LATE-ONSET PSYCHOSIS WITH PERSISTENT POSITIVE ANTI-NMDAR ANTIBODIES: A CASE REPORT

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Background and aims

- Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune condition caused by IgG **autoantibodies directed against NR1 subunit of the NMDA glutamate receptor**. A majority of adults first present with behavioural and psychiatric symptoms, predominantly psychosis, but the disorder usually progresses rapidly to include several neurological features like seizures, movement abnormalities, autonomic instability or hypoventilation.¹
- Detection of anti-NMDAR antibodies has also been described **in first psychotic episodes and, rarely, in established schizophrenia**. Its clinical significance in isolated psychiatric syndromes is still a subject of debate and uncertainty remains about the utility of immunotherapy in this cases.^{2,3}

OBJECTIVES: To report a case of a chronic psychotic patient with repeated positive anti-NMDAR antibodies and discuss their relevance and management.
MATERIALS AND METHODS: Case report and literature review.

Case Report

64 year-old man was brought to our psychiatry inpatient department in June 2017 with **persecutory delusions (worries about being spied on and stolen by his neighbours)** and **auditory (second and third person voices) and visual (laser beams) hallucinations**.

PAST MEDICAL HISTORY:

- 10 YEAR CHRONIC PSYCHOTIC DISORDER** (probable diagnosis of **schizophrenia**), with multiple psychotic exacerbations, prescribed with quetiapine 400mg bid and lorazepam 2.5mg id;
- Probable neuroleptic malignant syndrome in 2010;
- Alcohol abuse (abstinent for many years);
- JULY 2016:** admitted to our department for psychotic exacerbation. After a serum syphilis positive test, it was performed a lumbar puncture to rule out neurosyphilis, with the following cerebrospinal fluid (CSF) test results:

- Increased level of proteins (1.08g);**
- Positive anti-NMDAR autoantibodies;**
- Negative VDRL and TPHA;
- Normal cell count and normal IgG index;
- One oligoclonal band with no serum correspondent.

In collaboration with Neurology department, it was performed the following additional investigation:

Serum anti-NMDAR antibodies	Positive
Brain Magnetic Resonance Imaging	Small periventricular and deep white matter hyperintense ischemic lesions
Formal cognitive assessment	Significant deficits in attention, executive function, visuospatial abilities, working memory and language.
Electroencephalography (EEG)	Intermittent slow activity with no “extreme delta brush” pattern.
Serum anti-neuronal (onconeuronal) antibodies	Negative
Underlying tumor was excluded.	

CURRENT EPISODE (June 2017):

Admitted for another psychotic exacerbation. There were **no abnormal movements, seizures, catatonia or autonomic instability**.
Blood count, hepatic and renal function remained normal, as well as thyroid functions tests.
He repeated serologic evaluation for anti-NMDAR antibodies with **positive results**.

He also repeated EEG, which showed generalized slowing and frontal, central and temporal paroxysmal activity.

Besides the atypical presentation and the long course of the psychotic disease, it was **hypothesized a diagnosis of anti-NMDAR encephalitis** and it was decided to start directed treatment.

- First we tried a 5 days course of iv methylprednisolone (1gr/day). After 2 days of treatment, the patient became confused, with incoherent speech and worsening of psychotic symptoms, which led us to stop the steroids;
- After that, he completed **5 sessions of plasmapheresis**.

The patient also stopped quetiapine and started lamotrigine 100mg id and olanzapine 15mg id.

At hospital discharge (November 2017), the patient showed an improvement in positive psychotic symptoms, with residual persecutory delusions and no hallucinations. He kept **cognitive deterioration** and **negative symptoms**.

Positive and Negative Syndrome Scale (PANSS)	July 2017	November 2017 (discharge)
POSITIVE SCALE	20	15
NEGATIVE SCALE	31	28
GENERAL PSYCHOPATHOLOGY	37	33

Discussion and conclusions

- In summary, this is a case report of a patient with a **10-year course of late-onset psychosis and cognitive deterioration**, with positive anti-NMDAR antibodies (detected in 2 time points, 10 months apart). We tried high dose iv steroids (not tolerated) and plasmapheresis, with no clear response.
- There are some case reports and case series of patients with positive anti-NMDAR antibodies and purely psychotic presentations (**first psychotic episode**) who were successfully treated with immunotherapy.^{2,4,5} The longer the disease course, the less likely is encephalitis a phenocopy of schizophrenia. Data regarded immunotherapy in chronic psychotic patients is scarce and treatment options after a 10 year disorder are not established.
- In our case, the patient had no clear response to immunotherapy. Doubts remain whether this represents a treatment failure or if anti-NMDAR antibodies are an incidental finding without physiopathological relevance in this case.

¹Kayser MS, Dalmau J. Anti-NMDA receptor encephalitis, autoimmunity, and psychosis. *Schizophrenia Research*. 2016;176(1):36–40.²Kayser MS, Titulaer MJ, Gresa-Arribas N, Dalmau J. Frequency and Characteristics of Isolated Psychiatric Episodes in Anti-N-methyl-D-aspartate receptor encephalitis. *JAMA Neurol*. 2013;70(9):1133-9.³Lennox BR, Palmer-Cooper EC, Pollak T, et al. Prevalence and clinical characteristics of serum neuronal cell surface antibodies in first-episode psychosis: a case-control study. *Lancet Psychiatry*. 2017;4(1):42-48. ⁴Scott JG, Gillis D, Ryan AE, et al. The prevalence and treatment outcomes of antineuronal antibody-positive patients admitted with first episode of psychosis. *BJPsych Open*. 2018;16;4(2):69-74. ⁵Zandi MS, Deakin JB, Morris K, et al. Immunotherapy for patients with acute psychosis and serum N-Methyl D-Aspartate receptor (NMDAR) antibodies: a description of a treated case series. *Schizophre Res*. 2014;160(1-3):193-5