



Title	Anti-NMDA-R encephalitis: an encephalitis lethargica-like illness
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A girl of 3 years and 9 months with a 3-day history of fever and upper respiratory tract infection (URTI) was admitted with a generalised tonic-clonic convulsion, and delirium with screaming, non-sense talking, and agitation. For the first week after admission, she was lethargic with fluctuating awareness and mutism during the day but poor sleep at night. Workup for acute encephalopathy including autoimmune, infective, toxicology, metabolic and vasculitic screening showed negative findings. Erythrocyte sedimentation rate was markedly elevated and cerebrospinal fluid showed positive oligoclonal bands. Urgent MRI brain showed bilateral periventricular, multifocal hyperintense lesions on T2W and FLAIR images over the frontal, parietal and occipital regions without enhancement. Urgent electroencephalogram showed generalised slowing compatible with encephalopathic picture. Acute demyelinating encephalomyelopathy was initially suspected, and she was first given intravenous (IV) methylprednisolone, 30 mg/kg/day, for 5 days without evident response, and then IV immunoglobulin, 1 g/kg, for 2 days. After this treatment, there was some improvement in conscious level but the child remained mute. Repeated electroencephalogram showed improved slowing and sleep changes. In the second week, she developed dyskinesia with mouth chewing, tongue thrushing and finger rolling, and developed rigidity, dystonia and oculogyric crises. The dystonia caused mild rhabdomyolysis with raised creatine kinase level. Encephalitis lethargica was suspected and L-dopa was started. After dose titration, she responded well to L-dopa at 1.5 mg/kg qid with improvement of dystonia and rigidity. At the third week, however, she developed recurrent generalised tonic-clonic convulsions. Phenytoin and sodium valproate were started. Repeated MRI brain confirmed increase hyperintensity and size of the previously demonstrated lesions (T2W and FLAIR images) with additional pons involvement, and evidence of cerebral atrophy. In view of both clinical and radiological evidences of active ongoing encephalitic process, a second course of IV immunoglobulin followed by methylprednisolone was given. After the second course of treatment, the child responded well with ongoing improvement. She regained full consciousness and remained seizure-free. After half a month of rehabilitation training, she could walk on her own recommenced full oral feeding. She remained mute, but had normal understanding for her age. Her speech gradually returned 2 months after onset of illness. As this girl has encephalitis lethargica-like illness, NMDA-R encephalitis was suspected. NMDA-R antibodies in both serum and cerebrospinal fluid confirmed raised titres. Ultrasonogram of pelvis was normal.

In summary, this 3-year-old girl who developed a post-URTI encephalopathy with neuropsychiatric presentation, movement disorder, mutism, sleep disorder and seizures, symmetrical white matter changes, improvement after IV immunoglobulins and steroids, has anti-NMDA-R encephalitis. Her clinical features were typical of anti-NMDA-receptor encephalitis¹ which is associated with antibodies against the NR1-NR2 heteromers of the NMDA receptor, and often ovarian tumours in young adult females. The same antibodies have been shown in children with 'encephalitis lethargica'.² Long-term follow-up and monitoring of antibody titres are important as relapse may occur in some of the affected patients. This is the first case of anti-NMDA receptor encephalitis reported in Hong Kong.

References

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