

## Anaesthetic management of a patient with anti-NMDA receptor encephalitis

### INTRODUCTION

Anti-N-methyl-D-aspartate (NMDA) receptor (NMDA-R) encephalitis is a recently described neurological disorder, an immune-mediated encephalitis caused by production of antibodies to the NMDA-R, now a recognised cause of psychosis, movement disorders and autonomic dysfunction.<sup>[1,2]</sup> Though it is the second most frequent cause of immune-mediated encephalitis, it is usually under-diagnosed. Many anaesthetic medications interact with NMDA-Rs with risks during induction and maintenance of anaesthesia.<sup>[3]</sup> We report a patient with documented anti-NMDA-R encephalitis who was scheduled for surgery for right salpingo-oophorectomy under general anaesthesia.

### CASE REPORT

A 32-year-old female (154 cm, 73 kg) with no remarkable medical history was admitted to the hospital with complaints of insomnia, headache and irrelevant talk followed by three episodes of generalised tonic

clonic seizures. Electroencephalogram (EEG) showed generalised slowing with normal magnetic resonance imaging (MRI) study. She subsequently became drowsy and was intubated. Cerebrospinal fluid (CSF) showed pleocytosis with raised protein. She was being treated for aseptic meningitis with no improvement in her general condition. MRI pelvis revealed right ovarian complex cystic lesion. Limbic encephalitis was suspected because of her age, the clinical presentation and the absence of alternative aetiology. The anti-NMDA-R encephalitis was confirmed by indirect fluorescent antibody test. Serum anti-NMDA antibody level of 1:160 (normal < 1:10) and CSF level of 1:10 (normal < 1:1). Patient was started on steroids (methylprednisolone 100 mg thrice daily) and intravenous (IV) immunoglobulins (IgG type – injection glob Ex<sup>R</sup> 2 g/kg over 5 days). The patient remained confused, disoriented, agitated, depressed airway reflexes requiring restraint and ventilator dependent with a tracheostomy done on 14<sup>th</sup> day of admission. Subsequent neurological improvement was seen, with seizures controlled with multiple anti-convulsants. Patient was scheduled for right salpingo-oophorectomy, lasting 1 h and 45 min. No pre-medication was administered. On arrival to the operating room, her vitals were: Blood pressure of 110/70 mm Hg, heart rate of 74/min, oxygen saturation 100% on T-piece. General anaesthesia was induced with fentanyl (1 µg/kg), midazolam (0.05 mg/kg) and propofol (2mg/kg) and atracurium (0.5 mg/kg) and was maintained with fentanyl (0.3 µg/kg) IV, oxygen (1L/min) and compressed air (1.5 L/min), isoflurane (0.5%) through the tracheostomy. Patient was monitored with electrocardiography, non-invasive blood pressure, capnography, pulse oximetry and bispectral index. Surgery was completed without any complications. Patient was sent to the intensive care unit on mechanical ventilation. Subsequent follow-up after a week showed improvement in her neurological status; she was more alert with decreased convulsions, obeyed simple verbal commands. Tracheostomy was decannulated, but her psychiatric symptoms persisted with irrelevant talking and restlessness and agitation intermittently. EEG suggested improved activity. Repeat anti-NMDA-R antibodies titre was positive but reduced. She was subsequently mobilised and discharged with instructions for regular follow-up. At 3 months follow-up, she was alert, oriented, and had occasional episodes of agitation.

## DISCUSSION

N-methyl-D-aspartate receptor, α-amino-5-methyl-

3-hydroxy-4-isoxazole propionic acid receptor and kainate receptor are the three subtypes of ionotropic glutamate receptors. Ectopic brain tissue found in teratoma leads to the formation of anti NMDA-R antibodies and induces glutamatergic transmission impairment. NMDA-Rs are excitatory, tetrameric receptors. In NMDA-R encephalitis, NMDA-R antibodies decrease NMDA-R surface density and synaptic localisation via selective antibody-mediated capping and internalisation of surface NMDA-Rs that correlates with antibody titres.<sup>[4,5]</sup> Originally described by Dalmau *et al.*, in 2007 in women of age 19–24 years, it is associated with ovarian teratomas in 54% cases.<sup>[1]</sup> It has a characteristic presentation with psychiatric symptoms, behavioural or personality disturbances, central hypoventilation, paroxysmal sympathetic hyperactivity, seizures and then progresses to an unresponsive state during which periods of catatonia and agitation alternate.<sup>[1,2]</sup>

Immunotherapy is based on steroids, and subsequently on IV immunoglobulin or plasma exchange. Early removal of an underlying tumour may be associated with a good prognosis; most of the patients fully recover or have mild sequelae after removal and immunotherapy. The improvement is over several months. Coma, psychosis and dyskinesia improve first, then social behaviour and executive function.<sup>[1]</sup>

The anaesthetic considerations are related to autonomic instability, including hyperthermia, tachycardia, hypertension and bradycardia. Various anaesthetic drugs like ketamine, propofol, opioids and inhaled agents like nitrous oxide, sevoflurane acting on NMDA-R, may behave unpredictably. Ketamine binds to phencyclidine site of ion channel of NMDA-R, acting as an antagonist to inhibit the influx of Na<sup>+</sup> and Ca<sup>2+</sup>, causing similar clinical features as the disease itself. Propofol inhibits the NMDA subtype of glutamate receptor. Depression of NMDA-mediated excitatory neurotransmission may contribute to the anaesthetic, amnesic and anti-convulsant properties of propofol.<sup>[6]</sup> Inhalational gases like nitrous oxide reduces the excitatory currents induced by NMDA-R in the basolateral amygdala. This is associated with anaesthesia-induced amnesia of nitrous oxide.<sup>[7,8]</sup> Xenon has been shown to inhibit the NMDA-activated currents in hippocampal neurons.<sup>[9]</sup> Sevoflurane inhibits NMDA-gated currents and NMDA-induced mitochondria membrane depolarisation, could possibly worsen the clinical presentation of these

patients.<sup>[8,10]</sup> Pascual-Ramírez *et al.*,<sup>[2]</sup> reported using propofol/sevoflurane/fentanyl in a case with no complications.

## CONCLUSION

General anaesthesia using non-depolarising neuromuscular blocking agents, benzodiazepines and opioids should be preferred in patients with anti-NMDA-R encephalitis as their effects not associated with NMDA pathway. Regional anaesthesia as an option may be considered in patients diagnosed with early disease keeping in mind the autonomic dysfunction associated with the disorder.

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