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Case Report

Anaesthesia Section

Anaesthetic Considerations in Myasthenia Gravis: Strategies to Mitigate Cholinergic Crisis during Thymectomy

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ABSTRACT

Myasthenia Gravis (MG) is an autoimmune neuromuscular disorder characterised by muscle weakness due to antibodies directed against acetylcholine receptors at the neuromuscular junction. Patients with MG presents with significant anaesthetic challenges, including prolonged neuromuscular blockade, higher risk for perioperative myasthenic or cholinergic crises and risk of postoperative respiratory failure, chances of delayed extubation, potential need for postoperative ventilator support and risks associated due to close proximity to mediastinal structures. Thymectomy is the key treatment for MG and these challenges are to be anticipated during procedures like Video-Assisted Thoracoscopic Thymectomy (VATS). We present the anaesthetic management of a 24-year-old female with MG and co-existing hypothyroidism, who underwent laparoscopic VATS. Anaesthesia was induced using a non-depolarising muscle relaxant under neuromuscular monitoring, along with thoracic epidural analgesia and left-sided Double Lumen Tube (DLT) to facilitate one lung ventilation. Despite thorough preoperative optimisation, the patient exhibited intraoperative signs suggestive of cholinergic crisis, most likely due to excessive anticholinesterase therapy. The crisis was promptly recognised and effectively managed by providing appropriate supportive care and discontinuing anticholinesterase therapy. Postoperatively, the patient was extubated successfully without the need for ventilator support. This case emphasises the critical role of comprehensive preoperative assessment, vigilant intraoperative monitoring, and the ability to accurately distinguish between myasthenic and cholinergic crises. It also illustrates the anaesthetic challenges associated in managing MG, particularly in patients with coexisting endocrine disorders such as hypothyroidism. Timely recognition and a tailored anaesthetic approach are essential for optimising outcomes in such complex cases.

Keywords: Double lumen tube, Myasthenia crisis, One lung ventilation, Video-assisted thymectomy

CASE REPORT

A 24-year-old female with a 5-year history of MG, classified as Osserman type IIB presented with ptosis, dysphagia, difficulty with chewing, and both limb weakness. Her medications included Pyridostigmine 60 mg four times daily, Prednisolone 40 mg once daily, Azathioprine 50 mg twice daily, and Thyroxine 75 mcg once daily for her co-existing hypothyroidism. She had a myasthenic crisis three years prior, which was managed with mechanical ventilation, intravenous immunoglobulin, and plasmapheresis. Preoperative assessment revealed generalised muscle weakness with prominent ocular and bulbar involvement. Respiratory function remained stable; pulmonary function tests, including vital capacity, negative inspiratory force, and peak expiratory flow rate, were all within normal limits.

She was started on preoperative respiratory physiotherapy and incentive spirometry to enhance and preserve pulmonary function. Routine investigations, including chest X-ray and echocardiography were normal. Acetylcholine Receptor (AChR) antibody titers were elevated – 13.31 nmol/L (reference value ≤0.02 nmol/L). Repetitive nerve stimulation test showed a decremental response in the orbicularis oculi muscle. Computed tomography revealed thymic tissue of 5×1.3×3 cm in the anterior mediastinum. In view of her clinical status, she underwent plasmapheresis two weeks prior to surgery to reduce risk of perioperative complications. She was scheduled for laparoscopic VATS and pyridostigmine was discontinued on the morning of surgery. The anaesthesia plan comprised – thoracic epidural analgesia and one-lung ventilation, with restricted use of Neuromuscular Blocking Agents (NMBA). Considering the patient's prior crisis history and moderate disease severity, elective postoperative ventilation was considered, and an ICU bed was reserved for close monitoring. Difficult airway cart was prepared, and aspiration prophylaxis was initiated. During anaesthesia induction, the patient was closely monitored for respiratory compromise, with no adverse responses observed.

