International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Anesthetic Approach in Anti-N-methyl-D-Aspartate Receptor Encephalitis Associated with Ovarian Teratoma: A Case Report

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ABSTRACT

Autoimmune encephalitis associated with ovarian teratoma has recently been related to the development of antibodies to specific heteromers of the *N*-methyl-d-aspartate receptor. Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune condition that is brought on by the production of anti-NMDAR antibodies. It frequently presents on young females and manifests in different ways, including psychiatric symptoms, seizures, hypoventilation, and instability of the autonomic nervous system. Patients who have early surgical tumor excision in addition to immunotherapy had better outcomes than the other patients with this condition. Because the NMDAR is one of the main sites of action for frequently used anesthetic drugs, it is crucial to comprehend the pharmacological interaction between the anesthetic agents and the impaired NMDAR in order to build an anesthetic plan. This study describes a young female patient with autoimmune encephalitis who needed to have an ovarian teratoma surgically removed. Surgery was done under general anesthesia and peripheral nerve block (PNB). Sevoflurane and propofol did not appear to alter psychoneuronal function or cause autonomic instability despite their indirect effects on anti-NMDAR. A quadratus lumborum block was performed to reduce the amount of opioids required for anesthesia.

Keywords: anesthesia, ovarian teratoma, autoimmune encephalitis, anti-NMDA receptor

INTRODUCTION

An umbrella term for a variety of inflammatory illnesses of the central nervous system including neuronal autoantibodies is "antibody-mediated autoimmune encephalitis." Memory impairment, seizures, mental symptoms, autonomic derangement, involuntary movements, and cognitive dysfunction are the hallmarks of this uncommon condition, which is typically paraneoplastic. It has recently been linked to the development of antibodies against particular heteromers, such as those that are directed against NMDA receptors. [1] The second most common immune-mediated encephalitis cause and likely underdiagnosed is anti-NMDA-R encephalitis. In addition, young ladies frequently show signs of it. Approximately 38–58% of cases have tumors, and ovarian teratomas make up 94% of all tumors.[2] Consequently, the combination of therapies also includes surgical tumor removal and immunotherapy.

Many anesthetic drugs interact with the NMDA receptor and may therefore alter the anesthetic management of patients with anti-NMDA-R encephalitis. This paper presents a case of a 22-year-old

woman who was diagnosed with autoimmune encephalitis suspected with anti-NMDA receptor antibodies who underwent left salpingo-oophorectomy under general anesthesia and peripheral nerve block

CASE DESCRIPTION

This is a case of a 22-year old female who presented with an intermittent headache that is throbbing in character and allegedly triggered by light. The increase in severity and persistence of headache accompanied by undocumented fever and chills prompted the patient to seek consult. She was initially diagnosed with Viral meningitis and was sent home.

Her symptoms gradually worsened despite the pain medications given. She still experienced diffused headache and she developed progressing behavioral change described as decreased in verbal output, requiring assistance in bathing, and sudden urge to leave the hotel room in the middle of the night. The said symptoms prompted the patient to seek consult to a psychiatrist who medicated her with Risperidone, however, there was no noted improvement of the said symptoms.

After a few days, patient suddenly experienced onset of seizures described as tonic extension of both arms lasting for approximately one to two minutes occurring eight to ten times a day with post ictal regain of consciousness and spontaneous purposeful movements of all extremities, however, now with no verbal response and mostly stays in bed. Consequently, consultation was done and she was managed as a case of Status epilepticus and Tuberculosis Meningitis. She was given Levetiracetam and anti-tuberculosis medications (Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol). However, despite all the medications, there was still persistence of seizures. Diagnosis of exclusion was done by ruling out presence of other bacterial and viral causes of encephalitis with patient's CSF as specimen (Table 1). At this point, Autoimmune Encephalitis (anti-NMDA receptor antibody induced) was considered. The patient was then admitted to undergo plasma exchange treatment. Further work-ups were done which then revealed presence of ovarian teratoma which further supports the diagnosis (Figure 1). Hence, the patient was advised to undergo left salpingo-oophorectomy.

