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CLINICAL INFORMATION

Anesthesia in anti-N-methyl-D-aspartate receptor encephalitis – is general anesthesia a requisite? A case report



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Abstract Anti-N-methyl-D-aspartate receptor encephalitis is a recently described neurological disorder and an increasingly recognized cause of psychosis, movement disorders and autonomic dysfunction. We report 20-year-old Chinese female who presented with generalized tonic-clonic seizures, recent memory loss, visual hallucinations and abnormal behavior. Anti-N-methyl-D-aspartate receptor encephalitis was diagnosed and a computed tomography scan of abdomen reviewed a left adnexal tumor. We describe the first such case report of a patient with anti-N-methyl-D-aspartate receptor encephalitis who was given a bilateral transversus abdominis plane block as the sole anesthetic for removal of ovarian tumor. We also discuss the anesthetic issues associated with anti-N-methyl-D-aspartate receptor encephalitis. As discovery of tumor and its removal is the focus of initial treatment in this group of patients, anesthetists will encounter more such cases in the near future.

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PALAVRAS-CHAVE

Encefalite antirreceptor de N-metil-D-aspartato;

Anestesia em encefalite antirreceptor de N-metil-D-aspartato – a anestesia geral é um requisito? Relato de caso

Resumo A encefalite antirreceptor de N-metil-D-aspartato (NMDA) é um distúrbio neurológico recentemente descrito e uma causa cada vez mais reconhecida de psicose, distúrbios do

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Bloqueio do plano transversal abdominal; Encefalite antirreceptor de NMDA e anestesia

movimento e disfunção autonômica. Relatamos o caso de uma paciente de origem Chinesa, 20 anos de idade, que se apresentou com crises tônico-clônicas generalizadas, perda de memória recente, alucinações visuais e comportamento anormal. Encefalite antirreceptor de NMDA foi diagnosticada e uma tomografia computadorizada de abdome revelou um tumor anexial à esquerda. Descrevemos o primeiro relato de caso de paciente com encefalite antirreceptor de NMDA submetida ao bloqueio de plano transversal abdominal (PTA) bilateral como única anestesia para remoção de tumor ovariano. Também discutimos as questões anestésicas associadas à encefalite antirreceptor de NMDA. Como a descoberta e a remoção do tumor são o foco do tratamento inicial nesse grupo de pacientes, os anesthesiologistas encontrarão mais desses casos no futuro próximo.

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Background and objective

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis was first described in 2007.¹ Although more than 400 cases have since been diagnosed, literature regarding anesthetic management is scarce, with only 3 cases reported in recent years.^{2–4} This is surprising because most patients will need anesthesia for removal of tumor. Clinicians have to be aware that the pathology of this specific encephalitis is likely to affect the actions of many drugs that act upon the NMDA receptor.

We describe the first such case report of a patient with anti-NMDA receptor encephalitis who was given a bilateral transversus abdominis plane (TAP) block as the sole anesthetic for removal of ovarian tumor.

Case presentation

A previously well 20-year-old female presented with sudden onset of generalized tonic-clonic seizures which was preceded by recent memory loss, visual hallucinations and abnormal behavior. She was afebrile and haemodynamically stable. Her white cell count, MRI brain and lumbar puncture were normal and electroencephalogram showed slow background activity. She was treated as a case of aseptic meningitis with intravenous acyclovir and antiepileptics. After one week she was referred to our institution for further management.

In our institution, she was given intravenous methylprednisolone for five days while being continued on intravenous acyclovir, lamotrigine and risperidone. Her behavioral abnormalities and seizures persisted. Her serum was tested by indirect immunofluorescent antibody test (Luebeck, Germany) and was positive for antibodies against the NMDA receptor (Specificity 100%). Abdominal CT scan revealed a 4 cm × 4 cm × 4 cm left adnexal mass, likely to be an ovarian teratoma.

She was scheduled for laparotomy and cystectomy. Regional anesthesia with a bilateral TAP block was planned after a joint discussion with her parents.

