Thymectomy in a patient with thymoma -related myasthenia Gravis and recent recovery from adult respiratory distress syndrome

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ABSTRACT

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Thymoma is one of the most common tumors of the anterior mediastinum in adults, arising from thymic epithelial cells. Complete surgical resection is the treatment of choice in myasthenic patients with thymoma. A 41 year-old male, with myasthenia gravis and thymoma was scheduled for thymectomy. Ten months ago, he developed pneumonia. He had a history of pneumonia (10 months ago) complicated by severe adult respiratory distress syndrome (ARDS), managed successfully with a short-term support with extracorporeal membrane lung assist device NovaLung. Long-term impairments in lung volume and diffusion capacity have been reported in adult respiratory distress syndrome survivors. Total intravenous anesthesia technique and especially muscle relaxants infusion require special attention in this group of patients. Our management strategies in this case included careful assessment of respiratory function, avoidance of premedication, use of short-acting anesthetic agents (propofol, remifentanil), use of suggamadex for reversal of rocuronium-induced neuromuscular block, and intraoperative monitoring with a train-of-four monitor and monitoring in an intensive care unit for 24 hours after surgery.

INTRODUCTION

Approximately 30-50% of thymoma patients have myasthenia gravis (MG), an autoimmune disease that affects the neuromuscular junction of skeletal muscles and that is characterized by muscle weakness and fatigue.

Thymectomy due to thymoma-associated myasthenia gravis (tMG) is very interesting to anesthesiologists because of the affected mus-

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cle groups, the pharmacology of the neuromuscular junction and the interactions of the disease and treatment with many drugs. Patients require detailed preoperative evaluation, proper anesthetic management and optimal postoperative care to avoid respiratory complications[1]. Adult respiratory distress syndrome (ARDS) survivors may experience respiratory disorders and ICU acquired neuromuscular impairments[2].

In our case, a recent history of ARDS raised concerns about perioperative management for a scheduled thymectomy in a patient with MG.

CASE REPORT

Ten months prior to hospital admission, a 41 year-old white male, developed pneumonia which progressed to ARDS. Because respiratory failure was unresponsive to conventional mechanical ventilation, the patient was maintained on an extracorporeal membrane lung assist device NovaLung (iLA; Novalung GmbH, Heilbronn, Germany). After a 28-day ICU hospitalization, he was transferred to the High Dependency Unit.

Computerized tomography (CT) of the chest revealed ground-glass opacification of the lung parenchyma with peripheral cysts and an anterior mediastinal mass in the vicinity of the thymus, raising the possibility of thymoma. Laboratory tests found high antibody titers against acetylcholine receptors (AChR antibodies, 65 nM with normal values <0.5 nM), which confirmed thymoma-associated MG. The patient was initially treated with a four-month course of prednisone (maximum dose 1 mg/kg daily) and continuous treatment with pyridostigmine (30 mg three times daily). MG was classified as grade IIa (Osserman classification), which is a mild, generalized MG that responds well to therapy[3]. Thymectomy was the next potential therapeutic measure. The treatment team had concerns about MG-associated respiratory muscle weakness, excessive secretions from anticholinesterase therapy and persistent lung dysfunction due to ARDS. In follow-up CT, lung parenchyma appeared to be improved, but ground-glass opacities remained.

Magnetic resonance imaging (MRI) of the chest showed a 3.3 cm × 4.4 cm homogeneous mediastinal mass in contact with the thymus. Assessments of lung function (Table 1) revealed a mild restrictive pattern with a mild-to-moderate reduction in carbon monoxide diffusion capacity (DLCO).

The results of a 6-minute walk test were normal. Consequently, the patient was scheduled for trans-sternal thymectomy. He continued on his anticholinesterase medication, pyridostigmine, 30 mg X 3, until the morning of surgery.

Table 1. Patient's function lung tests and arterial blood gas analysis.

Function lung tests		
	Value	**% of predicted**
FEV1 (L)	3.74	95.2
FVC (L)	4.17	86.3
FEV1/ FVC		89.7
FEV 25-75 (L/sec)	5.58	110
Inspiratory Capacity (L)	2.74	
Forced Inspiratory Vital Capacity (L)	4.31	
Single breath CO diffusing capacity (ml/min/mmHg)	18.51	56.6
FRC (L) Multi Breath N2 Wash-out	2.18	62.3
TLC(L)	4.99	69.1
6-min walking test (Distance 580 m)	SpO_2 at rest 97%	SpO_2 at end 95%
Arterial blood gas analysis (FiO_2 0.21): PaO_2 85 mmHg, $PaCO_2$ 38 mmHg, pH 7.38		

Anesthesia Induction consisted of 2 mg/kg propofol and 0.1 mcg/kg/min remifentanil. Rocuronium bromide was provided at 0.3 mg/kg as a muscle relaxant during induction. The patient required a second dose of 1 mg rocuronium according to train-of-four (TOF) monitoring. Anesthesia was maintained with continuous infusions of propofol and remifentanil. Oxygen saturation, electrocardiogram, end-tidal carbon dioxide, invasive blood pressure, and TOF were monitored continuously. At the end of the 3-hour procedure, a bolus of 2 mg/kg sugammadex (Bridion) was administered to reverse the non-depolarizing action of rocuronium. This effect was verified by expected clinical changes and TOF > 90%. The patient was successfully extubated four minutes later with evidence of efficient muscle power. He was transferred to the ICU for 24 hours. Postoperative analgesia was maintained by paracetamol and lornoxicam. Thymoma was fully encapsulated (Masaoka stage I) and was histologically classified as type AB-mixed type (WHO classification for thymomas). The postoperative period was uneventful.

