ANAESTHETIC MANAGEMENT OF NMDA RECEPTOR ENCEPHALITIS IN A 19-YEAR-OLD PATIENT WITH OVARIAN DERMOID POSTED FOR CYSTECTOMY- A RARE CASE REPORT

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PRESENTATION OF CASE

A 19-year-old female patient presented with auditory hallucinations along with unusual phobias and abnormal behaviour for 1 year.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included psychosis, anxiety disorder, phobia, obsessive compulsive disorder, dissociative disorder and schizophrenia.

CLINICAL DIAGNOSIS

The patient was apparently well 1 year back when she started having auditory hallucinations along with unusual phobias and abnormal behaviour. She was diagnosed as dissociative disorder in Safdarjung hospital and was put on sedatives. After 2 days she was referred to RML hospital for admission where she was admitted for a period for 10 days. After 10 days of admission, she had sudden onset seizures and was started on sodium valproate for the same. She also had some autonomic disturbances and was then transferred to medicine ward for further management.

Her serum was tested for NMDA serology and the test turned out to be positive. Abdominal ultrasound revealed dermoid cyst in ovary.

She was given a course of intravenous immunoglobulin for 5 days and then the patient was shifted to AIIMS for further management.

In AIIMS she underwent CSF serology which turned out to be positive. MRI brain was normal. PET scan revealed dermoid ovary of 15cm.

She was started on Tab. Wysolone, Tab. Mycophenytyl, Tab. Quitipine, Tab. Calflash, Tab. Tegrital.

She was scheduled for laparotomy and cystectomy for which patient was transferred to Safdarjung hospital.

PATHOLOGICAL DISCUSSION

Anti NMDR encephalitis was first characterized in 2007.[1] This disease has been associated with malignancies such as germ cell tumours of ovarian teratoma and breast cancer with unclear aetiology and incidence.[1-7] It is classified as a paraneoplastic syndrome and involves the production of auto antibodies against NMDAR subunits in the tumour.[3,8] Early stages are characterized by psychiatric symptoms, late stage are often accompanied by paroxysmal sympathetic hyperactivity that includes hyperthermia, tachycardia or hypertension, hypoventilation, motor or complex seizures.[8-10] Various treatment modalities, including first line immunotherapy corticosteroid and or IV IG and/or plasma exchange and early removal of an underlying tumor, may be associated with a good prognosis.

Patients undergoing surgical resection of tumours commonly require general anaesthesia.[2] The anaesthetic considerations are related to autonomic instability including hyperthermia, tachycardia, hypertension and bradycardia.[11] Various anaesthetic drugs like ketamine, propofol, opioids and inhaled anaesthetic agents like N_2O, Sevoflurane acting on NMDA receptor may behave unpredictably. N_2O reduces NMDA receptor mediated excitatory currents in the basolateral amygdala and are associated with anaesthesia induced amnesia and the formation of aversion memories, fear and addictive behaviours.[12] Ketamine binds to phencyclidine site of ion channel of NMDA receptor acting as an antagonist to inhibit the influx of Na+ and Ca2+, causing similar clinical features as the disease itself.[11] Propofol acts by enhancing GABAergic transmission and may also inhibit NMDARs in vitro.[13-15] However, the clinical relevance of this inhibition has not been established. Moreover, drugs that primarily act on GABA receptors, including phenobarbital, diazepam and midazolam may also have indirect interactions with NMDA receptors. Sufentanil and Cisatracurium appear to have no significant effect on NMDA receptors.[16] Several important medications have been well tolerated during surgery such as fentanyl, Sufentanil, Remifentanyl, Propofol, Sevoflurane, isoflurane, desflurane, vecuronium, rocuronium and cisatracurium. Chen W et al reported that in three cases for ovarian teratoma resection anaesthesia was given with Midazolam, fentanyl, propofol and rocuronium for maintenance. All patient survived the surgery and were discharged with mild psychiatric symptoms.[17] Lapebic et al hypothesized that in anaesthesia combining propofol and sevoflurane simultaneously worsen the clinical presentation of anti NMDA receptor encephalitis by facilitating the inhibition of the NMDA pathway.[18] However most cases, did not provide a detailed anaesthetic procedure, and did not describe the postoperative course. Therefore, there is a requirement for additional studies to decide on the choice of anaesthetics for patients with anti- NMDAR encephalitis.[2]

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In a study by Chen W et al[17] and Lapebic et al[18] the condition of all the cases deteriorated to some degree after anaesthesia, but all of them ultimately survived. Chen W et el[17] reported extubation of 3 patients on the 1st, 5th and 90th day after surgery and were discharged on the 3rd, 5th and 8th week respectively after surgery according to the status of anti NMDAR encephalitis. However, all patients suffered with neurological and psychiatric symptoms and had to be treated with immunoglobulin after surgery.

