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LETTER TO THE EDITOR

Paraneoplastic encephalitis associated with ovarian teratoma and *N*-methyl-D-aspartate receptor antibodies

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Sir,

Recently, a new category of paraneoplastic encephalitis associated with ovarian teratoma (OTE) has been described.[1] This disorder results in prominent psychiatric symptoms, seizures, autonomic dysfunction, dyskinesias and hypoventilation, and associates with antibodies to NR1/NR2 heteromers of the N-methyl-D-aspartate receptor (NMDAR).[1,2] We lately described the clinical features of four patients with OTE, but the presence of these antibodies was not determined.[3] We now report the presence of these antibodies in archived frozen CSF of three of the patients with OTE.

All three patients (three women; age range 17–29 years, mean 20.7 ± 7.2 years) developed psychiatric symptoms, central hypoventilation requiring prolonged ventilatory support (range 30–44 days), seizures, involuntary movements, and autonomic instability associated with cardiac arrhythmias (bradycardia-tachycardia syndrome in three and sinus arrest in one) or hypersalivation. These neurological disorders preceded the diagnosis of ovarian teratoma. On neuroimaging studies, only one patient showed hyperperfusion in whole brain on perfusion MRI. The white blood cell count in cerebrospinal fluid was 47.0 ± 35.6/mm^3. Mature teratoma was diagnosed in all patients after ovarian tumor resection. They received immunotherapy: three patients received corticosteroids, two received intravenous immunoglobulins, and showed complete recovery (see[3] for details).

Immunocytochemical studies were performed as reported.[1] In brief, HEK 293 cells were transfected with NR1 and NR2 plasmids in order to express NR1/NR2

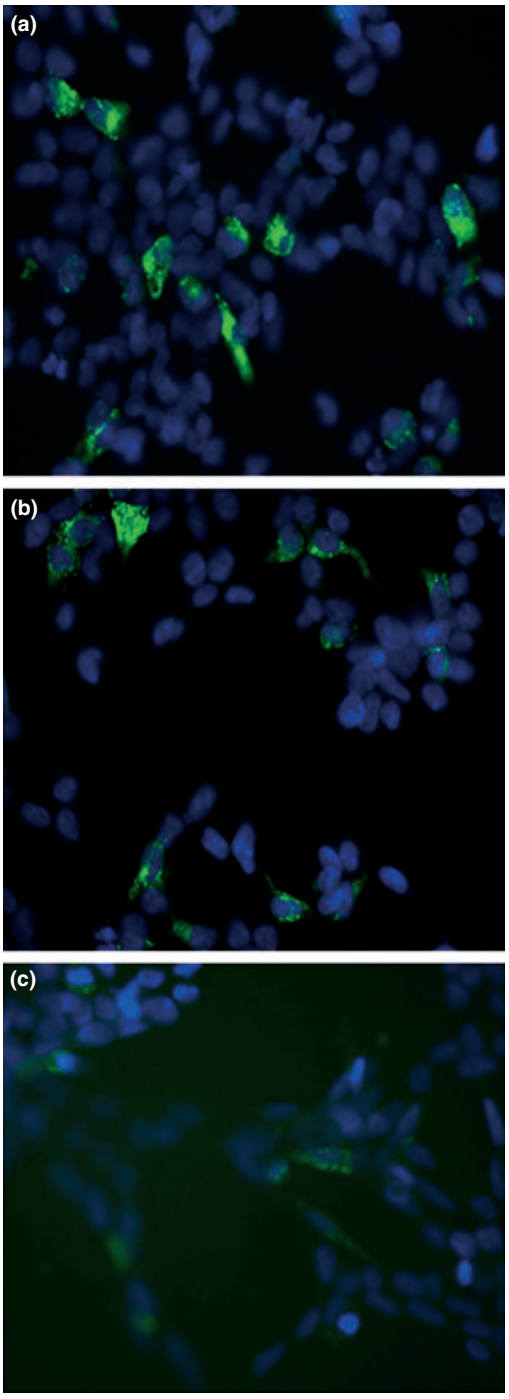

Figure 1 Reactivity of patients' CSF antibodies with NR1/NR2 heteromers of the *N*-methyl-D-aspartate receptor (NMDAR). HEK 293 Cells expressing NR1/NR2B heteromers show intense reactivity with the CSF (diluted 1:10) of patients 1 (panel a) and 4 (panel b) and weaker reactivity with CSF of patient 3 (panel c). Non-transfected cells (visible with nuclear staining by DAPI) show no reactivity.

heteromers. Cells expressing these heteromers, but not non-transfected cells, showed strong reactivity with CSF of patients 1 and 4 obtained at early stages of the disease (Fig. 1a and b), and weaker reactivity with the CSF of patient 3 obtained at a later stage of the disease (Fig. 1c). From patients 3 and 4, samples of CSF were available for follow-up of antibody titers. In both patients, the follow-up CSF samples were obtained while recovering from the neurological deficit. When compared with the antibody titers at symptom presentation, the follow-up CSF samples of both patients showed a substantial decrease of antibody titers. In patient 3 the antibodies were not longer detectable in her CSF and in patient 4 the antibody titers (obtained by serial dilutions of paired samples) were 1:160 at symptom presentation and 1:20 while recovering.

Taken together with previously reported studies[1–3], these findings suggest that patients with the above indicated syndrome should be evaluated for antibodies to NR1/NR2B heteromers of the NMDAR. Detection of these antibodies should prompt the search of an ovarian teratoma and immunotherapy.

References

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