Dear Editor,

Anti-NMDA receptor (NMDAR) encephalitis has only recently been described as a cause of paraneoplastic and autoimmune encephalitis (Dalmau et al. 2008). Herein we present a 13-year-old girl with NMDAR encephalitis characterized by acute mania at onset, which was initially misdiagnosed as a primary psychiatric disorder. No evidence of a tumor was found. Intravenous immunoglobulin (IVIG) was administered (table) and full recovery occurred 19 months after onset.

A 13-year-old previously healthy girl was hospitalized in our department (Department of Child and Adolescent Neurology of the National Institute of Neurology (Tunisia)) on the 5th of March, 2010 due to fluctuating behavioral disturbances. Her family reported that she had had been experiencing sudden changes in mood and was becoming increasingly irritable. Then, she exhibited acute manic symptoms (logorrhea, euphoric state, insomnia, inappropriate sexual behavior agitation, and extreme irritability alternating with a state of unresponsiveness). Neurological examination and brain MRI were normal. A primary psychiatric disorder was suspected. The patient developed tonic jerks of the right hemibody 3 d after onset of manic symptoms. Electroencephalography (EEG) showed a theta rhythm of 4-6 Hz. CSF analysis showed mild lymphocytic pleocytosis (WBC: 17 mL\textsuperscript{1}). Acyclovir and valproic acid were initiated on the 10\textsuperscript{th} of March, 2010 due to suspected viral encephalitis, and 9 d later she developed high-grade persistent fever and disturbed consciousness with complex abnormal movements (stereotyped episodes of brief repetitive dystonic posturing of the left hemiface and left upper extremity, orofacial dyskinesias, hypersalivation, and chewing movements).

Complex partial status epilepticus was suspected and as such, the patient was given intravenous clonazepam, but improvement was not achieved. Video-EEG showed that EEG activity and polymorphous dyskinesias were not correlated. On the 21\textsuperscript{st} of March, 2010, the patient developed autonomic imbalance and was given midazolam (0.1 mg/Kg/d) for 5 d. Viral serological findings were negative, as were the findings of extensive screening for systemic diseases. During the following 2 weeks, the patient had visual and auditory hallucinations, echolalia, echopraxia, and mutism. She was treated with neuroleptics without improvement. Autoimmune encephalitis was suspected and tests for onconeural antibodies (Hu, Yo, Ri, CV2/CRMP5, amphiphysin, Ma1, and Ma2) were negative. CSF screening for NMDA receptor antibodies (NR1-NR2) was positive. Following the diagnosis of NMDAR encephalitis, pelvic US and thoracic-abdominopelvic CT were performed, but provided no evidence of a tumor. IVIG (0.4 g·kg\textsuperscript{-1}·d\textsuperscript{-1}) was administrated for 5 d on the 4\textsuperscript{th} of April 2010 (Table).
During the next 10 d, the patient did not exhibit any movement disorder and was not febrile, although she still appeared perseverative. She was given 5 additional monthly IVIG trials from April to August 2010 (Table). On December 2010, neuropsychological tests showed improvement in memory and executive function (Table). Follow-up CSF screening for NMDA receptor antibodies performed on January 2011, showed low-level positivity. As such, 6 additional IVIG trials were administrated from April to August 2011 (Table) and 19 months after onset of manic symptoms, the patient had normal neuropsychological test results and had resumed attending school (Table and Figure).

The present patient presented with a non-paraneoplastic form of NMDAR encephalitis, with improvement after immunotherapy. NMDAR encephalitis is a newly described limbic encephalitis that has been primarily observed in young women with ovarian tumors (Irani et al. 2011; de Broucker and Martinez-Almoyna 2010; Dalmau et al. 2008); however, it is increasingly seen in females without tumors, in men, and in children (Florance et al. 2009). A high incidence (25 to 48%) of prodromal flu-like symptoms has been described (Irani et al. 2011; Dalmau et al. 2008). Psychiatric features associated with NMDAR encephalitis include catatonia, confusion, hallucinations, and memory deficit (Irani et al. 2011; de Broucker and Martinez-Almoyna 2010). In the presented patient, psychiatric disturbances were the initial presenting feature and were initially misdiagnosed as a psychiatric disorder. They included such manic symptoms as logorrhea, insomnia, inappropriate sexual behavior and irritability, which were followed by visual and auditory hallucinations, echolalia, echopraxia, and mutism.

Recently, cases of NMDAR encephalitis with pure psychiatric features, including late onset autism or childhood disintegrative disorder, have been reported in children (Creten et al. 2011). Additional research is needed to more clearly define the range of clinical presentation in children, because the impact of psychiatric symptoms may be especially challenging in the pediatric population (Creten et al. 2011). The psychiatric features, seizures, and abnormal movement disorders in the present case led to the suspected diagnosis of NMDAR encephalitis, which was confirmed via screening for specific an-

| Table 1. The course of cognitive assessment following immunoglobulin treatment |
|-----------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Time (months)               | 1           | 2           | 3           | 4           | 5           | 6           | 10          | 14→17       | 18          | 19          |
| Immunoglobulin (number of cure) | 0           | 2           | 1           | 1           | 1           | 0           | 4           | 1           | 1           |
| WISC-III                    |             |             |             |             |             |             |             |             |             |
| Immediate short-term memory:|             |             |             |             |             |             |             |             |             |
| Digit span forward (standard = 6) | Impossible | Impossible | 2           | 4           | 4           | 4           | 4           | 5           | 6           |
| Working memory:             |             |             |             |             |             |             |             |             |             |
| Digit span backward (standard = 4) | Impossible | Impossible | 2           | 2           | 2           | 2           | 3           | 3           | 4           | 4           |
| Intellectual quotient (PM 38) | Impossible | Impossible | Impossible | 80          | 85          | 85          | 85          | 90          | 100         |
| Executive dysfunction       | Impossible | Impossible | +++         | +++         | +++         | +++         | ++          | ++          | +            | –            |             |             |
| Mood disturbances           | ++          | ++          | +++         | ++          | ++          | +           | +           | +           | –            | –            |             |             |
| Behavioral disturbances     | +++         | +           | +           | +           | +           | –           | –           | –           | –            | –            |             |             |

-: Absent; +: mild; ++: moderate; +++: severe.

Figure. Simple Rey-Osterrieth Complex Figure Test.

A. Rey figure copy (type 1: time = 4 min).
B. Rey figure immediate recall (type 1: time = 3min28s).
tibodies. No evidence of a tumor was noted in the presented patient.

Because of the severity of the disease, NMDAR encephalitis patients are usually referred to an ICU (Wandinger et al. 2011). The treatment protocol is fairly well codified and usually consists of immunotherapy and tumor treatment (in the presence of a tumor). Interestingly, patients with non-paraneoplastic NMDAR encephalitis do not respond as well to immunotherapy as do patients with paraneoplastic encephalitis (Kuo et al. 2012). In the presented patient 12 IVIG trials given during a period of 19 months (table) led to recovery. As relapses can occur, neurological follow-up and periodic screening for ovarian teratoma for at least 2 years are strongly recommended.

NMDAR encephalitis is a complex immune-mediated disorder with polymorphous symptoms, including psychiatric features that may lead clinicians to misdiagnose a psychiatric disease. Despite its severe spontaneous course, NMDAR encephalitis has a good prognosis. Early recognition of this entity prevents cognitive sequelae; therefore, we think it essential that all clinicians be aware of NMDAR encephalitis.

Conflict of interest

The authors declare they have no conflicts of interest relevant to the materials presented herein.

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