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MODERN VIEW OF DIAGNOSIS AND TREATMENT OF MYASTHENIA GRAVIS. CASE REPORT

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Summary

Introduction. Myasthenia gravis (MG) or Erb-Goldflam syndrome is an autoimmune neuromuscular disease based on autoaggression of humoral immunity against elements of neuromuscular synapses and intracellular structures of muscle fibers (antibodies to acetylcholine receptors (AchR), muscle-specific tyrosine kinase (MuSK), protein 4 related to low-density lipoprotein receptors (LRP4), ryanodine receptors (RyR), titin, and skeletal muscle antigens). The exact causes of autoimmune processes in MG are unknown, but abnormalities of the thymus gland (hyperplasia and neoplasia), especially in patients with antibodies to AchR, as well as genetic predisposition are of indisputable importance [1].
Aim. To analyze the researches of pathogenesis, diagnosis and treatment for patients with severe MG from latest literature sources to optimize the treatment of this group of patients. To analyze the own experience of implementing a patient-oriented approach to the treatment and rehabilitation of MG.
Materials and methods. Bibliosemantic, comparative and system analysis methods, and clinical and neurological examination of patients with MG.
Results. The course of MG is variable and can be represented by episodic muscle weakness, stationary flow, slow or rapid progression [2]. Currently, the complex therapy of patients with MG has a clear tendency to move from symptomatic (acetylcholinesterase inhibitors, potassium preparations, potassium-sparing diuretics) treatment to pathogenetic, mainly etiopathogenetic concepts of therapy are being formed (immunosuppressive therapy, antigen-specific immunotherapy, monoclonal antibodies), and it is also being clarified effectiveness of early thymectomy [3].
Conclusions. Complex therapy of patients with MG is based on the use of a differential diagnostic algorithm for various pathogenetic variants of MG, which forms a mainly etiopathogenetic concept of therapy. Antigen-specific immunotherapy, aimed at restoring tolerance to the attacked autoantigen by targeting only the damaged part of the immune system, while leaving the rest intact, is considered more promising for the treatment of MG. MG treatment should be carried out in the conditions of a specialized neurological center, where a full examination and targeted pathogenetic therapy can be carried out.

Keywords: **myasthenia gravis, anticholinesterase inhibitors, corticosteroids, rituximab, plasma exchange**

INTRODUCTION

Myasthenia gravis (MG) or Erb-Goldflam syndrome is an autoimmune neuromuscular disease based on autoaggression of humoral immunity against elements of neuromuscular synapses and intracellular structures of muscle fibers (antibodies to acetylcholine receptors (AchR), muscle-specific tyrosine kinase (MuSK), protein 4 related to low-density lipoprotein receptors (LRP4), ryanodine receptors (RyR), titin, and skeletal muscle antigens). The exact causes of autoimmune processes in MG are unknown, but abnormalities of the thymus gland (hyperplasia and neoplasia), especially in patients with antibodies to AchR, as well as genetic predisposition are of indisputable importance [1]. According to various studies, the incidence of MG ranges from 1.7 to 10.4 cases per 100,000 population per year, and in the USA – up to 20 cases per 100,000 population [4]. The incidence of MG is approximately one case per 10,000-20,000 people per year. Today, the relevance of studying the problem of MG is determined by argumentation, because there is an undeniable increase in the number of patients from

3-7 people per 100,000 population in the 70s of the last century to 20 at the present time. The prevalence of the disease has been gradually increasing over the last decade, mainly in the elderly, despite significant progress in diagnosis, treatment approaches, and improvement in the prognosis of the disease as a whole [5]. In this regard, the total number of patients with MG in Ukraine is now about 9,200 people. Unfortunately, there are no reliable statistics on MG in our country [6]. The implementation of a complex multidisciplinary approach in the treatment of such patients allows to significantly reduce the mortality rate, prolong the life of patients and improve its quality, whereas even 50 years ago the average life expectancy for MG was 4-7 years. Knowledge of the essence of the disease, the main links of its pathogenesis, the spectrum of modern therapeutic agents and algorithms for their use can improve the quality of medical care for patients with MG [7].

AIM

To analyze the researches of pathogenesis, diagnosis and treatment for patients with severe MG from latest literature sources to optimize the treatment of this group of patients. To analyze the own experience of implementing a patient-oriented approach to the treatment and rehabilitation of MG.

