huang, Y., Liu, J., et al. (2019). *Front. Immunol.* 10:2611. doi: 10.3389/fimmu.2019.02611

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Recently, Gu et al. reported an epidemiological survey about autoimmune encephalitis (AE) in southwestern China, involving six large general hospitals in Chongqing (1). Their study revealed the underlying relationship between several factors and disease severity (1). Although there have been no large-scale epidemiological investigations of AE in China prior to this report (1), the conclusions of this research would have been more reliable had the following concerns been addressed.

First, the limited scale of this epidemiological investigation merits discussion. The detailed epidemiological features of AE in southwestern China were presented in this multicenter study involving six large general hospitals in the Chongqing area. These six general hospitals in Chongqing were limited to reflect the epidemiological features of AE patients in the southwestern region of China.

Moreover, it is noteworthy that researchers excluded patients with thyroid disease (1). However, some patients with Hashimoto's encephalopathy (HE), which is an important cause of autoimmune encephalopathy, may be neglected. High titers of thyroid peroxidase antibodies (TPO-Ab) is generally detected in HE patients (2). And morbidity of HE is estimated to be 2.1/100,000 in adults (3). Additionally, TPO-Ab detection was recommended to be tested in the systematic diagnosis per the clinical diagnosis criteria of AE published in 2016 (4). Therefore, it is quite likely to miss potential patients with AE by excluding patients with thyroid disease.

Also, the methods of antibody detection in the publication need to be further elaborated. According to the 2016 clinical diagnosis criteria of AE, antibody detection in definite AE-like encephalitis with anti-NMDA receptor antibody-positive status should include cerebrospinal fluid (CSF) testing with cell-based assay (CBA) and with confirmatory tests like tissue immunohistochemistry based on animals' brain tissue (4). The tissue immunohistochemistry has been widely used by some studies of AE (5–7). In the author's study, only CBA based on indirect immunofluorescence (IIF) assay was performed to analyze both the CSF and serum of each patient (1). Thus, owing to significant inter-operator variability in CBA performed by different technologists, the standard of determining antibody titers should be explained in detail.

Further, the assessment scale of disease severity in research needs more discussion. The authors have used the Glasgow Outcome Scale (GOS) to evaluate factors that may be associated with disease prognosis (1). The GOS was initially designed to predict the outcome after brain injury-like traumas (8–11). However, some researchers have indicated that GOS has some deficiencies because it cannot detect minor brain damage (12). Therefore, we suggest that it would be better if the researchers could combine GOS with some scales that are more appropriate to predict the outcome of AE. Although no specific scale has been designed yet to predict AE prognosis (13), some studies have supported the use of the modified Rankin Scale (mRS), which is more frequently used in the evaluation of AE prognosis (14–17). Another scale called the Response to Immunotherapy in Epilepsy and Encephalopathy score (RITE2 score) has also been used to evaluate and manage autoimmune-epilepsy (18, 19).

In summary, this is a meaningful report providing epidemiological data about the antibody distribution in AE

in the Chongqing area, along with revealing the factors associated with poor prognosis of AE. Despite some of the above-mentioned concerns, this study would be helpful to researchers and clinicians alike to gain more insight into AE.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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REFERENCES

