CASE REPORT

Important differential in a patient presenting with neuropsychiatric symptoms: Anti-N-Methyl-D-Aspartate receptor encephalitis

Jer Ming Low, MRCP

Department of Medicine, Hospital Tengku Ampuan Afzan, Kuantan Pahang, Malaysia

SUMMARY

Anti-N-Methyl-D-Aspartate receptor (NMDAR) encephalitis is an immune mediated condition, which remains relatively unknown in Malaysia outside tertiary hospitals with neurology unit. It is often misdiagnosed as a psychiatric illness before definitive treatment is instituted. We report here an 18-year-old man who initially presented to the psychiatry unit before he was subsequently diagnosed as having anti-NMDAR encephalitis. To our knowledge, this is the first reported case of anti-NMDAR encephalitis in the east coast of Peninsular Malaysia.

KEY WORDS:

Anti-N-Methyl-D-Aspartate receptor encephalitis; anti-NMDAR; Auto-immune encephalitis; neuropsychiatric symptoms; paraneoplastic syndrome

INTRODUCTION

Since the discovery of anti-NMDAR encephalitis in 2005, there has been a growing array of literature reporting this condition.[1] However, this condition is still under-recognised in Malaysia despite the University Malaya Medical Centre reporting that 50% of encephalitis admitted to their centre during an 18-month study period was due to anti-NMDAR encephalitis.[2] We report a case of anti-NMDAR encephalitis in a young man with no known prior medical illness.

CASE REPORT

An 18-year-old Malay man with no known medical illness presented to us with a 10-day history of behaviour change. His parents described him as impatient and withdrawn at home before becoming more aggressive. He also complained of visual and auditory hallucinations. He was admitted to the psychiatric ward where he was treated for brief psychotic disorder with antipsychotics as his parents mentioned that he was stressed with his upcoming examinations. There was no prior history of psychiatric illness.

On day five of admission, he was transferred to the medical ward after he developed two episodes of generalised tonic-clonic seizures. He was afebrile with normal vital signs. Neurological examination noted he was stuporous but arousable, and opened eyes spontaneously. Pupils were equal and reactive with no neck rigidity. Limb examination revealed normal tone with no hyperreflexia. Babinsky was downgoing bilaterally. Fundoscopy and power of all four limbs could not be assessed as he was uncooperative.

The contrasted computed tomography (CT) scan of the brain and electroencephalography (EEG) was normal. The family was undecided for lumbar puncture. Septic workout and other investigations done (Table I) were unremarkable and hence he was not treated as meningoencephalitis. On day 17 of admission, he was noted to have autonomic dysfunction where he developed transient hypertensive crisis and tachycardia together with hyperthermia. He was also noticed to have persistent 'lip smacking', or orofacial dyskinesia.

A repeat EEG (Figure 1) showed diffuse slowing of delta waves consistent with encephalopathy. The magnetic resonance imaging (MRI) of the brain revealed no significant abnormalities. Lumbar puncture was performed after the

Table I: Laboratory parameters

Laboratory parameters	Results
Haemoglobin (g/dL)	15.9
TWBC, x 10^3 cells/ml	8.03
Platelet count, x 10^3 cells/ µL	348
Serum creatinine, µmol/L	83
Total serum bilirubin, mmol/L	23.4
Serum aspartate aminotransferase, U/L	23
Serum alanine aminotransferase, U/L	52
Serum albumin, g/L	49
Random plasma glucose, mmol/L	5.1
Serum magnesium, mmol/L	0.86
Serum inorganic phosphate, mmol/L	0.80
Serum corrected calcium, mmol/L	2.24
Serum sodium, mmol/L	137
Serum potassium, mmol/L	4
Serum chloride, mmol/L	104
C-reactive protein, mg/L	1.5
ESR, mm/Hr	40
Beta h-CG	<2
ANA	Negative
CSF opening pressure	3cm H_2O
CSF FEME & gram stain	Clear
CSF glucose, mmol/L	4.4
CSF protein, g/L	0.148
CSF culture and sensitivity	No growth
CSF anti-NMDAR antibody	Positive
CSF indian ink & latex agglutination	Negative
Blood culture	No growth

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Corresponding Author: Jer Ming Low
Email: lowjerming@gmail.com

