

Anesthetic Management of Simultaneous Coronary Artery bypass Grafting with Cardiopulmonary bypass and Extended Thymectomy in a Patient with Myasthenia Gravis

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Abstract

A 61-yr-old male having myasthenia gravis MG (Osserman IIB), Hypertension HTN, hyperlipidemia, type II diabetes mellitus DM II, a single pelvic kidney, chronic obstructive pulmonary disease COPD with a positive history of smoking and coronary artery disease, was admitted for uncontrolled myasthenic symptoms, cardiology team was consulted, cardiac catheterization was performed and revealed a three vessel coronary artery disease. All the findings dictated the management, a combined coronary artery bypass graft CABG and an extended thymectomy was performed. Optimization of the patient was achieved preoperatively. Total intravenous anesthesia using propofol and remifentanyl was applied to this patient. Continuous monitoring of the neuromuscular transmission NMT was maintained throughout the perioperative period. Although neither muscle relaxants nor inhalational agents were used in the anesthetic management of this patient; the patient developed postoperative atelectasis and lung collapse; which was managed successfully, and extubation of the trachea was done after ensuring adequate recovery of the NMT and respiratory function. Myasthenic therapy was continued throughout the perioperative period.

Keywords: Myasthenia gravis; Coronary artery bypass grafting; Cardiopulmonary bypass; Perioperative management.

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Introduction

Myasthenia gravis *MG* is an acquired autoimmune disorder caused by failure of neuromuscular transmission, which results from the binding of autoantibodies to proteins involved in signaling at the neuromuscular

junction *NMJ*. These proteins include the nicotinic *AChR*, less frequently, a muscle-specific tyrosine kinase *MuSK* involved in *AChR* clustering.⁽¹⁾

Myasthenia gravis complicates the course of anesthesia and operation, because of the

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inadequate restoration of muscle function, especially of respiratory and swallowing muscles, inducing the prolonged mechanical ventilation, gastroesophageal reflux and pulmonary infection.⁽²⁾

The stress of surgery and some drugs used perioperatively may worsen myasthenic weakness. There are lots of different techniques of the anesthesia during *MG* (no use of any muscle relaxants, restriction of opioids, use an inhalational anesthetics and propofol, and continuous monitoring of neuromuscular junction function). As a rule local or spinal anesthesia is preferred over inhalation anesthesia, and neuromuscular blocking agents should be avoided or used sparingly.^(2,3)

Coronary artery bypass grafting for coronary artery disease and extended thymectomy for *MG* are both familiar operative procedures. However, the probability of their being performed simultaneously is extremely low and very few cases have been reported so far.^(2,4)

This case from clinical practice shows, that the correct choice of tactics of pre- and postoperative treatment makes simultaneous *CABG* with *CPB* and thymectomy possible.

Case report

A 61-year-old male patient, with a positive history for smoking and chronic obstructive pulmonary disease *COPD*, a 7-year history of arterial hypertension *HTN* a single pelvic kidney, hyperlipidemia and type II diabetes mellitus *DM II*, who, since the age of 54 years, had suffered from effort angina followed by myocardial infarction *MI* and, at the age of 60 years, had been diagnosed with *MG* from a

positive serum *anti-AChR* antibody (1.6 pmol/ml; 0.00-0.16 pmol/ml in normal patients), was to undergo coronary revascularization and simultaneous thymectomy for progressive *MG*.

A series of preoperative cardiologic examinations, including cardiac catheterization, revealed an old ischemic infarct and three-vessel disease with an estimated ejection fraction of 45%. Cardiologic drug therapy included acetylsalicylic acid, isosorbide dinitrate, nitroglycerin, enalapril maleate. His *MG*, which was classified as Osserman's IIB, became unresponsive to pyridostigmine. The attending neurologist adjusted the patient's medications to be pyridostigmine 60mg six times daily, oral prednisolone 80 mg daily and azathioprine 50mg twice daily. Preoperative examination revealed normal muscle strength but resistant ocular disease. Respiratory function tests revealed forced vital capacity (FVC) OF 3200 ml with 78% of predicted value and forced expiratory volume in one second (FEV 1.0%) of 70%. Respiration was 18 breaths per minute and arterial blood gases were as follows: pH: 7.48, PaCO₂: 38mmHg; HCO₃: 27mEq/L; TCO₂: 28mmol/L; BE: +4.2mmol/L; PaO₂: 55 mmHg and O₂%sat: 91% in room air. Chest radiography demonstrated a widened mediastinum and hyperinflated lungs.