Preoperatively, she was unable to follow commands and showed abnormal behaviors such as inappropriate laughing and jerking movements. Baseline blood pressure was 140/95 mmHg, heart rate 115 beats per minute (bpm) and saturations 98% on oxygen 3 L.min⁻¹.

In theater, under standard monitoring, ultrasound-guided (Sonosite M-turbo™, Sonosite Inc., Bothell, WA, USA) bilateral TAP block was done. A linear probe 13–6 MHz was placed at the lateral abdominal wall in the midaxillary line, between the subcostal margin and iliac crest. A 21G, 80 mm insulated needle (Stimuplex™ A, B. Braun, Melsungen AG, Melsungen, Germany) was directed to the TAP using in-plane technique. Twenty millilitres of levo-bupivacaine 0.25% was injected into the transversus abdominis fascial plane on each side.

After 15 min, the adequacy of block was assessed. As the patient was unable to follow commands, we relied on her facial expressions, movement and sympathetic responses such as heart rate. Surgery started when there was no response to pin prick up to T8 dermatomal level.

A Pfannenstiel incision was made, followed by excision of the tumor. Fentanyl 25 mcgs was administered intravenously as supplement for visceral pain. Intraoperatively she was stable with blood pressure of 110/75–140/95 mmHg, heart rate 100–115 bpm, respiratory rate 18–20 per minute and saturations 99–100%. A 4 cm × 5 cm left ovarian mass was removed uneventfully in 40 min with minimal blood loss. No episodes of hypoventilation or autonomic instability were seen.

Post-operatively her hemodynamics were stable and she remained calm. We prescribed morphine 5 mg QID subcutaneously, Tab Paracetamol 1 g QID and Tab Celecoxib 200 mg OD for post-operative analgesia.

A week after surgery she remained mostly unresponsive. She then underwent 5 cycles of plasma exchange. Histopathology examination of the excised tumor confirmed the diagnosis of mature cystic teratoma.

One week after plasma exchange, she showed marked clinical improvement. She was alert and talking coherently. Although she complained of occasional visual hallucinations, she had an excellent functional recovery and was discharged home after one month of hospital admission. Upon

questioning, she had no recollection of incidents during her stay and specifically could not recall anything about the operation.

Discussion

The NMDA receptor

NMDA receptors are ionotropic glutamate receptors. Eight different NR1, four NR2 and two NR3 subunits have been identified. The NMDA receptor most likely consists of four subunits, with at least one NR1 and one NR2 subtype.⁵

The receptor controls a cation channel that is blocked by extracellular Mg at resting membrane potential.⁶ Simultaneous binding of glutamate to NR2 and glycine, the coagonist, to NR1 is required for receptor activation.

Anti-NMDA receptor encephalitis

This was first described by J Dalmau and colleagues,¹ who reported a case series of 100 patients, mainly young women, who had antibodies against NR-1 NR-2 heteromers. All presented with psychiatric symptoms, and 59% had tumors, most commonly ovarian teratoma.

A prodromal phase of headache, fever, or upper respiratory tract symptoms is typically followed within 2 weeks by the psychotic phase, characterized by mood dysregulation and severe behavioral disturbances.^{7,8} This progresses to an 'unresponsive' state, in which periods of agitation and catatonia can alternate. Of interest to the anesthetist are the findings of autonomic instability during this stage, including hyperthermia, tachycardia, hypertension and bradycardia. Some patients require pacemakers for prolonged cardiac pauses.¹ There are frequently abnormal movements, increased muscle tone and dyskinesias. Another significant symptom is hypoventilation of central origin.^{7,8} Many patients require ventilation in the intensive care unit.