MATERIALS AND METHODS

Bibliosemantic, comparative and system analysis methods, and clinical and neurological examination of patients with MG. At the State Scientific Institution «Scientific and Practical Center of Preventive and Clinical Medicine» of the State Administrative Department, we conducted a clinical and neurological examination and treatment of patients with MG. To confirm the diagnosis, we used laboratory tests to detect serum antibodies to acetylcholine receptors (AchR) and muscle-specific tyrosine kinase (MuSK), as well as electroneuromyography (ENMG) and CT of the chest cavity, proserin test. Depending on the results of the examination, schemes were used for treatment according to the management protocols of patients with MG [3]. As a result of the examination of 24 patients with a diagnosis of MG, the patients were divided into 2 groups according to the nature of the neurological deficit and severity of symptoms and form of MG. The first group included 6 patients with ocular form with varying degrees of severity of oculomotor symptoms. The second group consisted of 18 patients with a generalized form of MG with varying degrees of severity (from moderate to severe) oculomotor and bulbar disorders.

RESULTS

MG is diagnosed on the basis of detailed history taking, clinical neurological examination, laboratory and instrumental studies [8]. However, it can sometimes take a long time to diagnose the disease, and the availability of tests performed to detect MG can vary depending on regional and institutional conditions [9]. Various research methods are used, as well as an algorithm for diagnosing MG (fig. 1).

The variety of clinical and pathogenetic variants of MG makes the task of finding a universal therapy for this disease very difficult. Regardless of the existing classifications proposed by V. S. Lobzin, A. G. Panov, L. V. Dogel, B. M. Hecht, K. E. Ossreman, the clinical manifestations of MG are mainly due to the age of onset of the disease, the spectrum of autoantibodies, the activity of the autoimmune process, the presence or absence of thymus pathology and the degree of generalization of muscle weakness. In this regard, patients suffering from MG can be divided into the following main groups: with ocular and generalized forms, in which MG with early and late onset of the disease combined with thymoma is distinguished, and with seronegative forms. The course of MG is variable and can be represented by episodic muscle weakness, stationary course, slow or rapid progression. In addition, muscle weakness can be aggravated by emotional and physical overstrain, high temperature, infections, menstruation, pregnancy, operations, diseases of the thyroid gland (hypo- or hyperthyroidism) and when using a number of medicines, especially during the first year of the disease [2]. Spontaneous long-term remissions of MG occur in 15-20 % of cases, and after thymectomy and active immunosuppressive therapy – in 28-34 % of cases [11].

Currently, complex therapy of patients with MG has a clear tendency to transition from symptomatic, anticholinesterase inhibitors (AChEI), potassium preparations, potassium-sparing diuretics, effectiveness of early thymectomy. AChEIs are drugs of the first line of therapy for MG, as they increase the amount of acetylcholine and the duration of its interaction with acetylcholine receptors, which provides compensation for the function of inactivated receptors per hour of drug action [3]. The most widely used is pyridostigmine (Kalimin, Mestinon) in tablet form of 60 mg (equivalent to a standard tablet of proserin (15 mg)), which has a short half-life. Treatment usually starts with 30-60 mg every 8 hours. The dose is increased gradually, depending on the patient's condition. The maximum dose is 60-120 mg every 4 hours (to be taken during meals). The effect occurs after 10-30 minutes, reaches a maximum after 2 hours and lasts for another 2 hours. In total, the effect of Kalimin can last up to 6-8 hours. The drug is used 3 times a day. Kalimin acts selectively on the cranial muscles, so it is especially indicated for ocular and bulbar forms of MG. The drug is low-toxic, in severe cases of the disease it can be combined with proserin. The most common side effects include gastrointestinal disorders, abdominal pain, diarrhea; muscle fasciculations. In high doses, the drug can provoke a cholinergic crisis [12].