The preoperative management of this patient aimed at optimizing the patient's general condition. Patient had stopped smoking for six weeks before admission; chest physiotherapy was instituted simultaneously with inhaled Combivent nebulizer therapy (Salbutamol and Ipratropium bromide). His oral hypoglycemic agents were substituted

with insulin for better glycemic control. The patient was put on intravenous immunoglobulin *IVIG* (0.4 g/kg) 35g over two hours for five days prior to the scheduled surgery.

The patient received his routine cardiac drugs, pyridostigmine and intravenous hydrocortisone 100mg on the morning of surgery. Intraoperative monitoring included a five lead electrocardiography ECG; pulse oxymetry; invasive radial artery and non-invasive blood pressure monitoring; capnography; urinary catheter; body temperature measurement at the nasopharynx and rectum; central venous pressure using right internal jugular vein; and a nerve stimulator (Fisher and Paykel)[®] applied to the facial nerve. After preoxygenation for three minutes with 100% oxygen; general anesthesia was induced with a total of 2mg/kg of propofol and 1.5mcg/kg remifentanyl over 100 seconds. Vocal cords were sprayed with 4% Xylocaine to blunt the sympathetic response that may result from airway manipulation. Direct laryngoscopy and tracheal intubation were performed without difficulty; mechanical ventilation was initiated with intermittent positive pressure ventilation *IPPV* using an air/oxygen mixture. The respiratory minute ventilation was set according to the patient's weight; and normocapnea was maintained with arterial blood samplings and capnography. Propofol infusion was commenced immediately after intubation, titrated at a variable rate of 3 to 8 mg/kg/hour according to hemodynamic response, and fixed at 3mg/kg/hour during and after hypothermic *CPB*. Remifentanyl was administered at a rate of 6-15 mcg/kg/hour; further boluses were injected prior to any known surgical stimulus (skin incision, sternotomy and retraction).

Neither muscle relaxants nor inhalational agents were used in this patient. Extended radical thymectomy was performed before *CPB*, with excision of a thymic tissue measuring 17x15x2.5 cm. The *CPB* technique included pump priming with 2.0L of ringer lactate solution, cardioplegic arrest, α -stat pH management, and moderate whole body hypothermia (30°C). Arterial carbon dioxide tension (PaCo₂) was regulated within normal limits. The flow was maintained at 2.5 L/m² body surface area. The great saphenous vein and left internal mammary artery aorto-coronary bypass grafts were anastomosed as scheduled. Following slow rewarming to 37°C at the oropharynx, weaning from *CPB* was carried out uneventfully without inotropic support or vasodilator therapy.

Throughout the procedure, there was no patient movement, abdominal muscle rigidity produced by rapid administration of large dose of opioids, or shivering.

At conclusion of the surgery, a single bolus of 10 mg morphine and 1 g of perfolgan[®] were given intravenously. The overall duration of general anesthesia was 295 minutes and the duration of surgery was 255 minutes, pump time was 64 minutes with 40 minutes cross clamping time.

The patient was transferred to the cardiac intensive care unit *CICU*, propofol infusion was continued at a rate of 150mg/hour for sedation, postoperative pain was controlled using; a continuous intravenous infusion of morphine at a rate of 2mg/hour supplemented with intravenous perfolgan[®] 1g three times daily. Monitoring of neuromuscular transmission was discontinued due to motion artifacts on the nerve stimulator. The patient