Upon arrival in the operating theater, standard monitors were connected, and thoracic epidural catheter was fixed at T3-T4 level. The patient was preoxygenated and premedicated with glycopyrrolate 0.004 mg/kg, midazolam 0.01 mg/kg, fentanyl 2 mcg/kg, ondansetron 0.1 mg/kg, metoclopramide 0.1 mg/kg, and hydrocortisone 2 mg/kg. General anaesthesia was induced with sevoflurane and propofol 2 mg/kg, followed by bag-mask ventilation with 100% oxygen, atracurium 0.3 mg/kg, and endotracheal intubation using a 37F left-sided (Robertshaw) DLT. The patient was positioned in the left lateral decubitus position for one lung ventilation, with low tidal volume (6 mL/kg), Positive End Expiratory Pressure (PEEP) 5 cmH_2O, and intraoperative recruitment maneuvers. Anaesthesia was maintained with sevoflurane, oxygen, air, fentanyl boluses, and Train-Of-Four (TOF) guided atracurium boluses (0.1 mg/kg, one-fifth the standard dose). The left radial artery was cannulated for invasive blood pressure monitoring. For intraoperative analgesia, 6 mL of 0.25% bupivacaine and 2 mg of morphine was infused, followed by continuous infusion of 0.25% bupivacaine through the epidural catheter at 3 mL/hr. Intraoperatively, vitals, pulse oximetry, and capnography were continuously monitored. The patient received 1200 mL of isotonic saline, with an estimated blood loss of 80 mL. Strict control of arterial blood gases was maintained. Throughout the procedure vital parameters remained stable, heart rate of 74 beats/min, blood pressure at 125/82 mmHg, end-tidal CO_2 of 34 mmHg, respiratory rate of 12 breaths/min, and oxygen saturation of 99%. VATS was completed, and the specimen was sent for histopathological examination.

At the end of the procedure, the DLT was replaced with 7.0 size endotracheal tube to facilitate continued monitoring. Once the

patient resumed spontaneous respiration and TOF ratio was >0.9, neuromuscular blockade was reversed with neostigmine 0.04 mg/kg and glycopyrrolate 0.008 mg/kg. Subsequently, the patient developed bradycardia (48 beats/min), excessive oral secretions, and tachypnoea (32 breaths/min). Pupillary constriction was also noted. Cholinergic crisis was suspected, and intravenous atropine 1.8 mg (0.03 mg/kg) was administered, followed by thorough oral suctioning. The patient was supported with ventilation till secretions ceased and vitally stable; she was extubated cautiously after meeting extubation criteria. Post-extubation, the patient was transferred to the surgical Intensive Care Unit (ICU), where her vitals remained stable and was continued on supplemental oxygen. Emergency reintubation equipments and difficult airway cart were kept standby at the bedside. She remained haemodynamically stable and maintained satisfactory blood gas status, and required no anticholinesterase drugs during this period.

DISCUSSION

A comprehensive preoperative anaesthetic evaluation encompassing disease severity, ongoing treatment, respiratory function, and bulbar involvement is essential for MG patients undergoing thymectomy [1]. Optimisation includes respiratory and chest physiotherapy, and in high-risk cases, plasmapheresis or intravenous immunoglobulin is recommended to reduce perioperative complications. Respiratory muscle weakness increases the risk of pulmonary complications - atelectasis and aspiration, often necessitating prolonged postoperative ventilation. Additionally, due to autoantibodies targeting adrenergic receptors, these patients have a higher risk of cardiac involvement, making preoperative cardiovascular assessment crucial [2]. Surgical outcomes are more favourable when performed during the stable phase of MG, with minimal reliance on immunomodulatory therapy and glucocorticoids, thereby reducing the risk of perioperative myasthenic crisis. In patients with pulmonary or bulbar involvement, steroid therapy and premedication with proton pump inhibitors or prokinetics is recommended to minimise aspiration risk [1].

In the index case, morning dose of Pyridostigmine (acetylcholinesterase inhibitors - AChEI)) was withheld. Nagre AS et al., reported that continued administration until the morning of surgery may increase acetylcholine availability at the neuromuscular junction, leading to an altered response to NMBAs [3]. Additionally, Gajendran R et al., and Sanders DB et al., noted that it might interfere with NMBA reversal [2,4]. However, Pal A et al., cautions that withholding anticholinesterases can cause respiratory and bulbar weakness in dependent patients [1]. Therefore, the decision should be individualised based on the preoperative disease stability of each patient before surgery.

The MG patients are highly sensitive to non-depolarising NMBAs; even small doses can cause respiratory compromise or impair airway protection [5]. TOF monitoring is essential to guide dosing and avoid prolonged neuromuscular blockade [6]. Rapid neuromuscular recovery has been observed in MG patients receiving rocuronium when reversed with sugammadex (2 mg/kg), making this a safer option when neuromuscular relaxation is necessary [7]. According to Pal A et al., incremental doses of atracurium can also be safely used for neuromuscular blockade [1]. In the present case, blockade was achieved with incremental doses of atracurium, which showed a prolonged effect compared to patients without MG reversal of steroidal NMBA, sugammadex is the agent of choice. While neostigmine may be used, lower-than-standard doses are recommended due to the risk of cholinergic crisis [8]. Kumar P et al., reported that inhalational and Total Intravenous Anaesthesia (TIVA) using agents like propofol and sevoflurane, without NMBA, can provide sufficient relaxation and facilitate early extubation, minimising the need for postoperative ventilation [9]. Similarly, Uchida S et al., managed a case of subclinical MG with thymoma with total intravenous propofol and remifentanil to assess the effect of neuromuscular effects of rocuronium [5]. Kiran U et al., also documented successful thymectomy using sevoflurane as the sole anaesthetic agent in a paediatric patient with juvenile MG and thymoma [10].