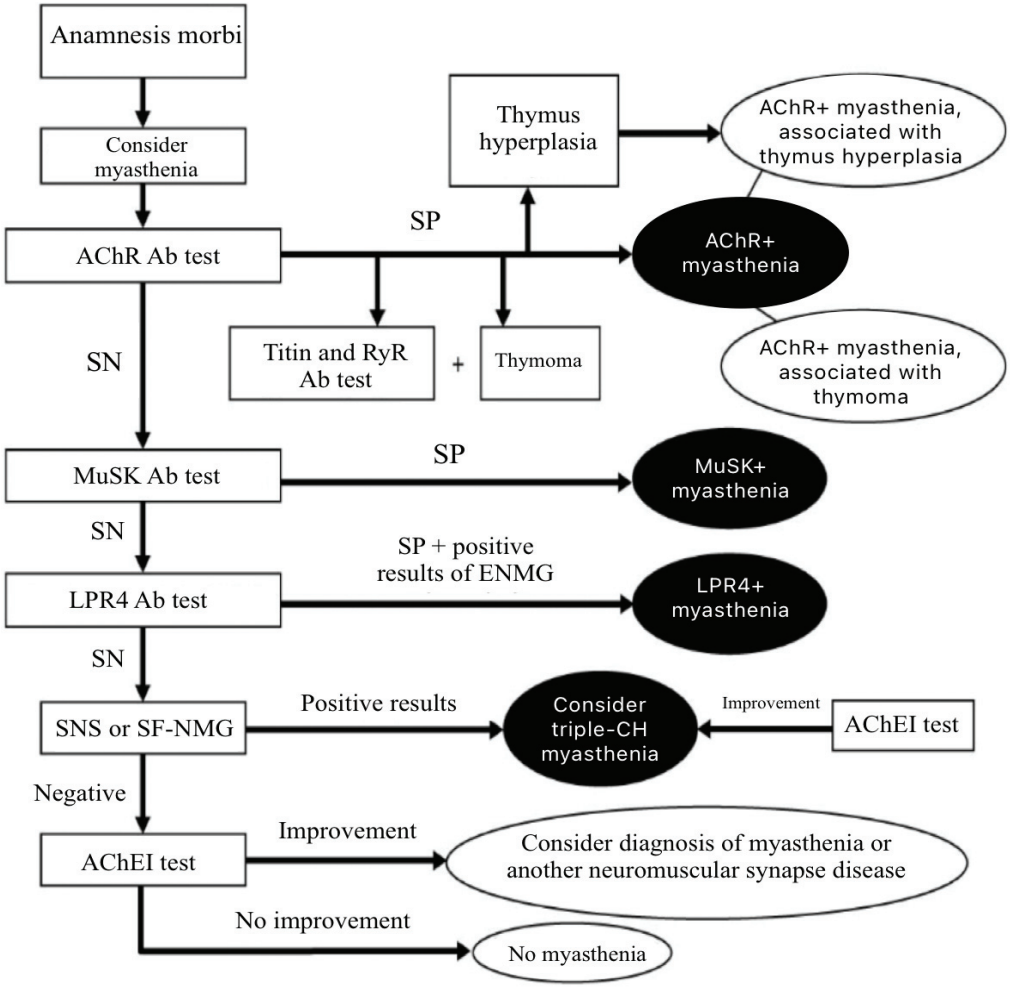

Figure 1. Diagnostic algorithm for different pathogenetic variants of MG (AchR – acetylcholine receptor; AChEI – anticholinesterase inhibitors; LRP4 – protein 4 associated with low-density lipoprotein receptors; MuSK – muscle-specific tyrosine kinase; RyR – ryanodine receptor; SNS – serial nerve stimulation; SF-NMG – single-fiber neuromyography; Ab – antibodies; SP –seropositive; SN – seronegative) [10].

Before the introduction of AChEIs in 1934, patients diagnosed with MG had a poor prognosis, and many died of respiratory failure and pneumonia within 1-2 years. Thymectomy was introduced in 1939 and its role in the pathogenesis of MG was later demonstrated, but its effect in MG was confirmed in randomized clinical trials only a decade later [13]. Treatment of MG with corticosteroids (CS) was introduced in the 1960s, followed by azathioprine, plasmapheresis (PLEX), and intravenous immunoglobulin (IVIG).

Data from four retrospective studies of corticosteroid therapy in different doses for the generalized form of MG indicate effectiveness (improvement or remission) in 73 % of 422 patients [14, 15, 16]. The appointment of corticosteroids (prednisolone, methylprednisolone) is advisable for progressive forms of MG, as well as for the stationary course of the ocular form of MG, which is resistant to AChEI therapy. There are many options for corticosteroid therapy for MG. The most rational is an alternating (every other day) intake of 0.7-1.0 mg/kg of DK in case of mild and moderate severity of MG, as well as severe forms without pronounced damage to the pharyngeal and respiratory muscles. In the case of severe forms of MG, it is rational to prescribe a daily GCS from a minimum dose of 10-25 mg of prednisolone or 8-12 mg of methylprednisolone, followed by an increase of 10 mg of prednisolone (8 mg of methylprednisolone), gradually increasing the dose (10 mg per dose until reaching) 60-80 mg (in one dose). Then it is possible to switch to alternating reception after stabilization of bulbar and respiratory disorders. Further intake of DC according to an alternating scheme is carried out until the state is reached, when on the day of skipping CS there is no increase in muscle weakness (this stage is called «zero day»), which indicates the restoration of sufficient compensatory mechanisms in the neuromuscular junction and development of a persistent anti-inflammatory effect. Further, the use of CS continues until full compensation of clinical manifestations within 1-1.5 months.