BIOFIRE FILM ARRAY MENINGITIS / ENCEPHALITIS (ME) PANEL	
BACTERIA	
Escherichia coli K1	Not detected
Haemophilus influenzae	Not detected
Listeria monocytogenes	Not detected
Neisseria meningitidis	Not detected
Streptococcus agalactiae	Not detected
Streptococcus pneumoniae	Not detected
VIRUSES	
Cytomegalovirus	Not detected
Enterovirus	Not detected
Herpes simplex virus 1	Not detected
Herpes simplex virus 2	Not detected
Human herpesvirus 6	Not detected
Human parechovirus	Not detected
Varicella zoster virus	Not detected

YEAST	
Cryptococcus neoformans/gattii	Not detected
MTB / RIF	
Myco. tuberculosis (MTB)	Not detected
SPECIMEN	CSF

Table 1. Pre-operative Laboratory Examination

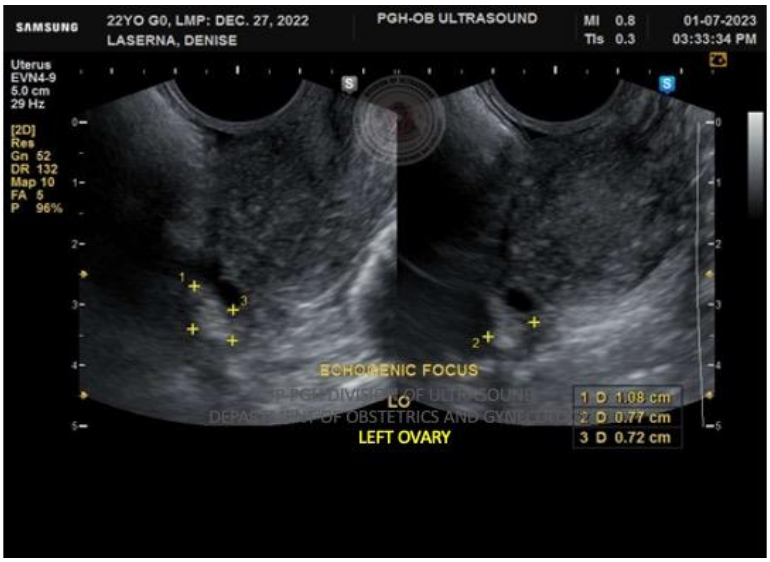

Figure 1. Bilateral polycystic ovaries; consideration of a dermoid focus 1.1 x 0.8 x 0.7cm (volume 0.3cc) within the stroma the left ovary

Medication was held on the operative day. General endotracheal anesthesia with peripheral nerve block were the chosen anesthesia techniques. Bispectral index (BIS) and invasive arterial monitoring were used intraoperatively. General anesthesia was induced with intravenous bolus administration of Propofol 2 mg/kg, Fentanyl 2 mcg/kg, and Rocuronium 0.6 mg/kg. Tracheal intubation was uneventful. Anesthesia was maintained with Sevoflurane. Quadratus lumborum block (QLB, type 1) was performed using ultrasound guidance with 0.25% Bupivacaine, 20 mL on each side (Figure 2). The BIS was about 60 during the operation. Surgery was done with no intraoperative events noted. Acetaminophen 600 mg was administered intravenously for postoperative analgesia. Sugammadex 4 mg/kg was administered intravenously to reverse the muscle relaxant. The patient was successfully extubated, with no signs of neurological or cognitive disturbances. She could breathe spontaneously without snoring or apnea after extubation. Her vital signs were stable and she did not complain of pain.

Figure 2. Quadratus Lumborum (QL, Type 1) Block

The patient significantly improved clinically one week after surgery. She spoke clearly and was talking coherently. Even though, the patient still complained of intermittent visual hallucinations, otherwise, she had an excellent functional recovery and was sent home.