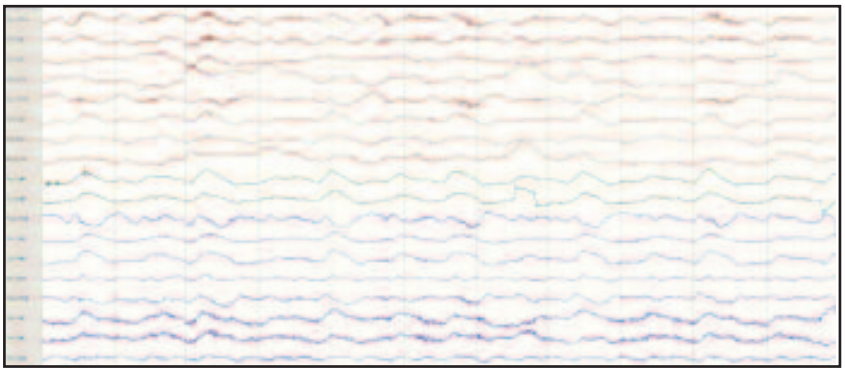

Fig. 1: Repeated electroencephalography.

family was counselled again. A provisional diagnosis of anti-NMDAR encephalitis was made. Further examination revealed no testicular mass. Tumour markers were normal. On day 19 of admission he was treated with IV methylprednisolone 500mg daily and IVIG 0.4g/kg/day.

On day 2 of treatment, he developed fever together with hypertensive and tachycardic episodes. Although this could be a manifestation of autonomic dysfunction, IV Tazobactam/Piperacillin 4.5g QID was started to cover hospital-acquired infection.

The following day, his condition deteriorated with episodes of labile blood pressure and severe tachycardia. Blood pressure ranged from 70-230 / 30-110 mmHg while the heart rate was 130-170 beats per minute.

Despite maximal resuscitative efforts, he ultimately succumbed to his condition. Anti-NMDAR antibody was subsequently detected in the Cerebrospinal fluid (CSF).

DISCUSSION

The diagnosis of anti-NMDAR encephalitis in our patient was based on the characteristic orofacial dyskinesia, prominent psychiatric manifestations, clinical features of encephalitis, absence of infective causes of encephalitis, and the presence of anti-NMDAR antibody.

The incidence of anti-NMDAR encephalitis is unknown, but it appears to be more frequent than any other known paraneoplastic encephalitis.[3] We believe that anti-NMDAR encephalitis is underreported due to the nonspecific symptoms that patients usually present. Apart from that, anti-NMDAR encephalitis is associated with ovarian teratoma or testicular tumours in more than half of the cases.[4]

The majority of patients present with symptoms consisting of nonspecific headache, fever, nausea, vomiting, and diarrhoea. They subsequently develop psychiatric symptoms progressing to abnormal movements, seizures and autonomic instability.[2,3]

A high index of suspicion is required especially in young patients presenting with encephalitis with prominent psychiatric and autonomic dysfunction.[5] CSF examination is vital as CSF anti-NMDAR antibody has been found to be highly sensitive and specific for anti-NMDAR encephalitis.[3]

The mainstay of management would be immunotherapy and the removal of malignancy if present.[3] First line immunotherapy consists of IVIG (0.4g/kg/day for 5 days) and methylprednisolone (1g/day for 5 days).

Second line therapy should be considered if the patient responded poorly to first line therapy within 10 days of treatment. Agents such as rituximab combined with cyclical cyclophosphamide are used.[3]

Although the majority of patients survive with prompt treatment, up to a quarter of cases result in severe disability or death.[4]

Many clinicians have limited experience or are unaware of this condition even though anti-NMDAR encephalitis might be more common than we thought, as shown in a case series by Suhailah A et al.[2] In the case series, out of 10 patients with anti-NMDAR encephalitis, nine survived when prompt treatment was given. Five of these patients had good outcome following treatment while four had partial recovery.[2]

This case highlights the importance of early diagnosis of this condition so that prompt treatment can be instituted to improve the outcome.

In conclusion, the diagnosis of anti NMDAR encephalitis should be considered in any young patient presenting with prominent neuropsychiatric symptoms associated with characteristic orofacial dyskinesia and autonomic instability.

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