Treatment consists of immunotherapy and removal of tumor. Corticosteroids, intravenous immunoglobulins, plasma exchange or drugs such as rituximab and cyclophosphamide have been used. Patients should be screened for an underlying tumor, most commonly an ovarian teratoma. Tumor removal resulted in substantial improvement in 80% of patients.⁸ Overall, about 75% of patients recover or have mild sequelae, whereas others remain severely disabled or die. The estimated mortality is 4%.⁸

Anesthetic considerations

Drugs acting at the NMDA receptor

Many anesthetic drugs act at the NMDA receptor. NMDA antagonists include ketamine, phencyclidine, nitrous oxide and xenon. Tramadol and methadone act both at opioid and NMDA receptors. These drugs may cause worsening of symptoms and should be avoided.

Halogenated volatile anesthetics may act indirectly at the NMDA receptor by reducing NMDA-activated currents, although their effects on GABA_A receptors may be dominant.⁹⁻¹¹ Therefore their effects may be unpredictable. Three previous case reports used desflurane,³ isoflurane³

and sevoflurane,^{2,4} and none reported increased sensitivity to the volatile anesthetics.

Although propofol is postulated to act via the GABA_A receptor and sodium channel, one patient had unexpected profound hypotension following a 3 mg.kg⁻¹ propofol induction.⁴ This shows that NMDA receptors are important in the action of many anesthetic drugs.

Effects of the disease

Temperature and invasive blood pressure monitoring should be considered as many patients show autonomic instability. Increased temperature may mimic malignant hyperthermia.

Central hypoventilation may lead to difficulty weaning, or to unexpected need for reintubation. Patients should be closely monitored in a high dependency setting following general anesthesia. Prolonged ventilation increases the risks of ventilator associated pneumonias and may necessitate a tracheostomy.³

Abnormal movements and dyskinesias may impede patient positioning or lead to nerve injuries and difficult intravenous access. Jaw clenching or broken teeth may lead to difficulties during intubation.

Is general anesthesia then the anesthetic of choice?

Patients with anti-NMDA receptor encephalitis are likely to already have a reduced perception of pain.¹² Pain involves NMDA receptor activation, especially the NR2B subunit.^{6,13} NMDA receptor antagonists are potent analgesics. Peripheral NMDA receptor antagonism may even be effective in preventing visceral pain.¹⁴ In anti NMDA receptor encephalitis, antibodies target the extracellular N-terminal domain of the NR1 subunit, followed by antibody mediated capping and internalization of NMDA receptors. This leads to reduced receptor density and NMDAR mediated currents.^{1,8,10} This may be why patients mimic the features of dissociative anesthesia produced by ketamine.

In addition, patients are unlikely to recall intraoperative events even without general anesthesia. Persisting amnesia of the entire process is characteristic, possibly due to disruption of synaptic plasticity.¹

We therefore felt that a TAP block would be sufficient as the sole anesthetic and would avoid the risks associated with general anesthesia. We were wary of a central neuraxial block due to its risks in recent encephalitis, possible increased intracranial pressure and difficulty positioning an uncooperative patient.

The block succeeded also because of the small tumor size that enabled the surgeon to perform a quick surgery with minimal handling.

Transversus abdominis plane block

This is an abdominal field block, with local anesthetic deposited in between the internal oblique and transversus abdominis muscles to block the anterior rami of spinal nerves T7 to L1 traversing in this plane. It blocks somatic sensation to the abdominal skin, muscles and parietal peritoneum but not visceral sensation.¹⁵ Therefore it is usually used to provide analgesia for lower abdominal surgery, and very rarely as the sole anesthetic.

Conclusion

We present a case of a patient with anti-NMDA receptor encephalitis who underwent laparotomy and cystectomy with a bilateral TAP block as the sole anesthetic. The anesthetic considerations are highlighted. Although a definite conclusion cannot be made until more is known about anti-NMDA encephalitis and its effect on pain signaling, we postulate that patients have an altered perception to pain. This may contribute to the feasibility of bilateral TAP block as the sole anesthetic for lower abdominal surgery in them and would also avoid the risks associated with a general anesthetic.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of interest

The authors declare no conflicts of interest.

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