If the patient is in a serious condition, CS should be used immediately from high doses every day (along with short-term therapy – PLEX or IVIG) until the condition

is stabilized. After achieving remission (usually after 4-16 weeks), the dose of CS begins to be gradually reduced to maintenance. Another scheme of large doses: immediately give a dose of 1-1.5 mg / kg of weight to achieve the effect (after a day), and then reduce by one tablet to the maintenance dose. On the other hand, because MG is usually a chronic disease, the side effects of long-term use of steroids or other immunosuppressants can dramatically affect the duration or quality of life [3]. In addition to the usual side effects, CS for patients with MG can lead to a sudden increase in muscle weakness 1-3 weeks (most often 5-7 days) after starting oral prednisolone (steroid deterioration). Symptoms usually develop within 24-28 hours. Pretreatment with PLEX or IVIG or a gradual increase in prednisolone from 25 mg every other day to 100 mg every other day can alleviate this phenomenon. In any case, careful monitoring of respiratory function is necessary during the initiation of CS treatment [12]. Nonsteroidal immunosuppressive drugs include azathioprine (Imuran), which is a purine antimetabolite that inhibits T- and B-cell proliferation. Azathioprine is effective in 70-90 % of patients with MG, but the therapeutic effect develops after 2-3 months. Azathioprine (initial dose – 50 mg/day) can be used both as monotherapy and as an adjunct to steroid therapy, but the use of a combination with prednisolone is more effective and safer. In the absence of systemic side effects, the dose is increased by 50 mg per week until reaching a daily dose of 2-3 mg/kg [17]. In 15-20 % of patients within 10-14 days after starting treatment with azathioprine, idiosyncratic reactions with flu-like symptoms occur, requiring discontinuation of treatment.

Mycophenolate mofetil (Celcept) selectively blocks purine synthesis, as a result of which the proliferation of T- and B-cells is inhibited. Clinical efficacy was proven in a retrospective analysis of 85 patients with MG. The standard therapeutic dose is 1,000 mg twice daily, but doses may be increased to 3,000 mg. A higher dose leads to suppression of red bone marrow function, in connection with which a general blood test is performed every month. The duration of the onset of the therapeutic effect can be compared with the effect of azathioprine, but the severity of immunosuppression is lower [18]. Cyclosporine (sandimune) suppresses T-cell proliferation through inhibition of calcium channels, by blocking the synthesis of interleukin-2 and other proteins necessary for the functioning of CD4+ T-cells. Cyclosporine is used mainly in patients with ineffectiveness of azathioprine, in seronegative patients and in the presence of invasive types of thymoma. The recommended initial daily dose of cyclosporine is 4-6 mg/kg, administered in two doses. The clinical effect develops after 1-2 months, and a maintenance daily dose of 3-4 mg/kg also provides a sufficient effect. Cyclophosphamide is used as an immunosuppressant in severe immunological diseases. The mechanism of action is based on suppression of T- and B-cells, as well as all other actively dividing cells of the body. Cyclophosphamide is rarely used – when the combined use of corticosteroids and azathioprine is ineffective; methotrexate; cyclosporine. Side effects include myelosuppression, diarrhea, amenorrhea, oligospermia, and alopecia. Approximately half of the patients have positive dynamics after 1-2 months from the start of treatment. Cyclophosphamide is used intravenously (IV) in a dose of 100-200 mg for 10-12 days, and then the patient is transferred to receive azathioprine daily or every other day for 3-6 months [19].

Methotrexate inhibits the process of division of actively dividing cells (including T and B cells). Side effects include myelosuppression, mucositis, nausea, alopecia, cystitis, etc. Methotrexate should be used as a reserve drug (in case of ineffectiveness of therapy with first-line drugs). Methotrexate is used intramuscularly (IM) at 0.02-0.08 mg 2 times a week for 2-4 weeks or IV at 25-50 mg 2 times a week. An effective combined scheme of treatment of patients with CS and cytostatics [20]. PLEX is carried out in a short course – in severe forms of the disease, in preparation for operative treatment, with a rapid rate of progression of the disease. IVIG for MG is used for the same indications as PLEX, only with significant symptoms of MG in hospital conditions. It is believed that the effectiveness of these methods is the same [21].

