Immune Modulating Therapy: An Effective Add-on Intervention for Psychosis of Anti-NMDAR Encephalitis in Taiwan

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Running head: Anti-NMDAR encephalitis mislabeled schizophrenia

Schizophrenia (SCZ) is a heterogeneous disease with approximately 10% of patients initially diagnosed with schizophrenia having autoantibodies binding to the NMDA receptor and presenting as anti-NMDAR encephalitis.[1] Therefore, immune modulating therapy may frequently respond well and timely for treating patients with anti-NMDAR encephalitis characterized by psychosis.[2]

In this paper we detail a series of seven cases where anti-NMDAR encephalitis was misidentified as SCZ (Table 1). The research protocol was approved by the Mackay Memorial Hospital Institutional Review Board (IRB). Written informed

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consent was obtained from each participant per the IRB guidelines.

These patients with anti-NMDAR encephalitis presented with psychosis and several neurological symptoms, including epilepsy, gait disturbance, speech problems, and memory impairment. Each patient received anti-NMDAR autoantibody testing, which confirmed a diagnosis of anti-NMDAR encephalitis with psychosis.

Our first patient was a woman with the symptoms of focal epilepsy during a psychotic period characterized by auditory hallucinations. The patient had previously received treatment with anticonvulsant and antipsychotic drugs but remained resistant to the treatment until testing positive for the anti-NMDAR antibody.

The most serious case was that of the sixth patient, a 42-year-old man with impaired speech function. The patient became agitated and displayed an uncontrolled outburst of anger and frustration, accompanied by unintelligible shouting.

The seventh patient, a 24 year-old male student, presented with memory impairment, which caused the patient to leave home because of a failure to identify the problem. This was the only patient to receive all therapies—pulse therapy with plasmapheresis and intravenous immunoglobulin (IVIG) because the patient's parent was willing to pay for IVIG. In all seven cases, the patients' conditions improved after receiving first-line immune therapy, pulse therapy with plasmapheresis and/or IVIG, as judged using the Clinical Global Impression scale.

We recommend an autoimmune serum test to rule out anti-NMDAR encephalitis for patients with acute onset of a first episode of SCZ following an upper respiratory infection, marked by an atypical disease course with symptoms of memory impairment, epilepsy, the absence of a family history of SCZ, and resistance to previously used antipsychotic treatment.

Disclosure Statement:

There is no conflict of interest.

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Table 1. Seven cases of anti-NMDAR encephalitis misdiagnosed as schizophrenia

Age		Sex	Clinical feature	Psychosis	Duration of illness	Treatment
1.	22 y/o	F	Focal epilepsy	AH	3 years	MP + P
2.	22 y/o	F	Acute psychosis	AH	Onset after URI	MP + P
3.	32 y/o	M	Chronic psychosis	AH	Onset on 17 y/o	MP + P
4.	22 y/o	M	Unsteady gait	AH	Onset after URI	MP + P
5.	20 y/o	M	Acute psychosis	AH, self talking	Onset after URI	MP + P
6.	42 y/o	M	Speech problem, regression	AH	Onset after URI	MP + P
7.	24 y/o	M	Misidentification, Memory impairment	AH	Onset after URI	MP + P+IVIG

y/o: years old; F: female; M: male; AH: auditory hallucination; MP: methylprednisolon ;P: plasmaphoresis ; IVIG: intravenous immunoglobulin