Case report

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Postoperative myasthenia crisis (PMC) after thymoma debulking surgery

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Abstract

***Background*: Debulking surgery is a common procedure performed in myasthenia gravis due to invasive thymoma. Postoperative myasthenia crisis is a life-threatening complication that can occur after this procedure even though plasma exchange has been given before.**

***Case presentation*: We present a case report of a 44-year-old male who was diagnosed with myasthenia gravis due to thymoma and performed debulking surgery. He had progressive respiratory failure and he was diagnosed with myasthenia crisis. Because of limited resources and cost, we treated the patient with combination therapy of 3 cycles plasma exchanged and steroids over 8 days. The patient recovered and was successfully extubated on day 10 and discharged from the Intensive Care Unit (ICU) on day 12 postoperative.**

***Conclusion*: Some of the therapeutic strategies, in this case, provided modulating therapy, overcoming infections, oxygen therapy, and adequate nutrition. Plasma exchange and intravenous immunoglobulin (IVIg) are the therapeutic standard modalities for myasthenia crisis. In conditions where it is not able to provide optimal plasma exchange, therapy can be combined with steroid administration, although until now steroid administration is still controversial.**

Introduction

Thymoma is a neoplasm of the thymic gland that is 96% located in the anterior or superior mediastinum. (1) Thymoma that happens in adults leads to autoimmune diseases like myasthenia gravis. Myasthenia gravis (MG) is an autoimmune disorder that deteriorates neuromuscular transmission and leads to muscle weakness locally or generally. Thymectomy is a common procedure to reduce the risk of exacerbation, but thymectomy has complications that decrease neuromuscular junction function and causes respiratory muscle paralysis, prolonged mechanical ventilation, or re-ventilation after extubation. These are called postoperative myasthenia crises (PMC). (2) Patients with MG performed a surgical procedure needing intubation and mechanical ventilation and who experience delayed extubation of >24 hours after surgery are also considered PMC. The incidence of post thymectomy PMC is approximately 3-30% and it is a serious condition, rapid worse of MG, life-threatening, and potentially become bulbar disfunction. The mortality rate of PMC is high, approximately 6-10%. (3) Because PMC is the main cause of mortality after thymectomy with myasthenia gravis, it is important to detect early PMC and appropriate management therapy resulting in decreased mortality rate and another secondary complication. How to prefer and use modulating therapy, setting of mechanical ventilation, manage infection, and other drugs that are still controversial for PMC, are still challenging for intensivists in treating patients.

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Case report

A 41-year-old male had symptoms of fatigue, ptosis, difficulty of swallowing, and sometimes difficulty to breath. He was diagnosed with myasthenia gravis 3 months ago. He had been treated with methylprednisolone PO, vitamin B1, pyridostigmine, and acetylcysteine. The patient was a smoker before being diagnosed with MG. Thorax multisliced computed tomography (MSCT) scan revealed a mass in anterior mediastinum suggestive of thymoma, and atelectasis detection in medium lobe right pulmonary, but chest X-ray was normal (**Figure 1**). The spirometry test showed mild chest restriction. Another evaluation was normal. Preoperative optimizations, he got 3 cycles of plasma exchange using replacement fluid of 1000 ml Plasmanate® and 800 ml saline.

The procedure was carried out for 2 hours, monitoring during the procedure was stable, and bleeding was 650 ml. Postoperative, he was treated in the Intensive Care Unit (ICU) and got ceftriaxone 1 g/12 hours IV, pyridostigmine 80 mg/8 hours PO, methylprednisolone 8 mg/8 hours PO, and nebulized with a combination of N-acetylcysteine, steroid, and bronchodilator. Hemodynamic was stable, and also was respiration, therefore we extubated him on day 1 after surgery.

On day 2, or 24 hours postoperative, he presented a complaint of difficulty to breathe. Blood gas evaluation showed hypercapnia, hypoxemia, and acidosis. Chest X-ray showed pneumonia in medium and inferior lobes of the right lung (**Figure 1**), then he was performed reintubation and was put on mechanical ventilation. Then we took sputum and blood culture samples. The dose of ceftriaxone was raised to 2 g/12 hours and methylprednisolone injection was added 125 mg/6 hours. The patient has performed 3 cycles of plasma exchange with 1000 ml Plasmanate® and 800 ml saline per cycle over 6 days. The sputum culture revealed Pseudomonas aeruginosa that was still sensitive with ceftriaxone.

On day 9 in ICU, the patient was performed an evaluation where clinical presenting and chest X-ray showed improvement (**Figure 1**). The patient was carried out weaning and extubation on day 10. The patient's condition tended to be stable and he was discharged from ICU after 12-day treatment.