DISCUSSION

Autoimmune encephalitis anesthesia should take three factors into account: the choice of anesthetic and anesthetic type, suitable anesthesia maintenance, and post-operative care. Anesthesiologists should select the best anesthetic for a patient with autoimmune encephalitis especially since most anesthetics have some impact on the NMDA receptor. This implies that the postoperative condition may be impacted by the anesthetic decision. Anesthesia side effects that go unnoticed can make recovery more difficult. These include aspiration and aspiration pneumonia, among others, as well as delayed awakening from anesthesia, confusion, seizures, apnea and hypoventilation after extubation, need for tracheal reintubation, and others.[3] In order to avoid the said adverse effects, understanding of the clinical entity of autoimmune encephalitis is crucial.

The NMDAR is one of two major receptors associated with the effect site of anesthetic agents, along with the gamma-aminobutyric acid type A (GABAA) receptor, [8] therefore can induce the same symptoms with autoimmune encephalitis.

Propofol was also shown to inhibit NMDA-R at the concentrations typically employed to maintain a general anesthesia in vitro by preventing the phosphorylation of the NR1 subunit in neurons. [7,9,10] Volatile anesthetics such as sevoflurane, isoflurane and desflurane are said to improve GABAergic transmission. [8] Its impact on the NMDA pathway has been indirectly shown through the suppression of NMDA-gated currents and NMDA-induced depolarization of the mitochondrial membrane. [11] An experimental study showed that effects of opioids (fentanyl, remifentanil, and sufentanil) on patients with anti-NMDAR are decreased because they are said to stimulate NMDAR of different subunit combinations (NR1A/2A, NR1A/2B). [13] As a result, a significant dose of opioid may be required for analgesia. However, due to the possibility of central hypoventilation, opioids should be given to these individuals

with caution.

Appropriate anesthesia technique

Ideal anesthesia for autoimmune encephalitis is still under discussion. General anesthesia has been chosen predominantly for patients with anti-NMDA receptor antibody encephalitis. Few case reports have described the use of a combination of propofol and volatile anesthetics [3,9], or total intravenous anesthesia (TIVA) with propofol and remifentanil for general anesthesia. [8,14] Moreover, the effects of TIVA or inhalational agents in patients with anti-NMDA receptor encephalitis are controversial.

Pain involves the activation of NMDA receptors, particularly the NR2B subunit. [15,16] NMDA receptor antagonists are powerful analgesics. Patients with anti-NMDA receptor encephalitis are likely to already have a diminished feeling of pain. [7,17] In anti NMDA receptor encephalitis, antibodies target the extracellular N-terminal region of the NR1 subunit, which is followed by antibody-mediated capping and internalization of NMDA receptors leading to reduced receptor density and NMDAR-mediated currents. [18,19] Peripheral NMDA receptor antagonism may even be effective in preventing visceral pain. By blocking both somatic nerves and the lower thoracic sympathetic trunk, the QLB could theoretically relieve both somatic and visceral pain. Hence, a peripheral nerve block can provide better analgesia for open lower abdominal surgery such as ovarian cystectomy, but rarely as the sole anesthetic.

CONCLUSION

We described a 22-year old woman suspected to have autoimmune encephalitis who required surgical resection of ovarian teratoma under general anesthesia and peripheral nerve block. In the anesthetic course presented, neither psychoneuronal modification nor autonomic instability was evident.

Although a definite conclusion cannot be made until more is known about anti-NMDA encephalitis and its effect on anesthesia. We imply that propofol and sevoflurane are safely used in patients with anti-NMDAR encephalitis, albeit their indirect pharmacological effects on NMDAR. Also, these patients have an altered perception to pain. This may contribute to the feasibility of peripheral nerve block on lower abdominal surgery.

INFORMED CONSENT

Physical copy is available upon request.

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