Old Thymectomized Patient Requiring Plasmapheresis Prior To Spinal Anesthesia For Gynecologic Surgery

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Abstract
Myasthenia gravis is an autoimmune disease which is characterized by muscle weakness and fatigue after exertion due to the decrease in the number of postsynaptic acetylcholine receptors. Medical treatment involves anticholinesterases and corticosteroids, while thymectomy remains the standard treatment. In the current case report a thymectomized old patient with high acetylcholine receptor antibody levels scheduled to undergo gynecologic surgery under spinal anesthesia following plasmapheresis was presented.

INTRODUCTION
Myasthenia gravis (MG) is a chronic autoimmune disorder which is characterized with varying degrees of skeletal muscle weakness and fatigue after exertion due to the decrease in the number of postsynaptic acetylcholine receptors (AchR)(1). The incidence is approximately 2-10 in 100 000 cases; two thirds of patients are young women and children account for 11-29% of all patients (2-4). Treatment options available for MG include anticholinesterases, immunosuppression, ACTH, plasmapheresis and/or thymectomy (2). Anesthetic management for surgery has been reported even in children where the incidence of the disease is very low in the literature (5, 6). Since the disease is rarely seen in the old population, we present an old thymectomized patient with exacerbated MG scheduled to undergo gynecological surgery and revisit the anesthetic management options associated with the status of the disease.

CASE REPORT
A 75 year-old female patient was scheduled for conisation because of cervical epidermal neoplasia. The patient had a history of thymectomy because of MG diagnosis determined by anti-striated muscle antibodies in 2002. She was receiving pridostigmine bromide (Mestinon 60 mg) 4X60 mg daily and was functional in her life except weakness and difficulty in walking since last 3 months. She had hesitation and inability to walk after walking 500 m. She was also suffering from hypertension and hypothyroidi. Preoperative EMG revealed abnormal neuromuscular transmission of right extensor digitorum communis muscle. Complete blood count results were unremarkable (hemoglobin: 11.6 g/dL, hematocrit: 35.9%, white blood cell count: 10000/mm3 and platelet count: 162000/mm3) while blood chemistry revealed low calcium, potassium and phosphorus levels. Preoperative AchR antibody level was 109 nmol/L (normal range: 0-0.5 nmol/L). Plasmapheresis was planned before anesthesia and operation. Three sequences of plasmapheresis were done and AchR antibody level decreased to 50 nmol/L. Hypocalcemia and hypopotassemia were corrected. The patient was scheduled for operation under spinal anesthesia. Patient received her daily oral pridostigmine dose on the morning of the operation and continued in the postoperative period as well. Spinal anesthesia was performed at the first attempt with 10 mg hyperbaric bupivacaine plus 15 µg fentanyl by midline approach between lumbal L3-4 intervertebral spaces with a 25 G pencan spinal needle. Full motor block was present in 5 minutes. When sensory block level reached to T10, operation was started. Operation lasted 30 minutes and was completed uneventfully. Complete motor block recovery was observed 3 hours after spinal anesthesia induction. Patient was able to urinate 4 hours after spinal anesthesia. She received oral regimen in the afternoon and was discharged from hospital the next morning. The pathology report revealed benign cervical epithelial cells requiring no further surgery.

DISCUSSION
Myasthenia Gravis is most commonly present in women between the ages of 10-40 years, while it occurs in men after
40 years of age (1). The disease has been classified according to its severity into ocular myasthenia (group I), mild generalized myasthenia (with slow disease progression and good treatment response) (group IIA), moderate generalized myasthenia (with bulbar and skeletal muscle involvement, and poor treatment response) (group IIB), acute progressive myasthenia (with rapid progression, high mortality and no response to treatment) (group III), and late severe myasthenia (progressing from class I or II over the course of 1-2 years) (group IV) (7). This is the first case report requiring plasmapheresis because of poor treatment response to thymectomy and anticholinesterase therapy prior to relatively urgent surgical anesthesia because of the pathology report in a 75 year-old female patient who had MG diagnosis at the age of 69. According to the classification, the present case was in group IIB.

