

Video-assisted thoracoscopic extended thymectomy in myasthenic children

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Abstract

Myasthenia gravis (MG) is an autoimmune disease marked by weakness of voluntary musculature. Medical and surgical therapy of adult myasthenia is well documented. There is little pediatric surgical evidence, only a few case reports being available. The aim of this paper is to verify whether the surgical and anesthesiological techniques can warrant an early and safe discharge from the operating room. The secondary aim is to assess the presence of perioperative indicators that can eventually be used as predictors of postoperative care. During the years 2006-2009, 10 pediatric patients were treated according to a surgical approach based on video assisted thoracoscopic extended thymectomy (VATET). Standard preoperative evaluation is integrated with functional respiratory tests. Anesthetic induction was made with propofol and fentanyl/remifentanyl and maintenance was obtained with sevoflurane/desflurane/propofol \pm remifentanyl. A muscle relaxant was used in only one patient. Right or left double-lumen bronchial tube (Rüsch Bronchopart® Carlens) placement was performed. Six patients were transferred directly to the surgical ward while 4 were discharged to the intensive care unit (ICU); ICU stay was no longer than 24 h. Length of hospital stay was 4.4 ± 0.51 days. No patient was readmitted to the hospital and no surgical complications were reported. Volatile and intravenous anesthetics do not affect ventilator weaning, extubation or the postoperative course. Paralyzing agents are not totally contraindicated, especially if short-lasting agents are used with neuromuscular monitoring devices and new reversal drugs. Perioperative evaluation of the myasthenic patient is mandatory to assess the need for postoperative respiratory support and also predict timely extubation with early transfer to the surgical department. Availability of new drugs and of reversal drugs, the current practice of mini-invasive surgical techniques, and the availability of post anesthesia care units

are the keys to the safety and successful prognosis of patients affected by MG who undergo thymectomy.

Introduction

Myasthenia gravis (MG) is an autoimmune disease marked by weakness of voluntary musculature. Although it can involve all the striate musculature of the organism, it mainly affects muscular groups innervated by brainstem motor nuclei (eye and eyelid muscles, masticatory and swallowing muscles, mimic musculature). Neuromuscular transmission can be compromised in three different ways: i) the antigen-antibody complex formation can be blocked; ii) complement-mediated destruction of postsynaptic receptors; iii) elevated receptor degradation ratio. From a biological point of view, specific antibodies against nicotinic receptor of acetylcholine (AChR-Ab) can be found in 85-95% of cases with a generalized presentation of the disease, while only 60% of ocular presentation of the disease shows this antibody.

MG is included in the group of neuromuscular diseases and junctional myopathies. There are some specific subgroups: newborn presentation, congenital presentation or the more frequent early presentation. Diagnosis can be complex and is not only clinical but based on the serum finding of AChR-Ab and muscle-specific kinase receptor antibodies (anti-MuSK). Edrophonium tests can also be used, such as electromyography and chest X-rays.

The incidence of MG is 150-400 new cases per million per year. There is a female prevalence in early presentation and a male prevalence in presentation in the patient's 50s and 60s.

Medical and surgical therapy of adult myasthenia is well documented while pediatric surgical evidence is very poor and only a few case reports are available.¹⁻³ The causes of this can be identified in the less frequent pediatric presentation, lack of availability of centers dedicated to pediatric MG, while both adult and pediatric patients are collected in the same centers.

Surgery offers a real chance of improvement in MG and although not a radical therapy, perioperative evaluation of the myasthenic patient (neurological functional capacity, grade of bulbar involvement, respiratory function) is mandatory to assess the need for postoperative respiratory support and also predict timely extubation with early transfer to the surgical department.^{4,5}

In this setting, myorelaxants are used less during anesthesia because of their unpredictable response, and preoperative sedation is also avoided in order to lower the risk of aspi-

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ration, especially in patients with reduced respiratory reserve.^{6,7}

Therefore, the main aim of this paper is to verify whether the surgical and anesthesiological techniques can ensure an early and safe discharge from the operating room leading to immediate discharge to the surgical ward.

The secondary aim is to assess the presence of perioperative indicators that can eventually be used as predictors of postoperative care.

Materials and Methods

This study was carried out from 2006 to 2009 at a reference institution for surgical treatment of MG. The surgical approach is based on video assisted thoracoscopic extended thymectomy (VATET). VATET was developed in the 1990s and is a mini-invasive option for thymic radical exeresis, avoiding sternotomy. It is useful in preserving the esthetic appearance of the thorax (cervicothoracic and thoracoscopic bilateral access), reducing postoperative pain and the length of hospital stay.

