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Case Report

Successful desensitization protocol for pyridostigmine in a 12 year old patient with myasthenia gravis

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ABSTRACT

Background. Myasthenia gravis is a chronic, autoimmune disease with muscle weakness. Acetylcholinesterase inhibitors are used in the symptomatic treatment of the disease. Allergic reaction to pyridostigmine bromide is rare. In the literature, no allergic reaction to pyridostigmine bromide has been reported in the pediatric population.

Case. A 12-year-old female patient diagnosed with myasthenia gravis consulted our clinic with the complaint of urticaria due to pyridostigmine bromide. The oral challenge test performed with pyridostigmine bromide was positive. As the patient was required to be continue pyridostigmine bromide with no suitable alternatives, it was decided that the patient had to be desensitized to pyridostigmine. During and after the desensitization protocol, no reaction was observed.

Conclusions. In this report, a successful desensitization protocol for pyridostigmine bromide in a child with myasthenia gravis is discussed.

Key words: allergy, desensitization, myasthenia gravis, pyridostigmine bromide.

Myasthenia gravis is a chronic autoimmune disease affecting the neuromuscular junction. In this disease, autoantibodies are formed against acetylcholine receptors located in the postsynaptic membrane of striated muscles. These autoantibodies may cause muscle weakness in patients. Muscle weakness can be generalized or localized. Generally, proximal muscles are affected more often than distal muscles. Since the disease often affects the eye muscles, diplopia and ptosis may occur. Muscle weakness may increase with exercise and fatigue. Complaints of patients tend to increase significantly towards the evening.[1]

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Annual incidence is 8 to 10 cases per 1 million individuals, and the prevalence is 150 to 250 cases per 1 million. Myasthenia gravis is the most common disease affecting the neuromuscular junction. Diagnosis of myasthenia gravis, the symptoms and signs of the patient are determined by electrophysiological tests, the Tensilon test and the demonstration of positive autoantibodies.[2]

The most commonly used drugs in the treatment of myasthenia gravis are acetylcholinesterase inhibitors. Acetylcholinesterase inhibitors act by slowing the degradation of acetylcholine at the neuromuscular junction, prolonging the interaction of acetylcholine with its receptor on the muscle membrane and enhancing neuromuscular transmission. Pyridostigmine bromide is the most commonly used acetylcholinesterase inhibitor.[1,3]

Pyridostigmine bromide has various side effects. Gastrointestinal side effects, such as abdominal cramping, loose stool and

flatulence, are the most common. Increased perspiration and muscle twitches and cramps are other side effects.[3] Allergic reaction to pyridostigmine bromide is rare.[4] To our knowledge, in the literature, no allergic reaction to pyridostigmine bromide has been reported in the pediatric population. Here, a successful desensitization protocol is described in the first reported pediatric myasthenia gravis case who developed an immediate type hypersensitivity reaction due to pyridostigmine bromide.

Case Report

A 12-year-old girl with myasthenia gravis presented to our clinic with the complaint of urticaria after using pyridostigmine bromide. In the patient's history, it was learned that the patient was diagnosed with myasthenia gravis and 60 mg pyridostigmine bromide was administered three times a day as a treatment. Twenty minutes after taking the drug on the seventh day of her treatment, urticaria developed on the dorsal side of her feet and arms (Fig. 1, 2). She had no other complaints. There was no history of any allergic disease in the patient's medical history. She had no allergic reaction to any drug or food in the history.

The patient was treated with an oral antihistamine. Then, the patient underwent an oral challenge test with pyridostigmine bromide after 4 weeks. We started the oral challenge test with 18 mg pyridostigmine bromide and

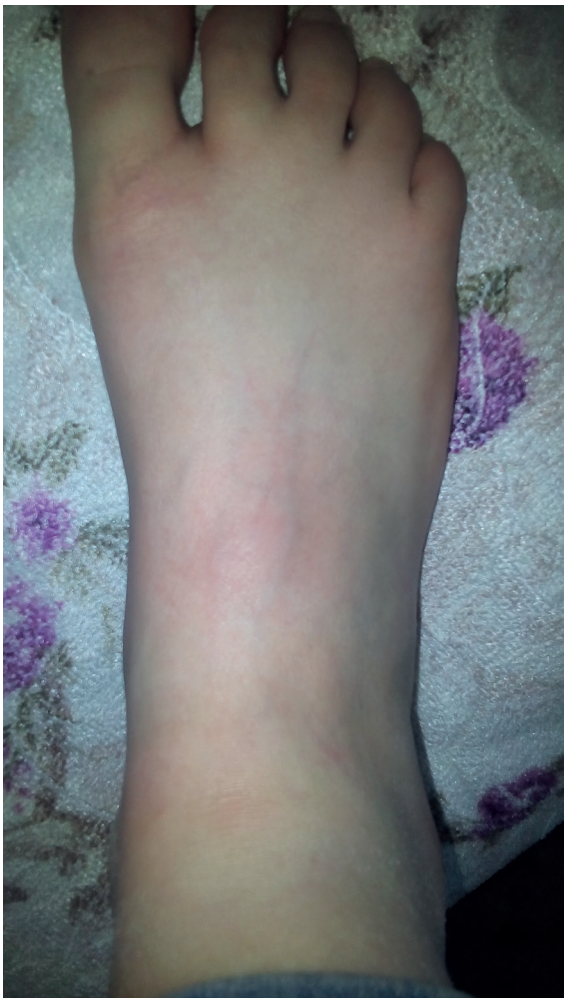

Fig. 1. Urticarial lesions on her foot.