DISCUSSION

Although thymomas are rare tumors arising from the epithelial cells of the thymus gland, they are one of the most common tumors of the anterior mediastinum in adults. Their prognosis depends on the macroscopic and microscopic invasion of their associated capsule and surrounding tissues. The Masaoka staging system is based on evidence for capsular invasion at the time of surgery. Stage I tumors are not invasive. The WHO classification is based on histology. Type AB thymomas are benign and are associated with long- term survival rate of

approximately 90% [4]. Surgical removal of thymus is the primary treatment in myasthenic patient with thymoma offering complete resection of the tumor. Adjuvant therapies, including chemotherapy and/or radiotherapy may be beneficial in certain cases[5]. Approximately 50% of thymomas present with one of a variety of associated parathymic syndromes, most commonly MG. Thymoma is associated with 10-15% of all patients diagnosed with MG, and 30-50% of patients diagnosed with thymoma develop MG. Myasthenia gravis (MG) is a chronic autoimmune, neuromuscular disorder affecting the neuromuscular junction. MG is caused by the production of antibodies against acetylcholine nicotinic postsynaptic receptors. Elevated levels of AChR antibodies are detected in 80- 90 % of MG patients. The manifestations of MG include skeletal muscle weakness and fatigability on exertion. Its clinical severity is assessed according to the Osserman classification[3].

Therapeutic strategies include include treatment with anticholinesterase drugs, such as pyridostigmine bromide, enhancing neuromuscular transmission, plasmapheresis, intravenous immunoglobulins, immunosuppressive agents, such as corticosteroids and azathioprine, and thymectomy[6]. Complete surgical resection of the thymus is indicated in all MG patients with thymoma. Since the thymus is a reservoir of B cells, that secrete antibodies, removal of auto-antibodies is one possible mechanism ofthymectomy in MG. This approach has resulted in significantly higher rates of clinical improvement, remission, and survival.

Most complications and surgically-related deaths can be attributed to MG crisis, which leads to delayed postoperative extubation or respiratory failure. Cholinergic crisis resulting from an excess of cholinesterase inhibitors may cause bronchospasm, bronchorrhea and respiratory failure. In such cases, a muscarinic antagonist is required.

MG patients treated with acetylcholine esterase inhibitors may manifest side effects during surgery. They also demonstrate enhanced sensitivity to competitive neuromuscular blocking agents. Patients with generalized MG often exhibit a characteristic “myasthenic pattern” with decreasing respiratory volumes during maximum voluntary ventilation (MVV) and reduced respiratory muscle endurance[7]. Respiratory muscle dysfunction can evoke upper airway obstruction, sleep apnea, or even respiratory failure.

In our case, the patient had an additional risk factor: a recent history of ARDS. ARDS survivors may develop pulmonary fibrosis and microvascular obliteration months after the initial event. Findings of ground-glass opacification by imaging in the early stages of ARDS usually represent edema and inflammation.

But, persistence of ground-glass opacities on follow-up imaging in our patient may be an indicator of fibrosis. Although protective mechanical ventilation strategies and usage of extracorporeal lung support improve survival rates, these strategies have not been proven to protect the lung parenchyma from fibrotic changes in long-term studies[8,9].

Ground-glass opacities on follow-up CT scans, probably represented intra-lobular fibrosis. Lung function tests with residual restrictive, 15 to 45%, and/or obstructive, 18 to 33%, defects are commonly identified in ARDS survivors, years after recovery. Low DLCO and a drop in PaO2 during exercise are the most frequent findings in ARDS survivors[10,11]. Despite a low diffusing capacity of the lungs for carbon monoxide (DLCO), the six minute walking test that was in the normal range. The anesthetic plan for our patient included maintenance of anticholinergic medications until the time of surgery, avoidance of premedication, use of short-acting anesthetic drugs with no effect on neuromuscular transmission, and the use of sugammadex for rocuronium reversal, according to TOF monitoring.

Non-depolarizing neuromuscular blocking drugs (NMBD), may lead to prolonged paralysis due to inadequate reversal using neostigmine. Sugammadex, a modified gamma cyclodextrin compound, encapsulates the nondepolarizing neuromuscular blocker rocuronium, providing a rapid reversal of residual neuromuscular blockade[12,13].

CONCLUSION

We present the management of a patient with the coexistence of two pathologies of the lung. He was an ARDS survivor, so a more detailed preoperative pulmonary functional assessment was performed, since this group of patients experience long term morbidity.Our ARDS surviror patient suffering from Myasthenia Gravis, was scheduled for thymectomy. A very careful anesthetic plan based especially on TOF monitoring and the use of sugammadex for rocuronium reversal, contributed significantly to successful outcome. It is encouraging that our patient with the coexistenceof ARDS and thymoma with MG, had an uncomplicated thymectomy.

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Author Disclosures:

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