Mini-cervicotomy at the jugular notch is indicated to identify thymic horns and prepare a retrosternal tunnel that is needed to lift up the sternum. Left 3-trocar thoracoscopy permits mobilization of the left hemithymus (after identification of anonymous venous trunk and phrenic nerve). Right 3-trocar thoracoscopy permits the mobilization of the right hemithymus from the pericardium (after identification of mammarian vessels, phrenic nerve,

and ascending aorta from heart to right anonymous vein). There is then a third left thoracoscopic surgery that permits full dissection. Finally, the extraction of the thyme from the thorax is made from a cervicothoracic access.

The need for surgical therapy is obviously assessed by the neurologist. Medication is stopped the day of surgery and restarted some hours after discharge to the ward, following further neurologist referral.

Standard preoperative evaluation with full blood tests, echocardiogram (ECG), chest X-ray (CXR) is integrated with functional respiratory tests (spirometry, blood gas analysis). The severity of the disease and evaluation of clinical stability are assessed by the neurologist using the MG Foundation of America (MGFA) scale, as described in Table 1.

Results

During the years 2006-2009, 10 pediatric patients from 9 to 17 years old (9 females, one male) were treated. Patients' characteristics are described in Table 2.

Diagnosis was at least two years before treatment and all patients were treated with steroids and cholinesterase inhibitors. Anti-AChR antibody titers were positive in 8 cases, and anti-MUSK in one. Only one patient was seronegative. No preoperative myasthenia crisis was detected.

Nine of the patients were defined to be in good clinical condition and only one was in partially satisfactory condition (MGFA Class III).

Blood gas analysis was normal in all patients while functional respiratory tests were normal in 8. One patient showed restrictive respiratory syndrome, while one patient showed obstructive respiratory syndrome. Gas

diffusion capability was mildly altered in one patient.

Two patients received preoperative sedation with benzodiazepine. Anesthetic induction was made with propofol 2.5-3.5 mg/kg and fentanyl 2 mcg/kg (6 cases) or propofol 2.5-3.5 mg/kg and remifentanyl 0.05-0.2 mcg/kg/min (4 cases). Anesthetic maintenance was obtained with sevoflurane (4 cases), sevoflurane/remifentanyl (4 cases), propofol/remifentanyl (one case) and desflurane/remifentanyl (one case). A muscle relaxant (cisatracurium 0.1 mg/kg) was used as induction in only one patient (who was later one of those to be transferred directly to the surgical ward). In this case, Train of Four monitoring (TOF) was used.

The radial artery was cannulated in order to measure invasive blood pressure; intra-operative monitoring consisted in internal temperature, functional respiratory data, end-tidal carbon dioxide (ETCO₂), oxygen saturation (SpO₂) and ECG. Left DLT (Rüsch Bronchopart® Carlens) was placed in 9 patients, a right DLT was placed in one case; sizes ranged from 32 to 35.

The average surgical time was 123±18.9 min, the average weight of thymus with fat tissue was 49.8±4.4 grams, the presence of thymoma was established in 2 cases and of thymic hyperplasia in the other 8.

Operating room (OR) discharge was 40±18.5 min after awakening (cumulative time for both transfer to the surgical ward or ICU). Six patients were transferred directly to the surgical ward. Four were discharged to the ICU, one of whom on the specific indications of the neurologist. The patients who went directly to the ward stayed in the recovery room for 47±19 min. During this time used the patient was monitored for sedation level and blood losses, to optimize pain control, and to gain ventilator weaning. The patients who

went into the ICU waited 28±8 min (Table 3).

Of the 4 patients discharged to the ICU, one was already extubated in the OR. Another patient was extubated after 20 min and the last 2 within 2 h of discharge from the OR. ICU stay was no more than 24 h.

Average blood loss was 35±3 mL and no treatment was needed; data are reported in Table 4. Drain tubes were removed on Day 2. Postoperative pain was treated by multimodal analgesia with acetaminophen plus intravenous (i.v.) morphine or acetaminophen plus iv tramadol. The Visual Analogue Scale (VAS) score was less than 4 at OR discharge and did not increase at any time over the following days. Length of hospital stay was 4.4±0.51 days. No patient was readmitted to the hospital and no surgical complications were reported.

A single episode of seizure requiring treatment was reported two days after surgery.

Discussion

In this paper we report the results we obtained with 10 VATET in 10 pediatric patients. Mainstay medical treatment of MG is based on anticholinesterases and immunosuppressants. Thymectomy is suitable in patients refractory to medical treatment or in patients presenting moderate or severe forms of the disease. Surgical removal of the thyme can be useful to lower the level of antigenic response, leading to remission in 30-70% of patients after three years.^{2,8} The thoracoscopic approach is also to be favored for esthetic purposes, but especially for the reduction in the use of chest drain tubes and painkillers, less blood loss and shorter hospital stays.