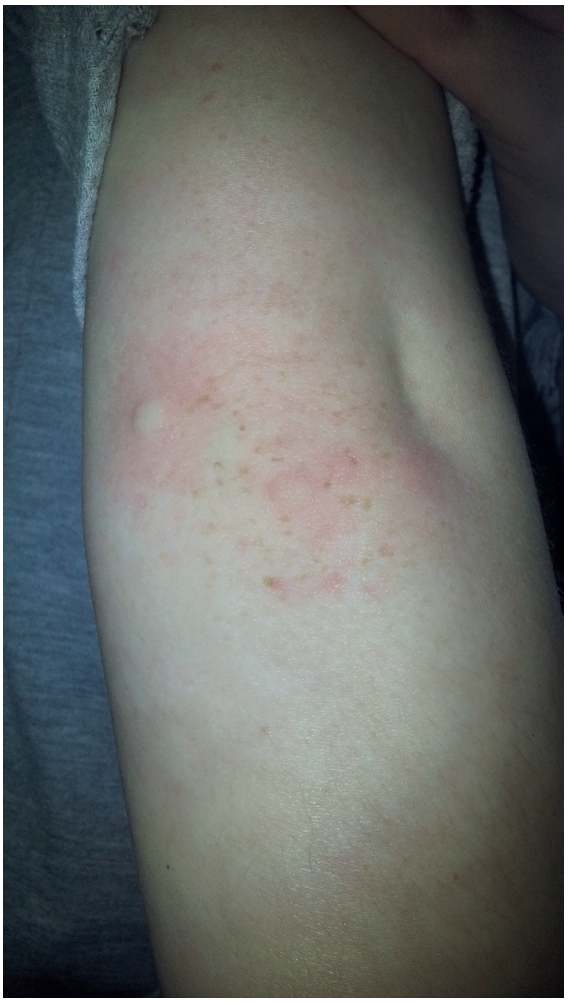

Fig. 2. Urticarial lesions in her arm.

Table I. Desensitization protocol for pyridostigmine bromide.

Time (minute)	Dose (mg)
0	0.6
30	1.8
60	5.4
90	16.2
120	36

doubled the dose every thirty minutes. In the third step of the oral challenge test the patient developed urticaria and flushing. Oral challenge test was accepted as positive.

The only drug used in the symptomatic treatment of myasthenia gravis in Türkiye is pyridostigmine bromide. Therefore, desensitization to pyridistigmine was decided for this patient. Written informed consent was taken from the patient's parents before the desensitization protocol. Premedication was performed with pheniramine, methylprednisolone and ranitidine before the initiation of the desensitization protocol. We started desensitization with 1/100 of the target dose and tripled the dose every thirty minutes. Desensitization for pyridostigmine bromide consisted of five steps and took 120 minutes in total (Table I). During and after the desensitization protocol, no reaction was observed. The patient continues the pyridostigmine bromide treatment at the normal dose.

Discussion

Myasthenia gravis is a chronic, autoimmune disease. It significantly impairs the quality of life of patients due to muscle weakness. Acetylcholinesterase inhibitors used in the treatment reduce muscle weakness by preventing the breakdown of acetylcholine, allowing it to stay in the synaptic gap longer.[3] Therefore, the they are indispensable for the treatment of myasthenia gravis. Pyridostigmine bromide is the only drug used in the symptomatic treatment of myasthenia gravis in Türkiye. Other acetylcholinesterase inhibitors neostigmine bromide and ambenonium chloride are not available. Therefore, we applied desensitized our patient to pyridostigmine bromide. To our knowledge, this is the first case of successful desensitization in a pediatric patient who developed immediate type hypersensitivity reaction to pyridostigmine bromide.

Acetylcholinesterase inhibitors may have various side effects. Gastrointestinal side effects, such as abdominal cramping, loose stool, and flatulence, are most common. Increased perspiration and muscle twitches and cramps are other side effects.[3] Immediate type hypersensitivity reaction to pyridostigmine bromide are rare.[4,5] However, Immediate type hypersensitivity reactions have not been reported in the pediatric population. To our knowledge, our patient is the first case who developed an immediate type hypersensitivity reaction to pyridostigmine bromide.

In patients with drug allergies, desensitization is administered only if it is absolutely required to administer the medication and no alternative treatment is available. The objective of desensitization in such patients is to temporarily suppress the response of the body to the medication. The patient is ensured to be administered with the medication without developing any reaction by administering the medication, starting with a low dose and increasing the dose gradually. Desensitization protocols are required to be based on general rules and be simple, safe, easy and amendable in accordance with the response of the patient. The initial dose for desensitization should be determined based on the severity of the reaction. Typically, the initial dose is required to be within the range of 1/100.000 and 1/100 of the complete therapeutic dose.[6] We initiated the dose of 1/100 of pyridostigmine bromide for our patient and reached a complete therapeutic dose, increasing by three-fold for each step. No reaction developed at any of the desensitization steps.

In conclusion, although rare, an immediate type hypersensitivity reaction can be occur with pyridostigmine bromide in patients diagnosed with myasthenia gravis. Desensitization is vital and inevitable for myasthenia gravis patients who develop urticaria to pyridostigmine bromide. The protocol that we propose here encompasses the general rules of desensitization: a regimen that is safe, simple, and effective. Although desensitization procedures have been conducted by different specialists, for the patient's safety, allergists should develop, review, and supervise treatments.

Ethical approval

Written informed consent to publish the case, was given by the patient's parents.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: FK, ET; data collection: FK; analysis and interpretation of results: FK, ET; draft manuscript preparation: FK, ET. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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