Discussion

There are several risk factors of PMC: 1) history of MG, 2) type of thymoma, 3) surgery technique. In case the patient experiences general MG, he is high risk to get PMC than local MG. Other factors that should be under control to minimize PMC risk are respiratory infection, aspiration, sepsis, exposure to drugs that may increase myasthenic weakness, and surgical operations. (3) Based on stage, thymoma has 4 stages: stage I, thymoma is still in its capsule; stage II, thymoma shows invasion through the capsule into the mediastinal fat or pleura; stage III, there is a macroscopic invasion into neighboring organs; and stage IV, there is an invasion to pleura, pericardial, or metastases. (4) Suggestive patient at stage II or III, so the choice of procedure was debulking thoracotomy. This procedure has a high risk of PMC because invasive thymoma has a greater risk of PMC estimated at 10-20%. (5)

Thymoma exports auto-reactive T cells that lead to deteriorating MG status, especially in debulking procedures, when thymoma was not removed completely. So auto-reactive T cells may be exported to peripheral continuously. (6) Technically, thymoma surgery is divided into 2 techniques: traditional thoracotomy and thoracoscopic surgery. Thoracotomy has a higher risk of PMC than thoracoscopic. This is maybe because tissue injury is greater in thoracotomy. An increase of respiratory secretion and diminished diffusion area of the alveolar membrane caused by pulmonary infection can contribute to the risk of PMC. (7)

The strategy of management therapy for this patient is oxygen therapy and ventilator setting, control of pulmonary infection, plasma exchange as modulating therapy, adequate nutrition, and other drugs that can improve the patient's condition. In this case, PMC occurred on day 2 postoperative while the patient had been extubated. He showed symptoms of breathing difficulty, hypoxemia, hypercapnia, and acidosis in blood gas test, and right lobe pneumonia showed by chest X-ray. These were maybe caused by hypersecretion and failure to swallow but aspirated.

Atelectasis and aspiration pneumonia is common consequence in PMC. However, atelectasis that is found in preoperative evaluation contributes to worsening PMC and pulmonary function. Aspiration pneumonia may lead to infection and infection is a precipitating factor of PMC (estimated at 38%). (8) Empiric or definitive antibiotic should be given to this patient. (9) First-line modulating therapies in PMC are intravenous immunoglobulin (IVIg) and therapeutic plasma exchange (TPE). The comparison of these two therapies can be seen in **Table 1** below.

The basic pathology of myasthenia has been known that thymus producing antibody against postsynaptic nicotinic acetylcholine receptors and thereby causing destruction and reduction of several receptors. (9,10) Plasmapheresis or TPE is an extracorporeal blood purification technique in which the plas-

ma is separated from the blood and replaced with a substitution fluid such as albumin or with plasma collected from a healthy donor. This is generally performed to remove high molecular-weight substances such as pathogenic autoantibodies, immune complexes, cryoglobulins, and toxins that have accumulated in the plasma. There is some evidence that mentions that TPE is more effective than IVIg. (11) Another study has found that the efficacy of both therapies was similar. (3) But complications caused by TPE are more than IVIg, such as hypotension, coagulopathy, and catheter-related complications. However, the effect of TPE is temporary, therefore it is recommended to combine TPE with other immunosuppressive therapy like IVIg, prednisone, and azathioprine. (1,9,10,12)

The administration of steroids until now is still controversial. In this case, the reason for steroids administration was as additional therapy while waiting for the family decision about TPE. As mentioned above that TPE has a temporary effect so a combination with steroids is more cost-effective than other immunosuppressants. (13-15) Diez et al in their study said that a combination of prednisolone with IVIg could prevent myasthenia exacerbation. Administration of high doses of steroids is not recommended because can lead to an exacerbation. (13)

Reintubation occurs in a quarter case of myasthenia gravis after extubation. Metabolic disorder (acidosis), not adequate forced vital capacity (FVC), atelectasis, and infection are factors that cause reintubation. The ventilator setting has an important role in management therapy, in this case, to prevent the increased atelectasis areas of the lungs and to make partial pressure of carbon dioxide and partial pressure of oxygen normal and correct acidosis. Using synchronized intermittent mandatory ventilation with positive end-expiratory pressure or bilevel positive airway pressure mode in the ventilation setting is recommended in this case. Weaning patients with PMC from mechanical ventilation is difficult. Several factors that should be considered in weaning and extubation are age, male, history of myasthenia crisis, other pulmonary complications, and prolonged ventilation of more than 10 days. (3) Besides clinical parameters, measurement of vital capacity and coughing ability are considered to be assessed whether the patient can be extubated or not.

