Myasthenic crisis and late deep vein thrombosis following thymectomy in a patient with myasthenia gravis

A case report

Cheng-Yuan Lin, MD, Wei-Cheng Liu, MD, Min-Hsien Chiang, MD, I-Ting Tsai, MD, Jen-Yin Chen, MD, PhD, Wan-Jung Cheng, MD, Chun-Ning Ho, MD, Shu-Wei Liao, MD, Chin-Chen Chu, MD, PhD, Cheuk-Kwan Sun, MD, PhD, Kuo-Chuan Hung, MD

Abstract

Introduction: Surgical stress and pain are potential provoking factors for postoperative myasthenic crisis (POMC). We report the occurrence of early POMC and late deep vein thrombosis (DVT) in a man with myasthenia gravis (MG) undergoing thymectomy, addressing possible link between reversal of opioid overdose with naloxone and the triggering of POMC.

Patient concerns: A 71-year-old man with impaired renal function (ie, estimated glomerular filtration rate [eGFR]: 49.1 mL/min/1.73 m²) with diagnosis of MG made 2 months ago was scheduled for thymectomy. After uncomplicated surgery, he experienced opioid overdose that was treated with naloxone. Hyperlactatemia then developed with a concomitant episode of hypertension. Three hours after reversal, he suffered from myasthenic crisis presenting with respiratory failure and difficult weaning from mechanical ventilation.

Diagnosis: Stress-induced hyperlactatemia and subsequent myasthenic crisis

Interventions: Pyridostigmine and immunosuppressive therapy with prednisolone were initiated. Hyperlactatemia subsided on postoperative day (POD) 5. Tracheal extubation was performed successfully on POD 6.

Outcomes: During the course of hospitalization, his eGFR (ie, 88.9 mL/min/1.73 m²) was found to improve postoperatively. After discharge from hospital, he developed DVT in the left femoral and popliteal veins on POD 24 when he was readmitted for immediate treatment with low-molecular-weight heparin. He was discharged without sequelae on POD 31. There was no recurrence of myasthenic crisis or DVT at 3-month follow-up.

Conclusions: Following naloxone administration, hyperlactatemia may be an indicator of pain-related stress response, which is a potential provoking factor for myasthenic crisis. Additionally, patients with MG may have an increased risk of DVT possibly attributable to immune-mediated inflammation. These findings highlight the importance of perioperative avoidance of provoking factors including monitoring of stress-induced elevations in serum lactate concentration, close postoperative surveying for myasthenic crisis, and early recognition of possible thromboembolic complications in this patient population.

Abbreviations: DVT = deep vein thrombosis, eGFR = estimated glomerular filtration rate, MG = myasthenia gravis, PACU = post-anesthesia care unit, POD = postoperative day, POMC = postoperative myasthenic crisis, TOF = train-of-four, WHO = World Health Organization.

Keywords: deep vein thrombosis, hyperlactatemia, myasthenia gravis, myasthenic crisis, thymectomy
1. Introduction
Myasthenia gravis (MG), an autoimmune antibody-mediated disease that affects the neuromuscular junction, is characterized by fluctuating weakness of voluntary muscles, in particular the extracocular, bulbar, and proximal limb muscles. It is considered to be a rare disease with an overall incidence rate of about 0.01 per 1,000 persons/yr in the United States. Although thymectomy is the first-line therapy for thymomatous MG patients, various medications, surgical stress, and anesthetic agents may trigger postoperative myasthenic crisis (POMC) after this procedure. We reported the occurrence of POMC in a man who developed hyperlactatemia after naloxone administration for opioid overdose. During the course of hospitalization, his renal function was found to improve after thymectomy. He also developed late deep vein thrombosis (DVT) after discharge from hospital. The associations among MG, DVT, and renal pathology as well as the possible link between perioperative hyperlactatemia and POMC were also discussed. Written consent was obtained from the patient.

2. Case presentation
A 71-year-old man, non-smoker (height: 155 cm; weight: 59 kg), was scheduled to receive video-assisted thoracoscopic extended thymectomy with the diagnosis of MG. Two months previously, he developed symptoms of right ptosis and progressive swallowing difficulty. Based on a positive response to edrophonium and increased titers of autoantibodies to acetylcholine receptor (19.3 nmol/L; normal < 0.2 nmol/L), he was diagnosed as having MG with severity belonging to Osserman’s classification IIb (ie, generalized moderate weakness and/or bulbar dysfunction). Thoracic computed tomography demonstrated glandular hyperplasia of the thymus (Fig. 1A). The patient was started on prednisolone 20 mg daily and pyridostigmine 60 mg three times daily. His past history included hypertension without evidence of previous myasthenic crisis or thromboembolic events (eg, history of lower limb swelling). The results of electrocardiography, pulmonary function test [eg, vital capacity: 93%], echocardiography (eg, left ventricular ejection fraction: 85.1%), chest radiography (Fig. 1B), and laboratory studies (eg, coagulation test) were unremarkable. On the other hand, impaired renal function [i.e., serum creatinine: 1.42 mg/dL; eGFR: 49.1 mL/min/1.73 m²] was observed after admission.