DISCUSSION OF MANAGEMENT

After the diagnosis of dermoid ovary was made on the PET scan she was started on Tab. Wysolone, Tab. Mycophenytyl, Tab. Quitipine, Tab. Calflash, Tab. Tegrital.

She was scheduled for laparotomy and cystectomy for which patient was transferred to Safdarjung hospital.

Preoperatively, MRI pelvis was done which revealed large cystic pelvic mass 12.8*8.7*11.8 cm containing fat and calcification with nonvisualisation of left ovary. Patient was conscious oriented. Baseline heart rate 70beats per minute, blood pressure 111/82 mmHg and saturation of 97% on room air.

In theatre, under standard monitored patient was given general anaesthesia with inj propofol 50mg and vecuronium 5mg IV after premedicating with Inj. Midazolam 1mg IV and Inj. Fentanyl 50+25 mcg IV. Airway was secured using Proseal laryngeal mask airway # 3. Anaesthesia was maintained with Oxygen and isoflurane.

Surgery was started, and cystectomy was done. Inj. Paracetamol was administered intravenously to supplement analgesia. Patient was given steroid cover intraoperatively with Inj. dexamethasone 8mg and Inj. hydrocortisone 100mg IV. Intraoperatively she was stable with blood pressure of 96/62 mmHg- 148/100 mmHg, heart rate 50-119 bpm and saturation 97-100%. A 12*10 cm cystic mass with smooth surface was removed successfully in 2 hours with minimal blood loss. No episodes of autonomic instability were seen.

Postoperatively she was reversed with inj neostigmine 2.5mg and Inj. glycopyrollate 0.4mg and was extubated. She was hemodynamically stable and remained calm. Then she was shifted to HDU for observation.

In our patient, we used Propofol, vecuronium for maintenance and PCM for analgesic supplement. Vasopressors, beta blocker antihypertensive and anticholinergics were readily available. Patient was reversed and extubated and was stable in postoperative course. Stable condition of the patient may be attributed to the remission of the condition pre-operatively.

FINAL DIAGNOSIS

The final diagnosis of NMDA receptor encephalitis with dermoid ovarian cyst was made and our patient was subjected to surgery.

Anti-N-methyl-D-aspartate receptor encephalitis is an immune mediated syndrome that remains under recognized despite a growing body of literature.[19] In 2007, the NMDA receptor encephalitis was first described and since then it has entered the mainstream of neurology and other disciplines.[20] The disorder predominantly affects children and young adults, occurs with or without tumor association and responds to treatment but can relapse. [20] Commonly associated with mature ovarian teratomas.[19] More frequent in women older than 18 years and slightly more predominant in black women than white women.[20] The symptoms include psychotic encephalopathy, epilepsy movements and facial abnormalities, alteration of consciousness and central hypoventilation.

In this case report we present the anaesthetic management of a 19-year-old female for ovarian dermoid cystectomy associated with anti NMDAR encephalitis highlighting on the specific aspects of anaesthetic management for this rare type of encephalitis. In patients with NMDA encephalitis, NMDA receptor antagonist such as ketamine, N_2O and tramadol, should be avoided whereas benzodiazepines, opioids muscle relaxants and curares are preferred as these drugs have no significant effect on the NMDA pathway. Medication with indirect interactions with NMDARs can be used with caution. Adequate preparation, availability of vasoactive agents and monitoring all throughout the perioperative period, particularly in the postoperative period is of vital importance. The literature is scarce to date for describing anaesthetic management for patient with anti-NMDAR encephalitis and there is a need for further investigations and detailed guidelines for anaesthesiologist to develop a stable perioperative anaesthetic plan for patients with this condition and to access surgery related risk factors of anti-NMDAR encephalitis.

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