Late onset autism and anti-NMDA-receptor encephalitis

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In December, 2009, a 9-year-old boy was admitted to our hospital with an acute onset of secondary generalised seizures. He had no medical or psychiatric history and functioned very well socially and academically. He presented with speech and swallowing difficulties, which after 10 days developed into a severely agitated catatonic state with opisthotonic posturing, tonic posturing of limbs, insomnia, and dyskinesia. Initially the electroencephalogram showed a normal background pattern with epileptic discharges, and oligoclonal bands were present in cerebrospinal fluid (CSF). Brain MRI and extensive blood tests were normal. The neurological diagnosis was atypical childhood epilepsy with centrotemporal spikes, for which oral corticosteroids and antiepileptic drugs were prescribed. His catatonia was treated with benzodiazepines. In January, 2010, our patient presented in a robotic state with complete mutism and negativism, and he did not respond to any form of contact. We provisionally diagnosed acute late onset autism with a differential diagnosis of childhood disintegrative disorder or early onset schizophrenia.

Childhood disintegrative disorder, early onset schizophrenia, and late onset autism often share a final common pathway: previous normal development, followed by sudden neuropsychiatric regression of social interaction and communication skills, and a decline in intelligence and daily activities.[1] The disorders are sometimes misrecognised and collectively called as autistic disorder. Although judged to be functional psychiatric diagnoses, the marked deterioration and poor prognosis suggest an organic cause, especially in children with catatonia, a normal development up to at least 5 years of age, or both.[1,2] In our patient, late onset autism was considered because: it is associated with neurological disorders;[2] it is a known end stage of acquired brain injury; progression of symptoms was fast and severe, unlike in early onset schizophrenia; the absence of positive symptoms made schizophrenia less plausible; the age of onset and rare prevalence made chronic disintegrative disorder unlikely;[1] and accompanying catatonic features were present.[3] After extensive diagnostic assessments, our patient was finally diagnosed with anti-NMDA-receptor encephalitis on the basis of slightly raised anti-NMDA-receptor antibody titres in serum and highly raised titres in CSF.[4] Clinical characteristics of this condition are acute major neuropsychiatric symptoms including anxiety, aggression, agitation, behavioural changes and catatonia, delusional thoughts, progressive speech deterioration, and hallucinations. Neurological symptoms such as dyskinesia, abnormal seizure-like movements, and diffuse and profound autonomic instability have also been reported.[4,5] Anti-NMDA-receptor encephalitis can occur in the context of malignant disease;[4] however for our patient extensive oncological investigations were negative. Electroconvulsive therapy was given for the severe catatonic state, and monoclonal antibody treatment (rituximab) was started because of the unsatisfactory response to the initial treatment with benzodiazepines. The acquired autism gradually subsided, he spoke fluently and was able to draw a happy picture (figure). In June, 2011, he only had some mild cognitive dysfunction.

Figure: **Drawing by the patient in February, 2011, after treatment**
"*Christmas with mice and me dancing at home***".**

Childhood disintegrative disorder, early onset schizophrenia, late onset autism and all stages of anti-NMDA-receptor encephalitis share core symptoms, as in our patient. We suggest that anti-NMDA-receptor encephalitis might be a possible organic cause underlying these three disorders. Patients previously diagnosed with these diagnoses might need to be re-examined for anti-NMDA-receptor encephalitis. We suggest that forthcoming editions of DSM-5 and ICD-11 exclude and define cases of regressive autism spectrum disorders due to anti-NMDA-receptor encephalitis.

Contributors
All authors looked after the patient, wrote and contributed equally to the report. Written consent to publish was obtained.

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