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Electroconvulsive Therapy in Myasthenia Gravis

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Background. ***Myasthenia gravis (MG) is a neuromuscular disease sometimes associated with severe psychiatric complications. The use of electroconvulsive therapy (ECT) in MG raises certain challenges.***
Methods. ***We describe a patient with MG and a steroid-induced major depressive episode with psychotic features treated with ECT. We also review the literature on similar cases and on the safety of ECT with muscle relaxation in this condition.***
Results. ***The use of ECT in patients with MG is a viable therapeutic option when psychiatric complications secondary to MG or its treatment do not respond to psychotropic medications.***
Conclusion. ***ECT with muscle relaxants could be administered safely, with appropriate precautions kept in mind.***

Keywords Electroconvulsive therapy; Myasthenia gravis; Depression; Psychosis.

INTRODUCTION

Electroconvulsive therapy (ECT) is a safe and effective treatment for a variety of psychiatric disorders (1). However, in a number of medical illnesses the use of succinylcholine is problematic. One of these is myasthenia gravis (MG), a neuromuscular disorder characterized by weakness and fatigability of skeletal muscles most often due to autoantibodies that target the acetylcholine receptors at the neuromuscular junction decreasing their number and interfering with their function (2). Various classification methods have been proposed (3,4). Osserman and Genkins described a dynamic clinical classification of adult patients with MG that includes four groups: group I: ocular MG, group IIA: mild generalized MG, group IIB: moderate generalized MG, group III: acute fulminating MG, and group IV: late severe MG (4). Therapeutic strategies have limited the physical morbidity of this illness. However, because of its debilitation as well as the treatment adverse effects, MG has been associated with an increased prevalence of psychopathology (5). A MEDLINE search of the literature yielded only three papers, in the English literature, reporting the use of ECT in the case of patients suffering from MG with an associated psychiatric illness. Martin and Flegenheimer warned about the possible delayed recovery from prolonged muscle relaxation and suggested avoiding succinylcholine administration in myasthenic patients (5). They also described a patient with MG, as well as orthopedic and neurological problems, in whom the use of succinylcholine was uneventful. In another report, the case of a 68-year-old female with MG and depression successfully treated with ECT was described (6). Finally, Gitlin et al. described a myasthenic patient who received multiple monitored ECT with mivacurium, a short acting non-depolarizing agent, for muscle relaxation (7). The most recent one of these three papers was published more than a decade ago. We, thus, felt it would be useful to report the case of a patient with MG and a steroid-induced major depressive episode with psychotic features treated with ECT. In addition, we discuss the safety of muscle relaxation in this condition.

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CASE

The patient is a 68-year-old married Caucasian male with a past medical history only significant for essential hypertension and hyperlipidemia. He denied cigarette smoking, illicit drug use or any personal or family history of psychiatric illness. He drinks alcohol rarely. Nine months prior to

his index admission, he was diagnosed with MG, ocular type (Osserman's type I), and was first treated with a short course of steroids, and later with pyridostigmine. He underwent a thymectomy three months afterwards. Just prior to the surgery his acetylcholine receptor antibody titer was 6.5 nmol/l (normal: < 0.5) and a lyme serology was negative. His medications were adjusted as indicated by the clinical course. The dose of pyridostigmine was gradually increased and azathioprine was added for symptom control. Six months later, his respiratory function rapidly deteriorated and he was admitted to the medical intensive care unit for management. The worsening of his condition was determined to have resulted from an exacerbation of his MG (Osserman's type IV). He was, as a result, treated with plasmaphoresis and prednisone 60 mg daily and discharged to home.

Ten weeks later, he was admitted to the medicine-psychiatry unit for management of a steroid-induced depressive episode with psychotic features. On admission, his physical exam and vital signs were within normal limits. His weight was 95 kg. His medications included: pyridostigmine 360mg daily given in divided doses, prednisone 60mg qam, azathioprine 50mg bid, hydrochlorothiazide/triamterene (25mg/37.5mg) qam, cerivastatin 0.4mg qam, atenolol 25mg qam, and ASA 325mg qam. A brain MRI was normal. His pulmonary function testing showed a forced vital capacity within normal limits (FVC=3.59L. or 78% of the expected value). Pre-ECT standard chemistries and CBC were unremarkable except for a mild hypokalemia (K^+=3.2 mEQ/L) and leukocytosis (WBC=14.8 K/ml). An ECG obtained revealed nonspecific anterolateral ST-T abnormalities.