Patients with MG, heterogeneous in pathogenesis and clinical diversity, differ in sensitivity to commonly accepted types of therapy: AChEI, CS and cytostatic immunosuppressants, thymectomy, immunomodulatory therapy, IVIG, PLEX. The effect of the listed types of therapy is absent in 15-20 % of patients with MG, who constitute the group with refractory forms of the disease [1, 6, 7]. Targeted therapy with the use of monoclonal antibodies is a new approach in the treatment of MG, giving hope for the possibility of changing the prognosis of the management of patients with refractory MG already in the coming years. Of greatest interest is the drug rituximab, which selectively binds to the CD20 antigen and initiates immunological reactions that mediate the lysis of B-lymphocytes, key links in the immunopathogenesis of MG [21].

A beneficial effect of rituximab has been demonstrated in patients with refractory or severe generalization of MG. In addition, uncontrolled studies have shown that the use of rituximab can significantly reduce or stop the use of steroids and other immunosuppressants. Efficacy of rituximab is more evident in MG with MuSK Ab+ antibodies compared to those with AChR Ab+ antibodies, with 70-89 % achieving minimal manifestation status (MMS) or better in MuSK Ab+ MG compared with 30-47 % in AChR Ab+ MG and the level of remission. MuSK Ab+ MG patients followed for a median period of 3.5 years, 58 % of patients treated with rituximab versus 16 % of those without had a favorable clinical outcome and lower doses of immunosuppressants. Rituximab was also shown to be safe and effective in a cohort of treatment-resistant patients with late-onset AChR Ab+.

