Letter to the Editor

Keeping pace with the world: improving the clinical practice of anti-NMDAR encephalitis in China

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The phenomenon and significance of low frequency of paraneoplastic cases in our Chinese cohort of anti-NMDAR encephalitis deserves clinical attention. Only 19.5% of the patients in our cohort of 220 cases had a tumor. But the fact that 29.4% of female patients had an ovarian teratoma warrants more oncological evaluation in the subgroup of young female (1). Other Chinese studies have reported even lower prevalence of tumors (6.7–8.1%) which may contribute to a relatively higher relapsing rate in these cohorts as the absence of tumor is a risk factor for relapses (2).

Whether the difference in oncological data indicates possibility of difference trigger factors and source of peripheral autoantigens remains a question. Except for a small portion of patients with post-HSE anti-NMDAR encephalitis, most patients, either tumor-positive or tumor-negative, have typical presentation and course of anti-NMDAR encephalitis. As for these tumor-negative cases in Asian and Chinese cohorts, to identify a potential source of autoantigens is theoretically reasonable and clinically practical. That is why we screen prominent melanocytic nevi in tumor-negative cases with refractory or relapse course (3,4).

The frequency of paraneoplastic cases is expected to decline as more cohorts of anti-NMDAR encephalitis accumulated. In fact, the decline in proportion of paraneoplastic cases will always be experienced in the series study of paraneoplastic encephalitis. Anti-NMDAR encephalitis was first described by Dalmau as a paraneoplastic autoimmune encephalitis (AE) in 2007 (5). Then Dalmau *et al*. described the clinical characteristics of 100 patients and reported that 59% of patients had tumors in 2008 (6). When Titulaer *et al*. reported the long-term outcome of more than 500 patients in 2013, the prevalence of an underlying neoplasm decreased to 38% (2). The research processes to discovery novel antineuronal antibodies emphasize on describing a novel neurological syndrome, usually the paraneoplastic one as the first promising step. Clinical indication of novel antibodies test tends to be more restricted to typical cases including paraneoplastic cases before a fully opening availability of the test.

According to our cohort and experience, re-enforced first-line immunotherapy based on repeated first-line therapy is effective with a good short-term outcome. Our team had respectively analyzed the immunotherapy strategy for 35 cases with severe anti-NMDAR mostly hospitalized to ICU in PUMCH from 2011 to 2015. All cases received intravenous immunoglobulin (IVIg), for one to a maximum of seven cycles, with an average of three cycles; 91.43% of cases received glucocorticoid therapy and 42.86% received long-term MMF therapy as add-on therapy for refractory course. Only 14.29% received second-line therapy

including rituximab and/or intravenous cyclophosphamide. All cases improved and were transferred out from ICU, the median length of stay in ICU was 6 weeks and the median duration of hospitalization was around ten weeks. Although the add-on immunotherapy with MMF as an alternative to rituximab warranted further study, the re-enforced first-line immunotherapy based on multicycle IVIg also achieved good long-term prognoses in other Chinese cohorts of severe anti-NMDAR encephalitis (7).

To some extent, the treatment strategy of AE will still depend on different centers in different countries. However, we can expect a better prognosis in future studies from different centers. Antibodies panel related to AE is among the first-line tests in many neurological centers in China which contributes to a more prompt and efficient immunotherapy. Increasing cases have enriched neurologists' experience in treating AE. Encephalitis has been considered as a novel subspecialty and encephalitis clinics or encephalitis centers have been established by the neurologists across China.

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Footnote

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