Since his psychopathology was believed to be secondary to steroids, prednisone was tapered. He was also started on sertraline 50mg daily and risperidone 1mg qam and 2mg qhs. However, during the first week of hospitalization he became more psychotic and quit eating; therefore, he was referred for ECT.

ECT was administered with a Spectrum 5000Q unit (MECTA corporation, Lake Oswego, OR, USA) and right unilateral electrode placement. A series of ten treatments were given using a stimulus intensity of 576mC in all but the first. The treatment protocol for ECT consisted of giving a stimulus of 120mC upon the first treatment of unilateral ECT to determine the threshold then a 576mC stimulus upon all the following treatments to improve the response rate (8). Treatment medications included 0.2mg glycopyrrolate IV and 60mg methohexital IV. Upon the first treatment, a test-dose of 10 mg of succinylcholine was given and his muscle response was assessed with a peripheral nerve stimulator. This dose suppressed the muscle contractions as would be expected. Under the guidance of an anesthesiologist, ECT was then administered with another 80mg of succinylcholine to achieve complete and sustained paralysis. He seized for an observed period of 38 seconds though the EEG was clearly ictal for only 33 seconds. His recovery was uneventful as he restarted breathing spontaneously at the completion of the ECT treatment. His dose of both methohexital and succinylcholine were increased to 100mg after the third and fourth treatments respectively in order to achieve a better sedation and muscle relaxation. All of the treatments were uneventful. He was finally discharged to home.

DISCUSSION

This case, along with the two others described recently, reports on patients with normal respiratory function and relatively few MG-related symptoms (6,7). It is still not known, however, how a compromised pulmonary function would influence recovery from ECT. Such patients would probably be at higher risk for prolonged apnea requiring tracheal intubation and ventilatory assistance. Several investigators have attempted to identify predictors of prolonged postoperative mechanical ventilation in patients with MG. Leventhal et al. found four risk factors in patients who had undergone a transsternal thymectomy (9). These include: a duration of illness of more than six years, chronic respiratory disease unrelated to MG, a dose of pyridostigmine greater than 750 mg per day, 48 hours prior to the surgery, and a preoperative vital capacity < 2.9L. Following a transcervical thymectomy, Eisenkraft et al. found that class III-IV MG, previous history of respiratory failure due to MG, and concomitant steroid therapy put patients at a higher risk for prolonged ventilation (10). On the day of his first ECT treatment, the patient was taking 360mg of pyridostigmine and 60mg of prednisone. Although he had had an acute episode of respiratory failure several months prior to his admission, his disease was well controlled when he received ECT. The post-thymectomy literature suggests that the patient's steroid therapy and his history of respiratory failure placed him at risk for delayed post-ECT recovery. It is possible that the more benign nature of ECT compared to a thymectomy, protected this patient from developing serious complications during the recovery from anesthesia.

The patient was taking several medications known to interfere with the action of succinylcholine and its metabolism. The acetylcholinesterase inhibitor pyridostigmine could prolong the half-life of succinylcholine resulting in increased neuromuscular blockade (11). Prednisone and cimetidine can also prolong its action (12,13). In addition, there is a potential interaction between prednisone and pyridostigmine resulting in decreased pyridostigmine effectiveness. Thus, the possible medication interactions are complex, potentially leading to alteration in the muscle relaxant half-life with unpredictable clinical consequences.

Myasthenics' response to muscle relaxants can vary from extreme sensitivity to resistance (14–16). A decreased number of functional receptors at the endplate can limit the response to succinylcholine. On the other hand, the

decreased "safety margin" (the rate of acetylcholine receptors present at the endplate but not required to maintain neuromuscular transmission) results in a marked sensitivity to nondepolarizing agents. Again, the acetylcholinesterase inhibitors used to treat MG could interfere with the metabolism of succinylcholine and potentiate the neuromuscular blockade. Because individual response is unpredictable, caution in dosing the muscle relaxants is warranted as well as close monitoring of neuromuscular transmission (14,15,17).

CONCLUSION

Since the combination of MG with ECT is rare, clinicians must rely on the collective experience of the field rather than clinical studies to guide them in this situation. In our experience ECT with succinylcholine was administered safely, with appropriate precautions kept in mind.

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