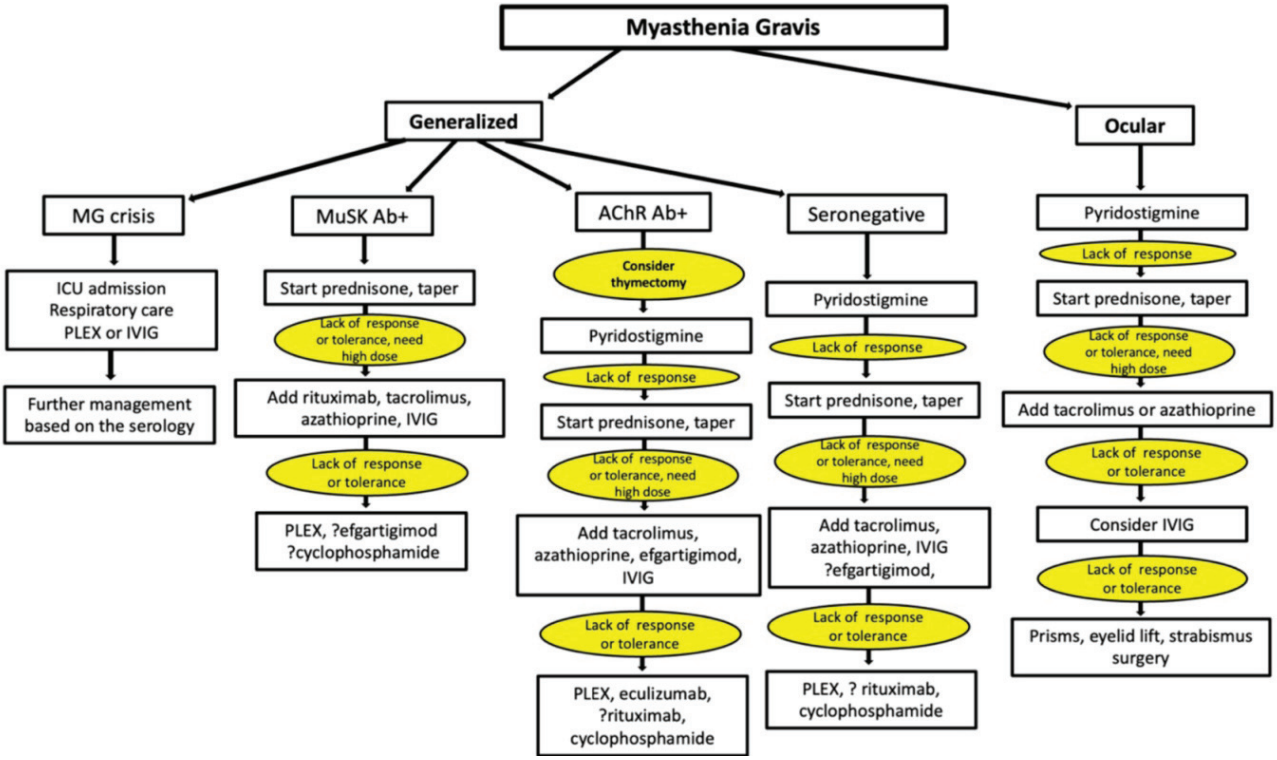

Figure 2. Overall treatment strategy of MG. MuSK: muscle specific tyrosine kinase; Ab: antibody; AChR: acetylcholine receptor; IVIG: intravenous immunoglobulin; PLEX: Plasma exchange [3].

Immunotherapy commonly used to treat MG is nonspecific and associated with serious long-term side effects. To mitigate this, some immunotherapies currently being developed target pathological mechanisms more specific to MG [22]. Antigen-specific immunotherapy, aimed at restoring tolerance to the attacked autoantigen by targeting only the damaged part of the immune system, while leaving the rest intact, is considered optimal for the treatment of MG. These treatments, such as complement C5 inhibitors (Eculizumab) and neonatal Fc receptor inhibitors (Efgartigimod) may be associated with fewer side effects, but they do not restore tolerance and are therefore not durable or curative [23].

In the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department patients with MG are treated in the neurology and neurophysiology department with the possibility of treatment in the intensive care unit. A patient-oriented approach to the treatment and rehabilitation of MG was determined by etiopathogenesis and the probability of neurological deficit according to the severity of symptoms and the form of MG.

Patients were divided into 2 groups according to the nature of neurological deficit and severity of symptoms and form of MG. The first group included 6 patients with ocular form with varying degrees of severity of oculomotor symptoms. The second group consisted of 18 patients with a generalized form of MG with varying degrees of severity (from moderate to severe) oculomotor and bulbar disorders. Spontaneous remission occurred in two patients of the first group of 6 patients with MG. All patients responded well to AChEIs, but required CS treatment.

With the help of a diagnostic algorithm, in patients of the second group (18 patients with a generalized form of MG with varying degrees of severity (from moderate to severe) oculomotor and bulbar disorders) a stepwise strategy of MG treatment was used (fig. 2) with the use of AChEI, CS, cytostatics. Episodic PLEX and IVIG were used.

Due to the fact that one patient with a generalized form of MG remained refractory to treatment with CS, AChEI and immunomodulatory drugs, targeted drugs, namely, rituximab, were used.

DISCUSSION

Here is an example of the implementation of a patient-oriented approach to the treatment and rehabilitation of a patient with MG. A woman, born in 1996, applied in October 2021 with complaints of drooping of the right eyelid, blurred vision, worsening of speech articulation, severe general weakness and weakness in the upper limbs, which had been bothering the patient for the last two weeks after childbirth. During her stay in the maternity hospital, she received pulse therapy with solumedrol for 2 days, Kalimin 60 mg every 6 hours, fluoxetine, and endoxan. Acetylcholine receptors, IgG antibodies – 71.15 nmol/l. ENMG was performed – signs of a generalized violation of neuromuscular transmission

of the myasthenic type. SCT of the OHP was performed, which revealed a thymoma. In neurological status: consciousness is clear, oriented, adequate. Eye slits D<S, pronounced ptosis of the right eyelid, pupils D=S. Movements of the eyeballs in full. No nystagmus, diplopia. The face is symmetrical. Tongue in the middle line. Dysphonia, dysarthria. There is no dysphagia. Muscle strength in the limbs is diffusely reduced, muscle tone is preserved. Tendon reflexes from arms and legs are symmetrically increased, D=S. Bekhterev, Jacobson-Lask symptoms «+» on both sides. Friedrich's feet. PNP performs satisfactorily. It is impossible to check stability in the Romberg pose. There are no meningeal signs, paresis, sensitivity disorders.

A diagnosis was established: AChR+ positive myasthenia gravis with early onset, generalized form, with moderately pronounced oculomotor and bulbar disorders in a state of decompensation. Lambert-Eaton syndrome is excluded.

