Journal of Biomedical Sciences
Research Article Peer-review, Open Access

Personalized Treatment of Myasthenia Gravis: Clinical Case Report

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Abstract

Myasthenia gravis (MG) is a rare autoimmune disorder based on the type II hypersensitivity immune response. Antibodies attack the nicotinic acetylcholine postsynaptic receptors, resulting in a decreased number of acetylcholine receptors (AChRs) at the neuromuscular junction (NMJ), resulting in the typical pattern of MG: fatigable general weakness after physical activities, fluctuating diplopia or ptosis, as well as any other skeletal muscle involvement. According to the statistics, 15–20% of MG patients experience exacerbation or crisis within the first 2 years after diagnosis. MG crises or exacerbations represent life-threatening and potentially lethal conditions, which should be evaluated and treated accordingly. Before deciding on the individualized treatment regimens, several factors, such as the severity and rapidity of symptom progression, the patient's medical history and the physician's clinical experience should be taken into consideration. A 64-year-old female diagnosed with myasthenia gravis presented with left-sided ptosis, diplopia, dysphagia, alongside difficulty breathing. The patient's medical history revealed arterial hypertension, type II diabetes, obesity and lacunar stroke. After a physical examination, the exacerbation was determined to be less severe and was assigned to MGFA Class II. Considered rapid treatments, such as 5-7 plasma exchange procedures were reduced to four procedures, and human immunoglobulin (IVIg) infusions were discontinued entirely. This action was taken as a result of the high cost of the plasma exchange and IVIg infusion treatments, which the patient could not afford and for which the insurance companies were unable to pay. We assumed the risk based on the personalized strategy, therefore we started therapy with Solumedrol (Methylprednisolone) 1000 mg intravenouslyover the course of three days. Additionally, we considered the urgent management of the high arterial blood pressure and blood glucose levels that showed a progressive positive effect on the patient's general health in addition to myasthenia gravis exacerbation symptoms within three days.

Key words: Myasthenia Gravis, Clinical Case, nicotinic acetylcholine, acetylcholine receptors (AChRs)

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World of Medicine : Journal of Biomedical Sciences Vol .1 No.4 (2024)
https://wom.semanticjournals.org/index.php/biomed

Introduction

Myasthenia gravis is a rare autoimmune neuromuscular disorder characterized by type II hypersensitivity immune responses that primarily affect middle-aged female populations. Autoantibodies form against nicotinic acetylcholine postsynaptic receptors (nAChR) at the neuromuscular junction, resulting in a decreased number of receptors[2]. When the neuromuscular transmission is breached, myasthenia gravis' characteristic fluctuating muscle and generalized weakness develop[1]. The disease progresses with remissions and exacerbations. Exacerbations may escalate rapidly and lead to life-threatening conditions such as respiratory failure. Medical treatment generally enhances symptomatic therapy with acetylcholine inhibitors, chronic immunotherapies such as glucocorticoids, immunosuppressive and immunomodulatory agents; rapid therapeutic measures such as plasmapheresis and intravenous immune globulin[3][4][5]. Choosing the appropriate treatment regimen should depend not only on given guidelines but also on clinical experience, and the patient's response to therapy. It may be reconsidered during the hospitalization.

Case presentation. We present the case of a 64-year-old female patient who reported symptoms such as ptosis, diplopia, dysphagia, alongside difficulty breathing. The patient has a long medical history of type 2 diabetes and essential arterial hypertension, both of which were managed on a regular basis. With a BMI of 27.0, the patient was also overweight. The abovementioned symptoms first appeared 2 years ago, after severe emotional stress; no other common risk factors were established. No family history of autoimmune diseases was known. The patient was diagnosed with an acute lacunar stroke, and the symptoms were managed as post-stroke manifestations. In September 2022, the patient was tested with repetitive stimulation electromyography, revealing characteristic decrement blocks for myasthenia gravis. To confirm the diagnosis, laboratory tests were performed, and the results were positive: anti-acetylcholine receptor antibodies (30,5 nmol/l), anti-titin antibodies (2,5 nmol/L) (the normal range under 1.25 nmol/L), and MuSK-antibodies were negative[8]. Based on an elevated amount of anti-titin antibodies, a chest CT scan was ordered, which showed a well-demarcated, lobulated, nonhomogeneous, soft-tissue mass (47X36X55mm) in the middle mediastinum, located caudally and on the right side of the thymus. A differential diagnosis between thymoma, dermoid cyst and lymphoma was needed, although it was not performed. The patient was prescribed Kalymin 60 mg TID (pyridostigmine). Several days before the doctor's appointment the patient noticed double vision in the left eye, partial left-sided ptosis, difficulty breathing and swallowing; no obvious exacerbating factors could be identified.

