*Age and Ageing* 2014; **43:** 725–726
doi: 10.1093/ageing/afu098


**CASE REPORTS**

# Anti-NMDA receptor encephalitis: an easily missed diagnosis in older patients

Katie Rainey, Bethan Gholkar, Mark Cheesman

ENT, North Bristol NHS Trust, Bristol, UK

Address correspondence to: Katie Rainey. Email; katiebewick@hotmail.com, katie.rainey@nbt.nhs.uk

## Abstract

Anti-*N*-methyl-D-aspartate (NMDA) receptor encephalitis is an important, treatable cause of encephalitis which remains under-recognised despite a growing body of the literature [1]. It is an immune-mediated syndrome which presents with a variety of neurological symptoms including headache, fever, personality change and seizures. Most case reports to date are of young adults, it is much less frequently reported in older adults. The syndrome has been associated with ovarian teratomas. The prognosis is good with early recognition and treatment, though may relapse. We present a case of NMDA encephalitis in an elderly patient who responded well to immunosuppressive therapy.

**Keywords:** *encephalitis, anti-NMDA receptor, immune, older people*

## Case report

A 75-year-old Caucasian woman was admitted with a 2 day history of fever and right-sided otalgia, progressing over 3 weeks to meningism and confusion. Computed tomography (CT) brain showed mild small vessel ischaemic change. Cerebrospinal fluid (CSF) analysis revealed elevated protein of 1.11 g/l, glucose of 3.4 mmol/l and white cell count of 48 with 100% lymphocytes. Treatment included 5 weeks of antibacterials and two of antivirals. Viral polymerase chain reaction for Herpes Simplex, Cytomegalovirus, Epstein Barr Virus, Enterovirus and Varicella-Zoster Virus was subsequently negative. CSF tuberculosis culture, mantoux and interferon tests were negative. An electroencephalogram revealed diffuse abnormal waveforms and magnetic resonance imaging showed a subacute frontal infarct and bilateral abnormal flair signal affecting the medial temporal lobes consistent with an encephalitis, most likely herpes (Figure 1). The subacute infarct raised the question of a vasculitic process, but the neurologists and rheumatologists felt an infective process was most likely. She failed to improve, and 3 months following the onset of meningism she was drowsy, following only simple commands and having myoclonus. The neurology team felt the scenario was typical of viral encephalitis causing significant damage. Tests were now executed for anti-NMDA-receptor antibodies and proved positive confirming a diagnosis of anti-NMDA-receptor encephalitis. She responded to immunosuppressive therapy with steroids. There was no evidence of associated malignancy. After 2 months rehabilitation, she was suffering mild cognitive impairment and able to transfer with a stand aid. Her mobility did not improve further and her cognition gradually declined. She passed away 1 year after discharge.

There is growing evidence that an autoimmune process underlies neurological disorders. It is well recognised that limbic encephalitis is associated with antibodies against voltage-gated potassium channels [2]. More recently has been discovery of antibodies against NMDA-receptors as an additional immune-mediated cause of encephalitis [3].

Anti-NMDA receptor encephalitis classically presents with viral prodrome, followed by psychiatric symptoms including psychosis and hallucinations. Such patients have been mistakenly diagnosed with schizophrenia [4]. Patients can develop dyskinesias and choreiform movements. Seizures are common. As disease progresses individuals become unresponsive and often develop autonomic instability. There is an association with ovarian teratomas [3]. In this report, psychiatric symptoms were not observed; she did develop myoclonus later in the illness. This atypical presentation and advanced age contributed to the delayed diagnosis.