was kept intubated and ventilated with synchronized intermittent mandatory ventilation *SIMV* mode using fraction of inspired oxygen FiO_2 80%, tidal volume *TV* 6-10 ml/kg with a rate of 12 breaths/ minute, 5cm H_2O positive end expiratory pressure *PEEP* was also applied. Intravenous methylprednisolone 80mg, mestinone 60mg three times daily, azathyoprine 50mg twice daily by nasogastric tube, a continuous intravenous infusion of insulin along with 5% dextrose water according to a sliding scale to control his blood sugar. His blood pressure was controlled using intravenous tridil®. Postoperative arterial blood gases *ABGs* showed a relative hypoxia with a PaO_2 55 mmHg of at FiO_2 80%, a chest radiography was obtained and showed atelectasis and collapse of the middle and lower lobes of the right lung (Figure I). The patient was kept intubated and ventilated under sedation; the

PEEP was raised to 10cm H_2O , FiO_2 was raised to 100%. Chest physiotherapy was initiated with frequent endotracheal suctioning, which yielded large amounts of viscid secretions; however, the patient's *ABGs* did not improve, so fiberoptic bronchoscopy with alveolar lavage was performed to washout the respiratory tract secretions, and chest physiotherapy with endotracheal suctioning was continued. Accordingly, a decision to keep the patient intubated and ventilated, with serial blood gas analysis was taken. The next morning; dramatic improvement was noticed on the patient's *ABGs* and chest radiography (figure II), and the trachea was extubated after fulfillment of the criteria; including maximum pulmonary inspiratory pressure of 25 cm H_2O and *TV* of 6-10 ml/kg. Clinically the patient did not show any signs of respiratory distress, and oxygenation was maintained using a 50% ventura face mask.

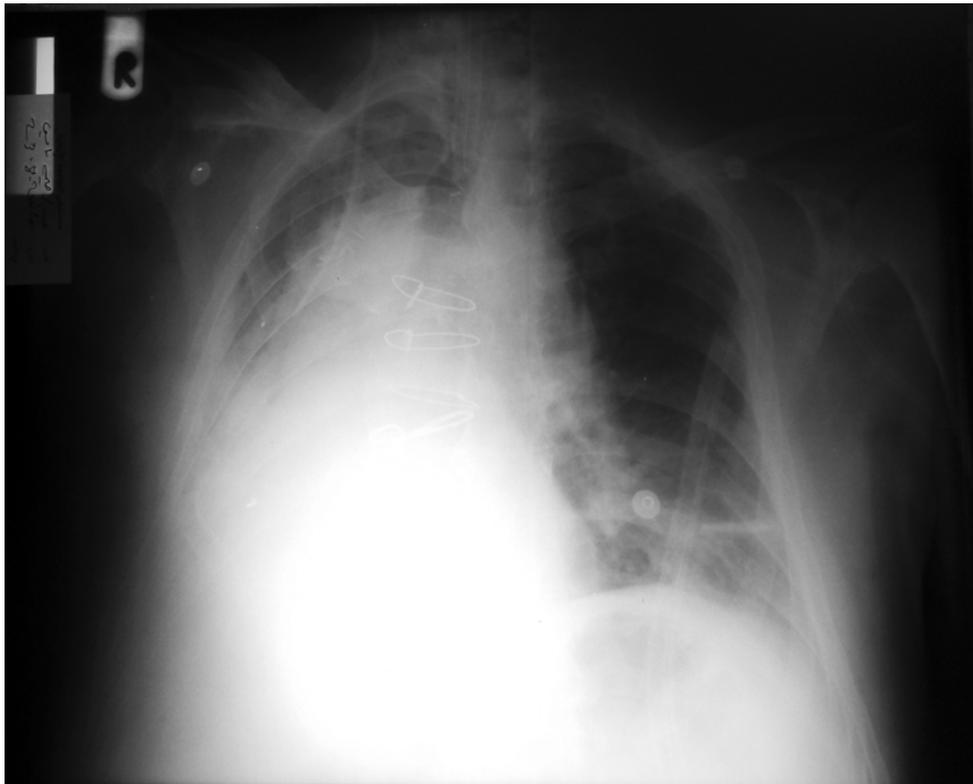


Figure 1: Immediate postoperative antero-posterior chest X-ray taken in supine position