- Gu Y, Zhong M, He L, Li W, Huang Y, Liu J, et al. Epidemiology of antibody-positive autoimmune encephalitis in Southwest China: a multicenter study. *Front Immunol.* (2019) 10:2611. doi: 10.3389/fimmu.2019.02611
- Li J, Li F. Hashimoto's encephalopathy and seizure disorders. *Front Neurol.* (2019) 10:440. doi: 10.3389/fneur.2019.00440
- Ferracci F, Moretto G, Candeago RM, Cimini N, Conte F, Gentile M, et al. Antithyroid antibodies in the CSF: their role in the pathogenesis of Hashimoto's encephalopathy. *Neurology.* (2003) 60:712–4. doi: 10.1212/01.WNL.0000048660.71390.C6
- Graus F, Titulaer MJ, Balu R, Benseler S, Bien CG, Cellucci T, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol.* (2016) 15:391–404. doi: 10.1016/S1474-4422(15)00401-9
- Ricken G, Schwaiger C, De Simoni D, Pichler V, Lang J, Glatter S, et al. Detection methods for autoantibodies in suspected autoimmune encephalitis. *Front Neurol.* (2018) 9:841. doi: 10.3389/fneur.2018.00841
- Liu T, Chen B, Yang H, Huang J, Liu S, Yang X, et al. Screening for autoantibodies in inflammatory neurological syndrome using fluorescence pattern in a tissue-based assay: cerebrospinal fluid findings from 793 patients. *Multiple Scler Relat Disord.* (2019) 28:177–83. doi: 10.1016/j.msard.2018.12.036
- Bien CI, Nehls F, Kollmar R, Weis M, Steinke W, Woermann F, et al. Identification of adenylate kinase 5 antibodies during routine diagnostics in a tissue-based assay: Three new cases and a review of the literature. *J Neuroimmunol.* (2019) 334:576975. doi: 10.1016/j.jneuroim.2019.576975
- McMillan T, Wilson L, Ponsford J, Levin H, Teasdale G, Bond M. The Glasgow Outcome Scale - 40 years of application and refinement. *Nat Rev Neurol.* (2016) 12:477–85. doi: 10.1038/nrneurol.2016.89
- Jennett B, Teasdale G, Galbraith S, Pickard J, Grant H, Braakman R, et al. Severe head injuries in three countries. *J Neurol Neurosurg Psychiatry.* (1977) 40:291–8. doi: 10.1136/jnnp.40.3.291
- Bates D, Caronna JJ, Carlidge NE, Knill-Jones RP, Levy DE, Shaw DA, et al. A prospective study of nontraumatic coma: methods and results in 310 patients. *Ann Neurol.* (1977) 2:211–20. doi: 10.1002/ana.410020306
- Langfitt TW. Measuring the outcome from head injuries. *J Neurosurg.* (1978) 48:673–8. doi: 10.3171/jns.1978.48.5.0673
- Beers SR, Wisniewski SR, Garcia-Filion P, Tian Y, Hahner T, Berger RP, et al. Validity of a pediatric version of the Glasgow Outcome Scale-Extended. *J Neurotrauma.* (2012) 29:1126–39. doi: 10.1089/neu.2011.2272
- Lim J-A, Lee S-T, Moon J, Jun J-S, Kim T-J, Shin Y-W, et al. Development of the clinical assessment scale in autoimmune encephalitis. *Ann Neurol.* (2019) 85:352–8. doi: 10.1002/ana.25421
- Huang X, Fan C, Wu J, Ye J, Zhan S, Song H, et al. Clinical analysis on anti-N-methyl-D-aspartate receptor encephalitis cases: Chinese experience. *Int J Clin Exp Med.* (2015) 8:18927–35. Available online at: <http://europepmc.org/article/PMC/4694417>
- Gresa-Arribas N, Titulaer MJ, Torrents A, Aguilar E, McCracken L, Leypoldt F, et al. Antibody titres at diagnosis and during follow-up of anti-NMDA receptor encephalitis: a retrospective study. *Lancet Neurol.* (2014) 13:167–77. doi: 10.1016/S1474-4422(13)70282-5
- Titulaer MJ, McCracken L, Gabilondo I, Armangué T, Glaser C, Iizuka T, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. *Lancet Neurol.* (2013) 12:157–65. doi: 10.1016/S1474-4422(12)70310-1
- Lee W-J, Lee S-T, Byun J-I, Sunwoo J-S, Kim T-J, Lim J-A, et al. Rituximab treatment for autoimmune limbic encephalitis in an institutional cohort. *Neurology.* (2016) 86:1683–91. doi: 10.1212/WNL.0000000000002635
- Husari KS, Dubey D. Autoimmune epilepsy. *Neurotherapeutics.* (2019) 16:685–702. doi: 10.1007/s13311-019-00750-3
- Dubey D, Kothapalli N, McKeon A, Flanagan EP, Lennon VA, Klein CJ, et al. Predictors of neural-specific autoantibodies and immunotherapy response in patients with cognitive dysfunction. *J Neuroimmunol.* (2018) 323:62–72. doi: 10.1016/j.jneuroim.2018.07.009

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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