Myasthenic patients with ocular MG or in remission, exhibit resistance to depolarising NMBA - succinylcholine, due to a reduced number of Acetylcholine Receptors (AChRs). Pyridostigmine may further prolong action of succinylcholine by inhibiting plasma cholinesterase, and repeated doses can result in a phase II block [11]. Hence, succinylcholine should be avoided unless airway management is anticipated to be difficult.

During one-lung ventilation for thymectomy, lung-protective strategies are critical to minimise atelectasis and ensure adequate oxygenation. These include low tidal volumes (4-6 mL/kg), appropriate PEEP (5-8 cmH_2O), low FiO_2, pressure-controlled ventilation, and alveolar recruitment manoeuvers [12].

Excess dosage of AChEI can lead to cholinergic crisis, caused by excessive Acetylcholine (ACh) and overstimulation of nicotinic and muscarinic receptors at the neuromuscular junction. Symptoms include salivation, lacrimation, urination, diarrhoea, gastrointestinal cramps, emesis, miosis, muscle weakness, fasciculations, respiratory paralysis, and blurred vision. Differentiating between myasthenic and cholinergic crises is crucial; using the edrophonium test intravenously (2 mg). If there is clinical improvement of symptoms, it is due to myasthenic crisis, and if there is worsening of symptoms, it is due to cholinergic crisis. Myasthenic crisis can be managed with AChEI to enhance neuromuscular transmission. Whereas cholinergic crisis results from excessive AChEI use, overstimulating cholinergic receptors. Management of cholinergic crisis includes airway protection, secretion clearance, and haemodynamic stabilisation and the antidote - intravenous atropine 0.03 mg/kg, which blocks muscarinic receptors. It should be titrated until signs of atropinisation (tachycardia, mydriasis, warm skin) are observed. Pralidoxime reverses nicotinic effects, particularly respiratory weakness and should be continued until muscle strength improves [13].

Patients with bulbar and respiratory involvement face greater risk of delayed extubation due to aspiration and compromised postoperative respiratory function. Incomplete reversal may result in delayed recovery, prolonged ventilation, and respiratory failure. Fluctuating muscle weakness in MG, particularly involving the diaphragm and intercostals impairs ventilation. Hence, adequate reversal is essential in these patients. Neostigmine carries a risk of cholinergic crisis, making sugammadex the preferred agent for reversing steroidal NMBA [5,11].

These patients often have reduced respiratory reserve, necessitating vigilant monitoring and strict extubation criteria, including adequate tidal volume, oxygenation, ventilation, and consciousness. Postoperatively, careful weaning from mechanical ventilation and monitoring for respiratory insufficiency are crucial. Extubation criteria for MG patients include: 1) adequate level of consciousness; 2) tidal volume >5 mL/kg; 3) PaCO2 <50 mmHg; 4) PaO2 >90 mmHg; and 5) respiratory rate <30 breaths/min. In our case, careful monitoring and timely intervention ensured airway clearance, stabilised respiratory status, and prevented aspiration, facilitating smooth transition from mechanical ventilation to spontaneous breathing.

CONCLUSION(S)

Careful preoperative evaluation, understanding of disease pathophysiology, and multidisciplinary approach, combined with a balanced anaesthesia technique minimising inhalational anaesthetics and muscle relaxants, enabled extubation on the operating table and ensured a safe outcome in this complex case. Awareness and prompt management of perioperative myasthenic and cholinergic crises remain essential. Although NMBA are ideally avoided in MG, the use of rocuronium with sugammadex for rapid reversal shows significant results, but warrants further investigation to establish standardised protocols on dosages. Future research should also compare the efficacy and safety of inhalational agents such as sevoflurane, either alone or combined with TIVA. Pyridostigmine

dosing should be carefully adjusted to balance the risk of myasthenic crisis against cholinergic toxicity and while continuation of anticholinesterases appears preliminarily safe, larger controlled studies are required to confirm their tolerability and impact on outcomes.

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