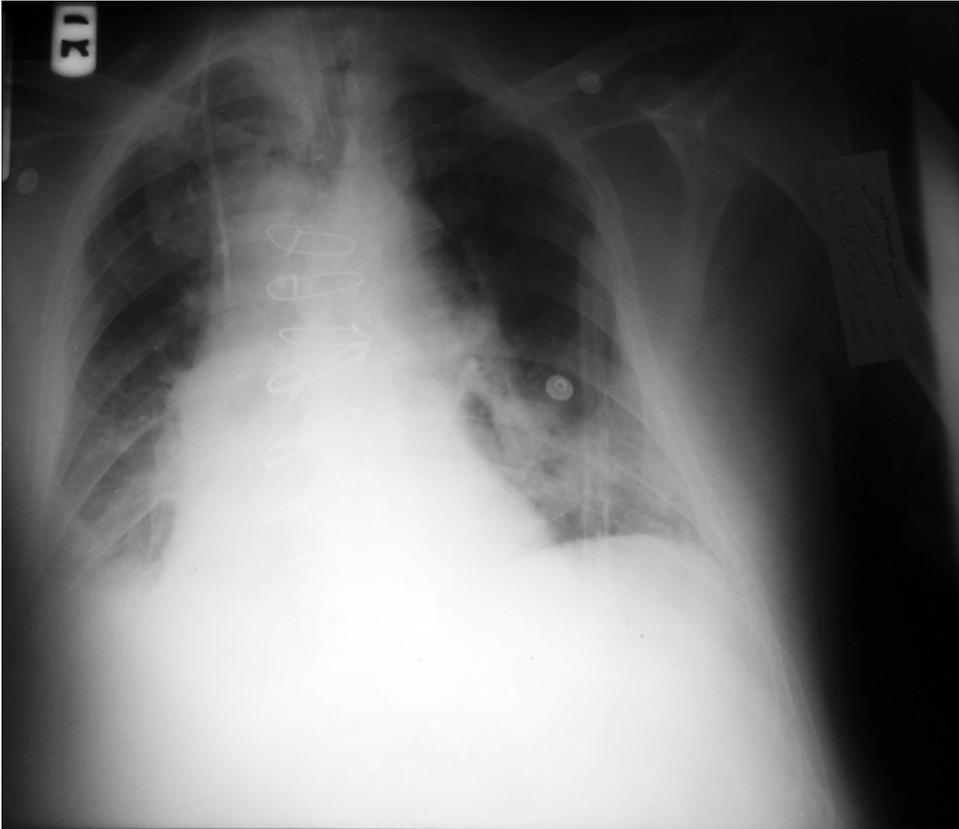


Figure 2: Antero-posterior chest X-ray taken in supine position after bronchial lavage

During the patient stay in the *CICU*, chest physiotherapy along with ipratropium nebulizer therapy was continued. Preoperative medications were resumed and the patient's myasthenic symptoms were similar to his preoperative ones. The excised thymic tissue was reported as fibrofatty tissue with some minute benign atrophic thymic tissue and no evidence of thymoma. The patient was discharged from the *CICU* on the 5th postoperative day, and subsequently home on the 11th postoperative day, with the radiography shown in figure III.

Discussion

Modern management of patients undergoing coronary artery bypass grafting (CABG) generally necessitates good

preoperative sedation, intraoperative adequate relaxation and analgesia, with hemodynamic stability, as well as sufficient postoperative analgesia keeping in mind the importance of as early as possible early extubation.

To date, there have been very few reports which describe perioperative management in patients with MG undergoing simultaneous CABG with CPB and extended thymectomy. Postoperative pulmonary complications are common in both types of surgeries.^(5, 6) Our aim during perioperative management in this case was to minimize postoperative pulmonary complications as possible, in a patient who has in addition a chronic lung disease. Despite our efforts, this patient developed atelectasis and lung collapse. Many factors played a role in this incident, and they are as follows:



Figure 3: Postero-anterior chest X-ray taken in erect position on discharge

1. Medications in the myasthenic patient:

Several medications taken by myasthenic patients have safety implications for the patient undergoing anesthesia. Cholinesterase inhibitors which act by blocking the degradation of acetylcholine include pyridostigmine and neostigmine may be necessary to maintain the patient's strength. Arrangements should be made so this medication can be administered prior to anesthesia induction and at appropriate time intervals after recovery from anesthesia. Corticosteroids are commonly used immunosuppressant drugs. As anesthesiologists are well-aware, steroids can produce many side effects. These include impaired wound healing, increased blood glucose, gastrointestinal *GI* ulceration, osteoporosis and increased infection risk.