Since thymoma is present in 10-15% of patients with MG, thymectomy is the treatment of choice (8). After thymectomy, 50% of patients showed clinical improvement, while 21-38% had complete remission comparing with 13% of those treated medically and exacerbations of the disease can occur in the rest of these patients several years after surgery (3). Medical therapy of MG includes anticholinesterases (e.g., pyridostigmine), immunosuppressive drugs (e.g., cyclophosphamide and/or azathioprine) and corticosteroids (9). Pyridostigmine is the most commonly used drug among anticholinesterases because it has fewer muscarinic side-effects than neostigmine (3). Additionally, plasmapheresis and intravenous immunoglobulin G are used when a patient is in crisis, or to optimize neuromuscular function preoperatively (10). If the patient is poorly controlled, plasmapheresis has been shown to be beneficial in the preoperative period (2). When such a myasthenic patient is scheduled for elective surgery, surgery must be postponed till the disease is under control. In this case report, despite surgery (tymectomy) and ongoing medical treatment with pyridostigmine, AchR antibody level was still high prior to surgery. Although it has been reported that no linear relationship was observed between plasmapheresis and decreasing antibody levels in all cases (3), we observed a marked decrease in the AchR antibody levels after 3 courses of plasmapheresis together with pridostigmine intake preoperatively. This patient was considered to be partly elective and relatively urgent because of the possibility of extending operation according to the final pathology report.

The preoperative management of the myasthenic patient will be influenced by the surgical procedure and the preferences of the surgeon and the anesthesiologist. The disease can be exacerbated by infections, physical and emotional stress, electrolyte abnormalities such as sodium and potassium (3). Our patient had hypocalcemia which was corrected preoperatively.

The anesthetic regimen should be planned to provide the least interference with both ventilatory and neuromuscular function. These patients exhibit marked sensitivity to nondepolarizing muscle relaxants under general anesthesia because of the receptor down regulation slight resistance to depolarizing muscle relaxants (succinylcholine). If a nondepolarizing muscle relaxant is needed, reduced doses of intermediate-acting agents (e.g., atracurium, rocuronium or vecuronium) should be carefully titrated and used by neuromuscular monitorization (9). In another study, rocuronium has been shown to be safe in adults with MG (11). Neuromuscular agent reversal may induce cholinergic crisis (9). Patients with MG exhibit also increased sensitivity to the ventilatory depressant effects of opioids therefore they should be used sparingly and cautiously during induction and maintenance of the anesthesia as well. Volatile anesthetics are known to affect neuromuscular transmission via prolongation of the refractory period, presynaptic inhibition of acetylcholine mobilization and release, and sensation of the receptors. In the myasthenic patients these effects are markedly exaggerated (12). Total intravenous anesthesia has been recommended and considered to be advantageous because the myasthenic patients, like normal individuals, experience less neuromuscular depression with propofol than with volatile agents (13). Therefore, we preferred spinal anesthesia for this short procedure.

In the literature, labor and cesarean section under regional anesthesia for parturients with MG and inguinal hernia repair under spinal anesthesia in children with MG have been recommended (5, 9). Local anesthetic agents decrease the sensitivity of the postjunctional membrane to acetylcholine. This could cause weakness in the myasthenic patients if blood levels are high enough. Ester local anesthetics, which are metabolized by cholinesterase, may present particular problems in patients taking anticholinesterases. Regional and local anesthesia should be performed using reduced doses of amide (rather than ester) local anesthetics to avoid high blood levels. Blockade of the innervation of intercostal muscles should be avoided to minimize the risk of...
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respiratory muscle weakness (2). In the present case report, spinal anesthesia was performed with an amide type local anesthetic bupivacaine which was combined with fentanyl to have a satisfactory block for surgical anesthesia without compromising ventilatory function.

In conclusion we reported successful preoperative approach and anesthetic management of a thymectomized old patient with high AchR antibody levels underwent gynecological surgery under spinal anesthesia following plasmapheresis. Preoperative evaluation of the patient, the current status of the disease and possible duration of the operation is of interest for decision making in the anesthetic management.

References
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