Inpatient treatment for 10 days: Plasmapheresis, Methylprednisolone 1000 mg IV, followed by Prednisolone 80 mg (16 tab.) in the morning after meals every other day, Kalimin 1/2 tab. in the morning, 1 tab. at lunch, 1/2 tab. in the evening, Calcium-D3 2 tab. in the evening, Caldium 600 mg 3 times a day, Veroshpiron 1 tab. 25 mg in the morning – 10 days, Gliaton 1000 mg in 200.0 NaCl – IV drops, Venokor 5.0 in 50.0 NaCl – IV, Neuromidin 1.0 1.5 % – IV. In November 2021, a thymectomy was performed.

After the treatment, the condition improved: ptosis of the right eyelid has almost completely disappeared, dandruff occurs only during fatigue, speech articulation and swallowing have improved, general weakness has significantly decreased. Prednisolone 80 mg (16 tab.) in the morning after meals was prescribed every other day – continued with subsequent dose adjustment, Kalimin 60 mg 4 times a day every 4-6 hours – continued with subsequent dose adjustment, Calcium-D3 2 tab. in the evening – continued, Caldium 600 mg 3 times a day – continued, Veroshpiron 1 tab. 25 mg in the morning – 10 days every month, Neuromidin 1 tab. 2 times a day – 3 weeks.

During the full-scale invasion of the Russian Federation into Ukraine, the patient's condition worsened, the severity of bulbar and oculomotor disorders increased significantly, despite the constant intake of Methylprednisolone and Kalimin. She was forced to go to the Czech Republic in March 2022 to receive medical help. The patient underwent several courses of IVIG without effect, after which Imuran was prescribed at a dose of 150 mg per day. In June 2022, the patient's condition stabilized: oculomotor and bulbar disorders completely regressed. A complete clinical remission was gradually achieved, after which, over the next six months, the doses of Imuran and Methyprednisolone were gradually reduced with their complete withdrawal, the patient continued to receive Kalimin (Mestinon) 30 mg 3 times a day. In December 2023, the condition began to deteriorate for no apparent reason in the form of sudden ptosis, diplopia, pronounced bulbar syndrome. In January 2024, treatment was prescribed: Methylprednisolone 64 mg in the morning every other day – continued, Mestinon 30 mg 3 times a day – continued, Calcium-D3 2 tab. in the evening – continued, Caldium 600 mg 2 times a day – continued, Veroshpiron 1 tab. 25 mg in the morning – 10 days every month, Neuromidin 1tab. 2 times a day – 3 weeks – without positive dynamics. In February 2024, the following course of treatment was prescribed: Potassium chloride 4 % 70.0 in 200.0 NaCl – IV, No. 5, Solumedrol 1000 mg in 200.0 NaCl – IV, No. 3-5, then 500 mg in 200.0 NaCl – IV, No. 3-5, then 40 mg in 200.0 phys. IV drop solution. No. 3-5, Neuromidin 1.0 1.5 % – IM No. 10, Imuran 50 mg in the morning, 50 mg in the evening, Mestinon 30 mg 4 times a day – continuously, Calcium-D3 2 tab. in the evening – with a slight improvement.

In connection with the lack of possibility of conducting PLEX, a decision was made to conduct targeted therapy. The patient underwent IV infusion of Rituximab 500 mg in 500.0 NaCl twice, with an interval of 2 weeks. Treatment with premedication, after which the patient's condition began to improve in the form of a gradual disappearance of oculomotor and bulbar disorders, a significant decrease in general weakness. In neurologic status: Consciousness is clear. Oriented, adequate. There is no ptosis or diplopia. Eye slits D=S, pupils D=S. Bilateral weakness of convergence of the eyeballs. No nystagmus, diplopia. The face is symmetrical. Tongue in the middle line. Pharyngeal and palatal reflexes are not high. There is no dysarthria or dysphagia. Moderate dysphonia. Muscle strength in the limbs is diffusely reduced, muscle tone is preserved. Dry p-sy from arms and legs are symmetrically lively, D=S. Symptom Bekhterev, Yakobson-Laska «+» on both sides. Friedrich's feet. In Romberg's pose, she is stable, and performs the PNP satisfactorily. There are no meningeal signs, paresis, sensitivity disorders.

Final diagnosis: AChR+ positive myasthenia gravis, generalized form, AChR+, with early onset, with moderately pronounced oculomotor and bulbar disorders in the state of insufficient compensation of AChE, state of initial recovery of functions. Thymectomy: 11/17/2021.

Final prescription: long-term Methylprednisolone 64 mg in the morning every day after breakfast, Mestinon 30 mg 4 times a day, Calcium-D3 2 tab. in the evening, Caldium 650 mg 3 times a day, Veroshpiron 1 tab. 25 mg in the morning – 10 days every month.