Patients who have been on chronic steroid therapy may need supplemental steroid doses to deal with the stress of moderate to major surgery, though this is a source of controversy. Azathioprine, a purine analog, targets immune cell replication. It may lead to bone marrow suppression, liver toxicity, nephrotoxicity and other less serious side effects. Again, these complications may alter the anesthetic management of the patient.⁽⁷⁾

2. Concomitant medical illness: The combination of disease processes, especially pulmonary comorbidity *COPD*, may severely hamper respiratory mechanics. This may lead an anesthesiologist to consider postoperative ventilation earlier in the course of evaluation, and make weaning from the ventilation a challenging issue.

3. Preoperative control of MG symptoms: Some myasthenics may benefit from being admitted to the hospital before the planned procedure. Such patients include those undergoing a relatively urgent procedure who have not yet been medically optimized and those undergoing thymectomy because they are refractory to medical treatment and those with a recent cholinergic crisis. In addition to adjustments in medication doses, these patients may benefit from plasma exchange or intravenous immunoglobulin therapy. The decision to admit a patient is usually made by either the treating neurologist or attending surgeon. However, an anesthesiologist who encounters a myasthenic patient whom he/she feels is not optimized prior to surgery should consider postponing surgery and suggesting that additional therapy take place as an inpatient.

4. The anesthetic technique used: Patients with *MG* may present for surgery for multiple reasons. In particular, patients who require general anesthesia present additional challenges. Based on their pathology, these patients have altered neuromuscular function and such, altered (exaggerated and prolonged) response to neuromuscular blockade *NMB*. In the non myasthenic patients, we frequently use *NMB* as an adjunct to our anesthetic agents to provide akinesis and a “balanced anesthetic”. The use on *NMB* in *MG* patients may defeat the goals of avoiding prolonged intubation/ventilation and limiting impairment of neuromuscular function postoperatively. If at all possible, we avoid the use of *NMB* in *MG* patients, which we have done in this case.

In order to safely and effectively use *NMB* in patients with *MG*, the anesthesiologist must have a sound understanding of the altered response to these drugs in association with

MG. The decreased number of motor end plates at the neuromuscular junction makes these patients more resistant to the depolarizing *NMB* agent succinylcholine *SCh*. *MG* patients require a larger dose to obtain the same degree of relaxation as seen in a patient without *MG*.⁽⁸⁾ *SCh* is metabolized by the enzyme pseudocholinesterase in the bloodstream, normally within minutes of administration. In patients treated with cholinesterases, pseudocholinesterase activity is also decreased. This means that the patient may have a more prolonged effect of the drug. By contrast, *MG* patients are extremely sensitive to nondepolarizing *NMB* agents. They display profound weakness after much smaller doses than would be expected from non-*MG* patients. This is due to the decreased number of acetylcholine receptors at the motor end plates becoming more saturated by the *NMB* agent, not because *MG* patients have altered clearance of these drugs. By this same reasoning, a given dose of a nondepolarizing *NMB* will have a more prolonged effect in an individual with *MG* than a nonmyasthenic.⁽⁹⁾ When one chooses to use these agents as part of an anesthetic, the use of small doses, the use of neuromuscular twitch monitor and vigilance on the part of the anesthesiologist are essential.