Anesthesiological and intensive care management of myasthenic patients is well known, as is the response of these to intravenous

Table 1. Myasthenia gravis Foundation of America clinical classification.

Class	Clinical signs
Class I	Any ocular muscle weakness; may have weakness of eye closure. All other muscle strength is normal
Class II	Mild weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
Class IIa	Predominantly affecting limb or axial muscles or both. May also have lesser involvement of oropharyngeal muscles
Class IIb	Predominantly affecting oropharyngeal or respiratory muscles or both. May also have lesser or equal involvement of limb, axial muscles, or both
Class III	Moderate weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
Class IIIa	Predominantly affecting limb, axial muscles or both. May also have lesser involvement of oropharyngeal muscles
Class IIIb	Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both
Class IV	Severe weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity
Class IVa	Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal muscles
Class IVb	Predominantly affecting oropharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles, or both
Class V	Defined by intubation, with or without mechanical ventilation, except when employed during routine postoperative management The use of a feeding tube without intubation places the patient in class IVb

anesthetics and gases.¹

Both volatile and intravenous anesthetics are used during induction or maintenance of anesthesia; these do not affect weaning, extubation, or the postoperative (neither early or delayed) period.⁹

Paralyzing agents are not totally contraindicated, especially if these are short-lasting agents used with neuromuscular monitoring devices and new reversal drugs.⁶ This and the introduction of mini-invasive techniques have made it possible to markedly reduce the risk of perioperative complications in thoracic surgery, as well as the duration of mechanical ventilation and the length of stay in the ICU, improving outcome. This can also be seen in pediatric patients for whom the poor experi-

ence available in specifically designed clinical studies often induced the anesthetist to follow procedures normal for adult patients.

Clinical evaluation and neurological health are to be considered in the choice of postoperative ICU or ward discharge.

Pulmonary function evaluation is mandatory in the stratification of risk and in case of postoperative complexity.¹ Anticholinesterase medications and corticosteroids are routinely stopped the day before surgery and are restored in the early postoperative phase. Premedication drugs (in our clinical practice, benzodiazepines) are not administered to avoid any additional risk of respiratory depression. We did not find any connection between the use of paralyzing drugs, delay in ventilator weaning/extubation time and discharge to ICU or ward.

The main cause of ICU discharge appeared to be preoperative borderline neurological status; certainly, early identification is made possible by interaction between the surgeon, the anesthetist and the neurologist.

Early extubation and discharge can be achieved in the majority of pediatric patients on completion of the surgical procedure. Only 40% of pediatric patients needed to be transferred to the ICU; all of them were in spontaneous ventilation and some of them were without the endotracheal tube. No delay in transfer from the ward to the ICU was required. Most of the conditions of discharge seemed to be inadequate and a post anesthesia care unit (PACU) appeared to be the ideal solution as an intermediate point of care between ward and ICU.

The ideal condition for choosing to transfer to the ward is also adequate analgesia, obtained with iv non-steroidal anti-inflammatory drugs (NSAID) and opiates. Paralyzing drugs seemed to be safe, thanks to the availability of monitoring of neuromuscular function and reversal drugs such as sugammadex.

by the neurologist and postoperative strategy was decided according to clinical status. Six patients were transferred to the ward, 4 to the ICU and extubated 2 h later. No intraoperative complications were reported; myoclonus was reported on postoperative day 2 in one case only. We did not observe any correlation between choice of hypnotic drug and discharge destination. Drugs were all reported to be safe and did not cause any respiratory depression. The single case needing a neuromuscular paralyzing agent was later transferred onto the ward. Availability of new drugs, of reversal drugs, the current practice of mini-invasive surgical techniques, and the availability of PACU are the keys to safety and successful prognosis of patients affected by MG who undergo thymectomy.

Table 2. Patients' characteristics.

N. of patients	10
Male:female	1:9
Age (years)	13.5±2.8
Body weight (Kg)	50±7.9
Height (cm)	157±9.5
Ongoing treatment	Steroid plus pyridostigmine

Table 3. Duration of surgery and anesthesia.

Duration of surgery	123±18.9 min
Time to ward discharge	47.5±19 min
Time to intensive care unit discharge	28.7±8.5 min
Intensive Care Unit stay	20 h
Length of hospital stay	4.4±0.51 days

Table 4. Hematologic values.

	Pre-operative	Post-operative
Hemoglobin (g/L)	13.5±1.3	12.8±1.1
Platelets (×10 ⁹ /L)	235±31	270±32
Blood loss (mL)	35±3	-
Blood trasfusions	None	None

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Conclusions

MG is a junctional myopathy. In pediatric patients, the disease usually presents as juvenile MG. Previous studies mostly regard adult patients, and in the case of pediatric patients are limited to single case reports.

We collected data from 2006 to 2009 of 10 pediatric patients. Surgery had been requested