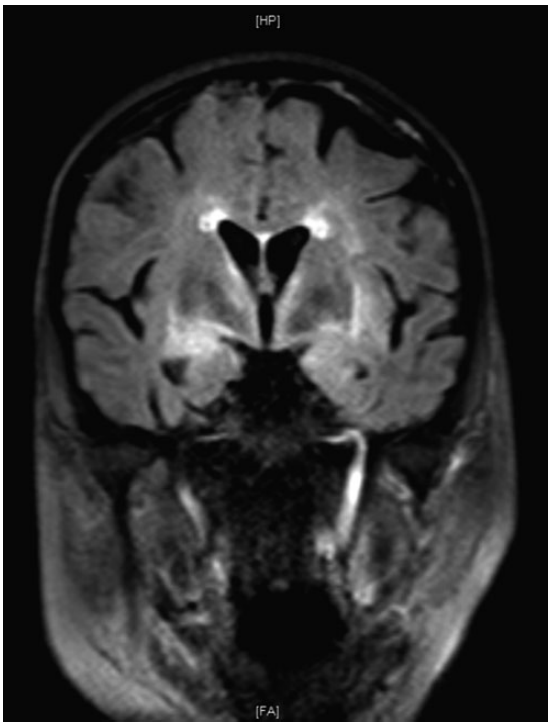


**Figure 1.** Bilateral medial temporal abnormal T2/FLAIR signal.

Clinically, differentiating anti-NMDA receptor encephalitis from viral encephalitis is difficult. Patients with viral encephalitis tend to be older and display fewer psychiatric symptoms [5], with movement disorders and autonomic instability being less frequent [6].

Diagnosis of anti-NMDA receptor encephalitis is supported by CSF lymphocytosis and elevated protein. Brain imaging is usually normal. Diagnosis is confirmed by antibodies against the NMDA-receptor in the serum and CSF. The mainstay of treatment is immunotherapy combined with tumour resection, where relevant. Based on data from 501 patients, the estimated mortality is 6% with relapse rate of 12% over 2 years. Predictors of a good outcome were early treatment and no admission to intensive care unit [7].

Despite a growing body of literature anti-NMDA receptor encephalitis remains under-recognised in clinical practice. Young females are most commonly affected. It is less recognised in elderly patients. There has been one other report, an 84-year-old woman who presented with a 6-day history of neurological disturbance and had anti-NMDA-receptor antibodies detected in CSF. She was treated with immunosuppression but remained unresponsive and died [8]. In a modest cohort of encephalitis patients in a tertiary referral centre 20% tested positive for antibody markers [9]. Larger studies are needed to estimate the true incidence of this condition. Meanwhile, clinicians need to remain vigilant when assessing patients with encephalitis.

## Key points

- Anti-NMDA receptor encephalitis is an important, treatable course of encephalitis.
- Consider testing for anti-NMDA receptor antibodies in patients not responding to antivirals/antibacterials.
- Anti-NMDA receptor encephalitis is under-recognized.

## References

1. Iizuka T, Sakai F, Ide T, Monzen T *et al*. Anti-NMDA receptor encephalitis in Japan: long-term outcome without tumor removal. Neurology 2008; 70: 504–11.
2. Buckley C, Oger J, Clover L *et al*. Potassium Channel antibodies in two patients with reversible Limbic Encephalitis. Ann Neurol 2001; 50: 73–8.
3. Dalmau J, Tüzün E, Wu HY *et al*. Paraneoplastic anti-*N*-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. Ann Neurol 2007; 61: 25–36.
4. Suzuki Y, Kurita T, Sakurai K, Takeda Y, Koyama T. Case report of anti-NMDA receptor encephalitis suspected of schizophrenia. Seishin Shinkeigaku Zasshi 2009; 111: 1479–84.
5. Gable MS, Gavali S, Radner A *et al*. Anti-NMDA receptor encephalitis: report of ten cases and comparison with viral encephalitis. Eur J Clin Microbiol Infect Dis 2009; 28: 1421–9.
6. Redington JJ, Tyler KL. Viral infections of the nervous system, 2002: update on diagnosis and treatment. Arch Neurol 2002; 59: 712–8.
7. Titulaer MJ, McCraken L, Gabilondo I *et al*. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. Lancet Neurol 2013; 12: 157–65.
8. Day GS, Hifh SM, Cot B, Tang-Wai D. Anti-NMDA-receptor encephalitis: case report and literature review of an under-recognized condition. 2011; 26: 811–6.
9. Davies G, Irani SR, Coltart C *et al*. Ant-*N*-methyl-D-aspartate receptor antibodies: a potentially treatable cause of encephalitis in the intensive care unit. Crit Care Med 2010; 38: 679–82.

**Received 29 September 2013; accepted in revised form 26 March 2014**