In general practice, *NMB* are used during induction of anesthesia along with narcotics and IV induction agents to achieve intubating conditions (akinesis, vocal cord relaxation and reduced hemodynamic response to airway manipulation). During the maintenance phase of anesthesia, *NMB*'s are often used to facilitate mechanical ventilation. For *MG* patients, other means of achieving these ends are available. One option for induction is to use an increased dose of the chosen IV induction agent (propofol, thiopental,

etomidate). Propofol is often chosen because it is more effectively cleared than other agents (barbiturates in particular) with more complete arousal and fewer residual effects. Akinesia during the maintenance phase of anesthetic can be achieved without *NMB*. The basic technique involves using one of a variety of agents to achieve a deeper plan of anesthesia than is typical for the particular case in a non-*MG* patient. Agents at one's disposal include an increased dose of inhaled volatile agent (e.g. Isoflurane) as well as various adjuncts, including propofol infusion, narcotic boluses or infusion (remifentanyl can be considered if rapid emergence is desired), or dexmedetomidine infusion. Bear in mind that all of these agents have the potential to cause hypotension and may need to be countered by pressor agent (usually a vasoconstrictor such as phenylephrine).

5. Postoperative pain control: Narcotics have a blanket warning for myasthenic patients. This is not due to *NMJ* dysfunction, but rather the depressant effect on respiratory drive. There is some evidence that cholinesterase inhibitor medications can exacerbate the depressant effect of narcotics.⁽¹⁰⁾ This combined effect, together with the baseline neuromuscular dysfunction in myasthenic patients, makes it critical that narcotics be given in monitored setting. This does not mean that narcotics should be avoided postoperatively. Narcotic analgesics are very

effective and necessary to treat postoperative pain, even in myasthenic patients.

Finally; With all the precautions we have taken in the management, the patient developed postoperative pulmonary complications; that necessitated keeping him intubated and ventilated till the second day, the risk factors involved but were not limited to: the disease duration, concomitant pulmonary disease, an old age, a major surgery in the chest, a poor preoperative pulmonary function and a large dose of myasthenia drugs. Nevertheless; by keeping in mind the postoperative pulmonary complications alone with taking in considerations all what an anesthesiologist can add in the management we could successfully wean the patient from the ventilator; these involve factors like; optimization of neuromuscular function preoperatively, limiting any agents we administer during surgery that may inhibit muscular strength or depress respiratory function, which is not limited to *NMB*, good postoperative analgesia and chest physiotherapy. The struggle in this case was to combine optimum preoperative treatment with effective intraoperative management in a cardiac patient with many risk factors, such that the patient can emerge from anesthesia with peak strength and have limited or no respiratory compromise. Effective postoperative analgesia is an important link in this chain as well.

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المقاربة التخديرية لعملية موسعة لوضع وصلات شريانية قلبية بالإضافة لاستئصال موسع للغدة الزعترية

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الملخص

الحالة تصف مريض يبلغ من العمر 61 سنة يعاني من الأمراض المزمنة الآتية: مرض الوهن العضلي والضغط والسكري من النوع الثاني، وارتفاع في دهون الدم، والداء الرئوي الإنسدادي المزمن، بالإضافة لوجود كلية واحدة موضوعة في الحوض، والمريض مدخن ويعاني من نقص التروية القلبية.

تم إدخال المريض بأعراض هجمة وهن عضلي، حيث تم استشارة أطباء القلب وأجري له قسطرة لشرايين القلب أظهرت وجود انسداد في 3 شرايين تاجيه. أجري للمريض عملية مضاعفه حيث تم وضع وصلات شريانيه لشرايين القلب بالإضافة لاستئصال موسع للغدة الزعترية.

تم تقييم المريض بشكل كامل قبل العملية، وتم تخديره عن طريق استخدام البروبوفول وريميونتاييل وريدياً. أثناء العملية وما حولها تم إجراء مراقبه مستمرة للتوصيل العصبي العضلي. لم يتم تستخدم مرضيات عضلية أو مخدرات استنشاقية. تم إزالة أنبوب التنفسي الاصطناعي بعد التأكد من سلامة التوصيل العصبي العضلي والوظائف التنفسية. تم الاستمرار بعلاج الوهن العضلي في الفترة ما حول العملية.

الكلمات الدالة: مرض الوهن العضلي، عمليات نقص التروية القلبية، ما حول العملية.