After the prescribed treatment, a stable remission occurs in all patients until the complete regression (disappearance) of all symptoms. Remission can be complete or incomplete. For example, taking drugs contraindicated in MG or severe stress can cause an exacerbation of MG even several years after the onset of remission.

CONCLUSIONS

1. Complex therapy of patients with MG is based on the use of a differential diagnostic algorithm for various pathogenetic variants of MG, which forms a mainly etiopathogenetic concept of therapy.

2. Antigen-specific immunotherapy, aimed at restoring tolerance to the attacked autoantigen by targeting only the damaged part of the immune system, while leaving the rest intact, is considered more promising for the treatment of MG.

3. MG treatment should be carried out in the conditions of a specialized neurological center, where a full examination and targeted pathogenetic therapy can be carried out.

Prospects for further research. The study can be used by neurology specialists for more detailed and specified algorithm of diagnosis and further treatment of patients with MG.

FUNDING AND CONFLICT OF INTEREST

The authors declare no conflict of interest. The research has no external sources of funding.

COMPLIANCE WITH ETHICAL REQUIREMENTS

The authors adhere to the standards of the Helsinki Declaration of the World Health Organization association, as well as Interdisciplinary norms and regulations on the use of animals in research, testing and educational programs, which are published by the appropriate committee dealing with animal research at the Academy of Sciences in the city of New York. The submitted manuscripts relate to the work patients and prepared in accordance with ethical standards.

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Резюме

СУЧАСНИЙ ПОГЛЯД НА ДІАГНОСТИКУ ТА ЛІКУВАННЯ МІАСТЕНІЇ. ВИПАДОК З ПРАКТИКИ

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Вступ. Міастенія гравіс (МГ) або хвороба Ерба-Гольдфлама-Джолі, – аутоімунне нервово-м'язове захворювання, в основі якого лежить аутоагресія гуморального імунітету щодо елементів нервово-м'язових синапсів та внутрішньоклітинних структур м'язових волокон (антитіла до ацетилхолінових рецепторів, м'язовоспецифічної тирозінкінази (MuSK), білку 4, пов'язаному з рецепторами ліпопротеїдів низької щільності (LRP4), ріанодиновим рецепторам (RyR), тітіну та антигенам скелетної мускулатури). Точні причини аутоімунних процесів при МГ невідомі, але безперечне значення мають аномалії вилочкової залози (гіперплазія та неоплазія), особливо у пацієнтів з антитілами до ацетилхолінових рецепторів (AchR), а також генетична схильність [1].
Мета. Проаналізувати проблематику патогенезу, діагностики та лікування тяжкої МГ із джерел сучасної літератури для оптимізації проведення лікування у цієї групи пацієнтів. Проаналізувати власний досвід впровадження пацієнт-орієнтованого підходу до лікування та реабілітації пацієнтів з МГ.
Матеріали та методи. Бібліосемантичний метод, метод системного аналізу та клініко-неврологічне обстеження хворих на МГ.
Результати. Перебіг МГ відрізняється варіабельністю і може бути представлений епізодичною м'язовою слабкістю, стаціонарною течією, повільним або швидким прогресуванням [2]. В даний час комплексна терапія хворих з МГ має чітку тенденцію до перехода від симптоматичного (інгібітори ацетилхолінестерази (ІАХЕ), препарати калію, калійзберігаючі діуретики) лікування до патогенетичного, формуються переважно етіопатогенетичні концепції терапії (імуносупресивна терапія, антиген-специфічна імунотерапія, моноклональні антитіла), а також уточнюється ефективність ранньої тимектомії [3].
Висновки. Комплексна терапія хворих з МГ заснована на використанні диференційного діагностичного алгоритму при різних патогенетичних варіантах МГ, що формує переважно етіопатогенетичну концепцію терапії. Антиген-специфічна імунотерапія, спрямована на відновлення толерантності до атакованого аутоантигену шляхом цілеспрямованого впливу тільки на пошкоджену частину імунної системи, залишаючи при цьому решту незайманої, вважається більш перспективною для лікування МГ. Лікування МГ доцільно проводити в умовах спеціалізованого неврологічного центру, де можна провести повноцінне обстеження та цілеспрямовану патогенетичну терапію.

Ключові слова: **міастенія гравіс, антихолінестеразні препарати, глюкокортикостероїди, ритуксимаб, плазмаферез**