Administration of other drugs should be more selective. Several drugs lead to myasthenic exacerbation, such as β-adrenergic antagonist, calcium-channel antagonist (nifedipine, verapamil), procainamide, quinidine, magnesium, antibiotic (gentamicin, ciprofloxacin, erythromycin, polymyxin, ampicillin, streptomycin), gabapentin, phenytoin, dan methimazole. (8) Perioperative pyridostigmine is controversial because on one side pyridostigmine prevents PMC, but on the other side pyridostigmine can precipitate a cholinergic crisis. Therefore, using a high dose of pyridostigmine is not recommended. (16) However, this case and Nazarbaghy's study show that using steroids and pyridostigmine in PMC patients can provide a good outcome. (5)

Conclusion

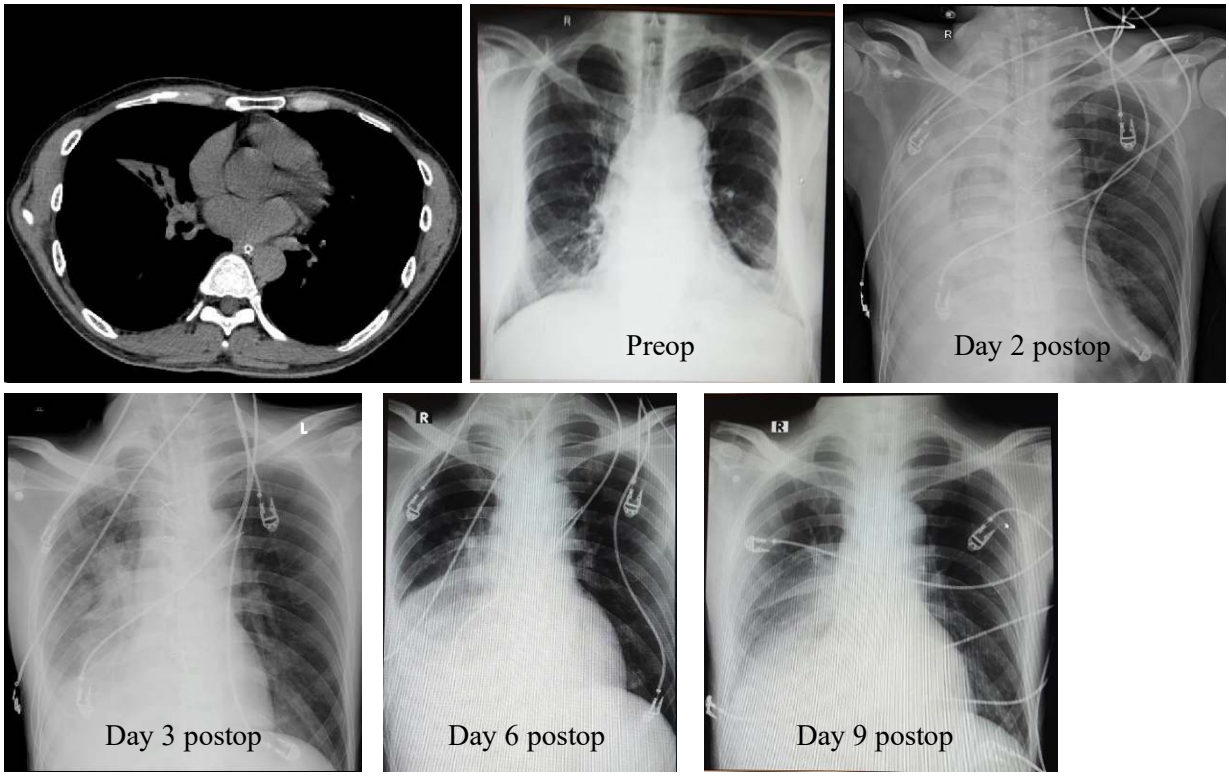
PMC can occur in postoperative thymoma, especially debulking surgery. PMC is a serious and life-threatening condition. Appropriate strategy management involves oxygen therapy, infection prevention, modulating therapy, and adequate nutrition can improve outcomes. Modulating therapies (IVIg and TPE) give the same effect. Therefore, the application of this therapy depends on the patient's condition, hospital resources, and cost.

Tabel 1. Comparison of intravenous immunoglobulin (IVIg) to plasma exchange (PE) (8)

	IVIg	PE
Dose	400 mg/kg BW x 5 days	One PE every other day over 10 days
Response	Improvement in 4-5 days, effect for 4-8 weeks	Improvement in 2 days, effect for 3-4 weeks
Advantages	More readily available	Faster treatment response
Disadvantages	Slower treatment response	Need for special venous access, equipment, and personnel
Contraindications	IgA deficiency	Hemodynamic instability, unstable coronary disease, current internal bleeding
Serious complications	Aseptic meningitis, cardiac arrhythmia, thrombocytopenia, thrombotic events	Hemodynamic instability, cardiac arrhythmia, myocardial infarction, hemolysis

Legend: BW=body weight; IgA=immunoglobulin A.

