

## Myasthenia Gravis Attack after Oral Risperidone Treatment: A Case Report

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### ABSTRACT

Myasthenia gravis (MG) is an autoimmune disease, which can be triggered by anticholinergic agents. The 6-year-old female patient was admitted to the outpatient clinic. She had been previously diagnosed with comorbid attention deficit hyperactivity disorder and conduct disorder and was receiving short-acting methylphenidate and risperidone, as recommended by a child psychiatrist. However, after using the drugs, she stated that she was overly tired during the day and that her eyelids drooped. Hence, the current treatment was stopped. She was hospitalized with a prediagnosis of ocular type MG and pyridostigmine (90 mg/day) treatment was started. The patient recovered and subsequently the treatment was stopped. Since psychiatric symptoms of the patient resurfaced, long-acting methylphenidate treatment was initiated. During this treatment, the symptoms of MG did not return. The Naranjo's scale of adverse drug reaction probability was completed. Consequently, there may be an association between risperidone and MG.

**Keywords:** Myasthenia gravis, risperidone, adverse effect

### Introduction

Myasthenia Gravis (MG) is a disease characterized by time-varying muscular weakness and fatigue resulting from an autoimmune response to acetylcholine receptors (AChR) in the post-synaptic neuromuscular region, generally due to the parasympathetic nervous system effect [1]. MG is a neuromuscular disorder that can be triggered by anticholinergic agents [2]. In addition to the trigger by anticholinergic agents, it was found that antipsychotics used during schizophrenia treatment worsen MG [3]. However, to the best of our knowledge, there has been no report in literature for the worsening of MG due to oral risperidone treatment. This patient is the first case of an MG attack followed by oral risperidone treatment. Written informed consent was obtained from the patient and her family.

### Case Presentation

A 6-year-old female patient was admitted to our clinic by her foster family with symptoms of inattention, distraction, hyperactivity, and impulsivity. She was insisting on her wills, and the family had problems with setting rules. According to the information received from her teacher, she would not pay attention to what the teacher said. Moreover, she extensively moved around in class, disturbed the order of the class, and talked a lot. A psychiatric assessment revealed that she had concentration problems, hyperactivity, and impulsivity. At the age of 5 years, she was beaten up by her biological family and was sent to an orphanage. With regard to her biological family, her mother had been diagnosed with MG, schizophrenia, and tonic-clonic type epilepsy, and her father had been diagnosed with epilepsy. The patient was diagnosed with attention deficit hyperactivity disorder (ADHD) according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, and was recommended behavioral interventions. Although a follow-up was suggested, the patient did not attend the follow-up visit.

One year later, it was reported that the patient was admitted to another clinic and was diagnosed with ADHD and conduct disorder and was prescribed methylphenidate (10 mg/day) and risperidone (0.25 mg/day). The symptoms benefited from the medication. After using the medications, the movements of the patient began to decrease considerably. The patient stated

that she started to feel extremely tired to move during the day and that her eyelids drooped. Subsequently, her gaze became stunned. Hence, the current treatment of the patient was discontinued, and she was directed to a neurology clinic and was hospitalized with a prediagnosis of ocular type MG. A neurological examination revealed that the eyelid ptosis was present and ptosis increased due to a challenged upward gaze. A thymoma-compatible lesion was detected in a thorax–neck computed tomography (CT) scan. In a blood analysis, the AChR antibody was established as positive (10 mg/dL).

Pyridostigmine bromide (90 mg/day) treatment was started for the patient. After the patient recovered, she was discharged and pyridostigmine was discontinued. Since the psychiatric symptoms of the patient returned to the initial severity, long-acting methylphenidate (10 mg/day) was restarted. Methylphenidate was gradually increased to 20 mg/day. She benefited from the drug at that dose and continued her follow-up regularly for 1.5 years. The Naranjo's scale score of adverse drug reaction probability was 5. Consequently, we hypothesized that risperidone has a probable association with MG.

## Discussion

MG is a complex disease caused by antibody-mediated damage to the neuromuscular junction. The frequency of MG is reported to be 20 in 100,000 [4]. MG is rare in childhood since it is primarily an adult-specific disease. Only 10%–15% of myasthenia patients are in the childhood group. This rate is detected as 4.2% in children under 10 years of age [5, 6]. Muscular weakness and fatigue that gradually increase during the course of activity and decrease during rest are characteristics of MG. In many patients, eyelid droop described as blepharoptosis is the first known symptom. The onset of the disease may be immediate, and the symptoms are usually transient and periodic [7]. In the present case, the patient had a rapid-onset eyelid droop as the first symptom of an early-onset MG.

In patients with MG, the usage of antipsychotics, mood stabilizers, and antidepressants are risk factors for potentially exacerbating symptoms. Antipsychotic agents are highly selective for muscarinic receptors. Additionally, acetylcholine

(ACh) blockade in nicotinic receptors is also minimal with antipsychotic agents. Nicotinic receptors directly affect MG. Thus, anticholinergic effects of antipsychotics have the potential to worsen the symptoms of MG. Antipsychotics with a high severity of these effects include chlorpromazine, thioridazine, clozapine, olanzapine, and haloperidol [3, 8].

Risperidone is a second-generation antipsychotic that has been shown to be effective with Dopamine D2 and Serotonin 5-HT2A receptor antagonistic mechanism. Reportedly, anticholinergic side effects of risperidone were very low compared to clozapine and olanzapine [9]. However, in a recently published case report, MG symptoms in a 29-year-old woman with MG and schizophrenia, who had no myasthenic crisis for 7 years, were found to worsen after the first, second, and third Risperidone Consta injection for antipsychotic treatment. In this case report, depending on the patient's use of fluoxetine, which increases the blood plasma level of risperidone by 2.5-fold, myasthenic symptoms might be caused by the increase of risperidone blood level [10].

Our case is the first to demonstrate that the use of oral risperidone may trigger MG symptoms. The AChR antibody was positive during the attack leading to a diagnosis of risperidone-induced MG. With regard to the use of methylphenidate, there is no literature stating its worsening effect on MG. Stimulants increase ACh levels by inhibiting acetylcholinesterase, and hypothetically, may improve MG symptoms instead of worsening [11]. Although the patient continued to use methylphenidate in follow-ups, MG symptoms did not occur. Hence, we hypothesized that methylphenidate may not trigger MG. The probable relationship defined at Naranjo adverse drug reaction scale explained that the main reason for the attack is risperidone. Therefore, it should be considered that oral risperidone may trigger and worsen MG and that it should be used with caution in MG patients.

**Informed Consent:** Written informed consent was obtained from patients and the parents of the patient who participated in this study.

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