Preoperative physical examination of the patient showed clear consciousness without respiratory distress. Vital signs included a blood pressure of 187/103 mmHg, heart rate of 82 beats/min, and respiratory rate of 14 breaths/minute. Under real-time neuromuscular monitoring with a train-of-four (TOF) monitor (TOF-watch SX, N.V. Organon, Oss, Netherlands), anesthesia was induced with propofol (130 mg) and rocuronium (0.85 mg/kg). Following successful tracheal intubation with a double-lumen tracheal tube (Broncho-Cath; Mallinckrodt, Athlone, Ireland), general anesthesia was maintained with sevoflurane, rocuronium (total dosage: 40 mg), and a continuous infusion of remifentanil. An 18-gauge peripheral intravenous line and an arterial line were introduced. The surgical time was 4 hours 15 minutes with an estimated blood loss of 100 mL. Upon completion of surgery, sugammadex 4 mg/kg was administered to reverse neuromuscular blockade, with a maximum TOF ratio of 0.93 following reversal. Additionally, intravenous morphine 8 mg was given for postoperative analgesia. After successful extubation in the operating room and resumption of spontaneous breathing, he was transferred to the post-anesthesia care unit (PACU) for further care.

During the immediate postoperative period, the patient was hemodynamically stable without respiratory distress. Because of surgical pain with a numeric rating scale of 5 (scale of 0–10), intravenous morphine was titrated to a total dosage of 7 mg. Forty-five minutes later, respiratory distress with drowsiness was noted. Physical examination found pinpoint pupils with a TOF ratio of 0.9. Blood gas analysis demonstrated severe hypercapnia (arterial carbon dioxide pressure: 117.7 mm Hg) and acidosis (pH: 6.996, lactate levels: 3.3 mmol/L). On suspicion of morphine overdose, intravenous naloxone was administered twice (0.08 mg

Figure 1. (A) Thymic hyperplasia on thoracic computed tomography (CT) (arrow); (B) Unremarkable finding on preoperative chest radiograph, indicating unlikely non-pulmonary origin of postoperative respiratory distress. CT = computed tomography.
3. Discussion

Owing to the reduced number of functioning nicotinic acetylcholine receptors, even small amounts of nondepolarizing neuromuscular blocking agents can lead to profound neuromuscular blockade in patients with MG. Reversal of neuromuscular blockade in patients with MG by sugammadex has been reported to result in rapid and complete recovery of neuromuscular function without signs of postoperative residual neuromuscular blockade.[9] In our patient with respiratory distress in the PACU, postoperative recurrence of neuromuscular blockade (ie, recurarization) was unlikely based on a TOF ratio of 0.9. The diagnosis of opioid overdose was made based on the typical clinical symptoms and signs (ie, pinpoint pupils, respiratory distress, drowsiness) as well as symptom improvement after naloxone administration. Since the serum half-life of naloxone is approximately 60 minutes,[7] surgical patients receiving naloxone for reversal of opioid overdose is recommended to be observed for 90 minutes.[7] Although our patient did not develop recurarization in the PACU after observation for 100 minutes, it occurred about 3 hours after initial reversal. Patients with MG have been reported to demonstrate enhanced sensitivity to opioid,[4,10] which may at least partially explain the delayed recurarization after initial reversal in our patient.

MG is a disease of young women and old men with an overall mortality rate of 2.2%,[1] Myasthenic crisis, which occurs in approximately 15% to 20% of MG patients within the first 2 years of the diagnosis[11] with a mortality rate of 4% to 4.47%,[11,12] is characterized by respiratory failure requiring invasive or noninvasive mechanical ventilation.[1] Old age and respiratory failure requiring tracheal intubation were identified as predictors of mortality.[1] Of all patients with MG undergoing thymectomy, 10% to 11.5% may experience POMC, including preoperative bulbar symptoms, intraoperative blood loss >1000 mL, preoperative serum level of anti-acetylcholine receptor antibody >100 nmol/L[14] and WHO histologic classification B2–B3 thymoma.[13] Accordingly, the risk factors for POMC in our patient included the presence of preoperative bulbar symptoms and WHO histologic thymoma grading of B2.
The clinical predictive score, which included vital capacity <80% (yes=3, no=0), disease duration <3 months (yes=2, no=0), and bulbar symptoms immediately before thymectomy (yes=1, no=0), yields a total score ranging from 0 to 6.\textsuperscript{[15]} The probability of postoperative crisis was 0.9% and 25.9% for low (less than 3) and high (3 or more) score groups, respectively. According to this scoring system, the risk score of our patient was 3, indicating a high risk of myasthenia crisis.

4. Conclusion

Myasthenic crisis and DVT are potential complications in patients with MG following thymectomy, underscoring the importance of avoiding intraoperative provoking factors and meticulous postoperative monitoring for early detection of myasthenic crisis to prevent life-threatening events as well as continual outpatient follow-up for possible thromboembolic complications. Hyperlactatemia may be a perioperative indicator of stress related to the triggering of myasthenic crisis.