Neurological exam: The patient is alert, oriented to person, place and time. No evident speech pathologies. Pupils are round, reactive to light and accommodation. Extraocular movements are intact, left-sided partial ptosis can be seen. A soft palate is lightly flaccid bilaterally. Tongue midline with normal movements. Strength is slightly reduced in the upper and lower limbs bilaterally (4/5). Biceps, brachioradialis, triceps, patellar, and Achilles reflexes are all decreased by 3/5. No pathological reflexes. Finger-to-nose and heel-to-shin tests were performed normally. In the Romberg test, mild incoordination can be observed. Both superficial and deep sensations are intact bilaterally. Based on the examination results, the exacerbation was considered less severe and categorized as Class IIb according to the MGFA.

The patient was hospitalized and placed in a neurological intensive care unit. Initial blood tests were within the normal range. A urinalysis showed elevated glucose levels of 250 mg/dL. Other imaging and laboratory investigations were intact. Depending on the clinical picture, concurrent medical conditions, MGFA class[7], the following personalized treatment plan was suggested: pulse therapy with Solumedrol (Methylprednisolone) 1000 mg intravenous for three days, 5–7 plasmapheresis procedures[6] human immunoglobulin (IVIg) infusions with a dosage of 0.75 mg/kg, calculated according to the actual weight of the patient. Human immunoglobulin infusions were refused and the number of plasma exchange treatments was reduced to four depending on the patient's socioeconomic situation and the inability of social insurance policies to cover the high costs. Solumedrol infusions were used to treat the exacerbation, with full knowledge of the potential risk that they could make the patient's concurrent diseases worse[9][10].During observation, new clinical manifestation was seen, including neck muscle weakness preceded by high arterial blood pressure with a max T/A of 220/100 mmHg. Only after administration of Urapidil (an A1-adrenoceptor antagonist and a 5-HT1A receptor agonist), was the patient able to extend her neck and hold it upright. During the treatment process, we were able to stabilize not only arterial hypertension but also high glucose numbers that led to improvementin MG symptoms. No other significant clinical symptoms or paraclinical changes were detected. After three days, the patient was discharged with a significantly improved general condition and referred to the specialized institution for plasmapheresis. The patient was prescribed Medrol (oral methylprednisolone) to maintain the therapeutic effect. We advised the patient to have a follow-up visit. Within a few days, the patient was checked in via virtual appointment, during which no problems with swallowing, breathing, gait, or vision were observed; only residual partial ptosis was visible. The patient's medical condition was stable and she was adjusting to her normal lifestyle.

Discussion. The benefits of a personalized approach to myasthenia gravis exacerbation treatment are highlighted in the case report above. Myasthenia gravis is the most common neuromuscular junction disorder, but at the same time, it is considered the most treatable. After evaluating the severity of the myasthenia gravis flare, multiple therapeutic methods can be initiated. Classically, first-line therapy for the exacerbation includes PLEX as well as IVIg infusions for immediate clinical improvements. To prolong the efficiency of PLEX and IVIG infusion, corticosteroids can be administered at the same time, the therapeutic effect will last up to 6 months.

In this instance, a customized strategy had to be chosen based on the level of neurological impairment, coexisting medical conditions, and high expense of immunomodulatory therapy regimens[4]. Despite the potential risk of severe arterial hypertension and diabetes mellitus, we chose to begin treatment with a high dose of glucocorticoids (Solumedrol, 1000 mg per day for three days) [9][10]. Both conditions were taken into consideration as secondary causes of the MG flare and were given the proper care. The monitoring of the patient's neurological status, combined with the clinical findings, revealed that symptoms improved significantly within a few days. After the full course of glucocorticoids, the patient

was transferred to the specialized plasma exchange center, and procedures were minimized to four after achieving minimal manifestation status (MMS).

Conclusion: In special cases the personalized treatment approach is reasonable despite the protocols and guidelines. In such cases physicians can risk with available treatment taking into consideration the patient's wellbeing and interests.

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