Figure 1. MSCT scan and X-ray of the chest



Legend: MSCT=multi-sliced computed tomography.

References

1. Takebayashi S, Yoshikawa Y, Morita M, Nagashima R, Nakazono Y, Miyamoto S. Myasthenic crisis appearing after resection of intracardiac ectopic thymoma with superior vena cava syndrome. Surg Case Rep [Internet]. 2021 Dec 15;7:144. Available from: https://surgicalcasereports.springeropen.com/articles/10.1186/s40792-021-01233-4
2. Krawczyk P, Adamczyk-Korbel M, Kieszko R, Korobowicz E, Milanowski J. Immunological system status and the appearance of respiratory system disturbances in thymectomized patients. Arch Immunol Ther Exp (Warsz) 2007;55:49-56.
3. Gamez J, Salvadó M, Carmona F, de Nadal M, Romero L, Ruiz D, et al. Intravenous immunoglobulin to prevent myasthenic crisis after thymectomy and other procedures can be omitted in patients with well-controlled myasthenia gravis. Ther Adv Neurol Disord 2019;12: 1756286419864497.
4. Truong MT, Sabloff BS, Gladish GW, Whitman GJ, Munden RF. Invasive thymoma. AJR Am J Roentgenol [Internet]. 2003 Dec [cited 2021 Jul 5];181:1504. Available from: https://www.ajronline.org/doi/pdf/10.2214/ajr.181.6.1811504
5. Nazarbaghi S, Amiri-Nikpour MR, Mahmodlou R, Arjmand N, Rezaei Y. Clinical outcomes of myasthenia gravis with thymoma and thymic hyperplasia undergoing extended transsternal thymectomy: A single-center experience. N Am J Med Sci 2015;7:503-8.
6. Geng Y, Zhang H, Wang Y. Risk factors of myasthenia crisis after thymectomy among myasthenia gravis patients: A meta-analysis. Medicine (Baltimore) 2020;99:e18622.
7. Liu C, Liu P, Zhang XJ, Li WQ, Qi G. Assessment of the risks of a myasthenic crisis after thymectomy in patients with myasthenia gravis: A systematic review and meta-analysis of 25 studies. J Cardiothorac Surg 2020;15:270.
8. Wendell LC, Levine JM. Myasthenic Crisis. Neurohospitalist 2011;1:16-22.
9. Kumar R, Birinder SP, Gupta S, Singh G, Kaur A. Therapeutic plasma exchange in the treatment of myasthenia gravis. Indian J Crit Care Med Internet]. 2015 [cited 2021 Jun 27];19:9-13. Available from: https://www.ijccm.org/doi/pdf/10.4103/0972-5229.148631
10. Saeteng S, Tantraworasin A, Siwachat S, Lertprasertsuke N, Euathrongchit J, Wannasopha Y. Preoperative Plasmapheresis for Elective Thymectomy in Myasthenia Patient: Is It Necessary? ISRN Neurol 2013;2013:238783.
11. Dhawan PS, Goodman BP, Harper CM, Bosch PE, Hoffman-Snyder CR, Wellik KE, et al. IVIG versus PLEX in the treatment of worsening myasthenia gravis: What is the evidence? A critically appraised topic. Neurologist 2015;19: 145-8.
12. Siahaan YMT, Ketaren RJ, Pangestu AR, Hartoyo V. Case Series: Clinical Impact of Plasmapheresis and Thymectomy on Early-Onset Myasthenia Gravis. Case Rep Neurol 2021; 13:1-8.
13. Díez-Porras L, Homedes C, Alberti MA, Vélez-Santamaría V, Casasnovas C. Intravenous immunoglobulins may prevent prednisone-exacerbation in myasthenia gravis. Sci Rep 2020; 10:13497.
14. Kato T, Kawaguchi K, Fukui T, Nakamura S, Hakiri S, Nakatochi M, et al. Risk Factors for the Exacerbation of Myasthenic Symptoms After Surgical Therapy for Myasthenia Gravis and Thymoma. Semin Thorac Cardiovasc Surg 2020;32:378-85.
15. Yamada Y, Yoshida S, Suzuki H, Tagawa T, Iwata T, Mizobuchi T, et al. Efficacy of perioperative high-dose prednisolone therapy during thymectomy in myasthenia gravis patients. J Cardiothorac Surg 2013;8:226.
16. Pêgo-Fernandes PM, de Campos JRM, Jatene FB, Marchiori P, Vargas Suso F, de Oliveira SA. Thymectomy by partial sternotomy for the treatment of myasthenia gravis. Ann Thorac Surg 2002;74:204-8.

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