Amyotrophic Lateral Sclerosis and Myasthenia Gravis: Comorbidities and Differential Diagnosis

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Abstract

Amyotrophic lateral sclerosis (ALS) and myasthenia gravis (MG) are both characterized by primarily motor deficit, and their differential diagnosis may be sometimes challenging. We present a case report of a patient with late-onset ALS, which was initially misdiagnosed for anti-acetylcholine (anti-AChR) antibody-positive MG. In some cases, ALS has been thought to be triggered by MG. In the presented case report, elevated anti-AChR antibody titers (positive anti-AchR Ab) had no clinical significance and possibly indicated an immune response to structural changes in the postsynaptic membrane of the neuromuscular synapse in the ALS patient.

Keywords: *amyotrophic lateral sclerosis; myasthenia gravis; anti-acetylcholine receptor antibodies; motor neuron disease*

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Боковой амиотрофический склероз и миастения гравис: коморбидность и дифференциальная диагностика

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Аннотация

Боковой амиотрофический склероз (БАС) и миастения характеризуются чисто двигательным неврологическим дефицитом, и в некоторых случаях их дифференциальная диагностика может вызывать трудности. Представлен случай позднего дебюта БАС, который изначально был ошибочно принят за миастению с положительными антителами к ацетилхолиновым рецепторам (АХР). В некоторых случаях миастения рассматривается как триггер БАС. В представленном случае положительный титр антител к АХР не имел клинического значения и, возможно, указывал на иммунную реакцию на структурные изменения в постсинаптической мембране нервно-мышечного синапса у пациента с БАС.

Ключевые слова: *боковой амиотрофический склероз; миастения; антитела к ацетилхолиновым рецепторам; болезнь двигательного нейрона*

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Amyotrophic lateral sclerosis (ALS) and myasthenia gravis (MG) are two diseases with motor disorders at the core of their clinical picture. However, a comprehensive examination of the clinical manifestations generally allows for a correct diagnosis to be established already at the screening. ALS is characterized by progressive mixed asymmetric paresis without oculomotor muscle involvement. The disease is irreversibly progressive and unresponsive to treatment. Myasthenia gravis (MG) is predominantly manifested by muscle weakness and abnormal fatigability. MG is classified by the distribution of paresis affecting mainly oculomotor, mimic, and bulbar muscles, as well as the muscles of upper and lower limb girdles and proximal limbs. MG course is usually fluctuating with MG patients quickly responding to acetylcholinesterase inhibitors (AChEIs).

A number of factors may impede differential diagnosis of ALS and MG. In some ALS subtypes, the peripheral motor neurons are primarily affected. At the early stages, only the bulbar muscles are involved, and there are no clear signs of tongue atrophy or fasciculation. This clinical picture resembles that of MG. On the other hand, MG may mimic ALS. For instance, MG with antibodies against muscle-specific tyrosine kinase (MuSK-MG) is characterized by asymmetric paresis sparing oculomotor muscles, although with an early onset of respiratory disturbances. In this subtype of MG, progression of paresis is rapid leading to atrophy and the patients show no response to AChEI [1].

Differential diagnosis of MG and ALS is of paramount importance as these two diseases require different treatment approaches. In MG patients, immunomodulatory therapy may be beneficial, while in ALS patients, glucocorticoid therapy fails and the most promising treatment options are associated with various neuroprotective strategies. We present a case report of an anti-AchR Ab positive patient who initially was diagnosed with late-onset MG. A more comprehensive review of the clinical and instrumental data ultimately led to the ALS diagnosis.

A case report

Patient N. aged 81 years.

Complaints: difficulty swallowing (both solid foods and liquids), impaired chewing, choking, nasality, and decreased voice pitch, severe generalized muscle weakness, especially in the neck ("dropping head") and legs.

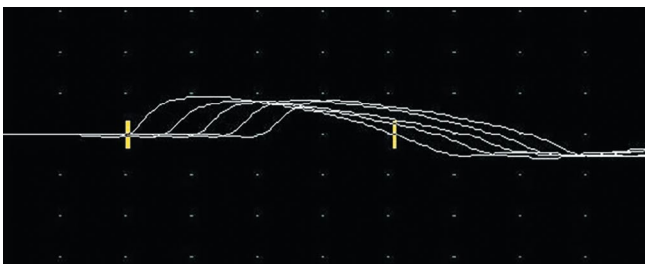
Medical history. Approximately one year ago, the patient first observed weakness in the right arm, which subsequently extended to the whole body. One year later, his close ones started noticing his slurred speech. One month prior to hospital admission, the patient experienced an acute decline in his condition, which manifested as acute dysphagia, including failure to swallow saliva, and weakness in the legs, which gradually increased over the course of the month.

Concomitant diseases. The patient had a history of basal cell skin carcinoma of the right anterior thorax which was operated in 2021; neither radiotherapy or chemotherapy was given; prostate adenoma (operated in 2021); stage III arterial hypertension > 10 years managed by triple antihypertensive therapy with combination of amlodipine, valsartan, and hypothiazid 5/160/12.5 mg. The patient had smoked for 40 years (one pack of cigarettes per day) and ceased smoking in 2004; worked at construction sites for a long time, and as a crane operator for the last 20 years before retirement at the age of 65. No family history of similar disorders, the patient's father died early in life because of the trauma, mother had symptoms resembling parkinsonism (limb tremor, bradykinesia, and muscle rigidity), we have no information about her diagnosis.

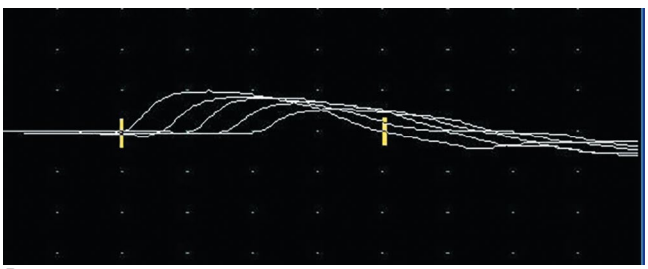
The patient was urgently admitted to the central district hospital. Diagnosis at admission: cerebrovascular disease. The complete blood count and metabolic panel test results fell within reference limits; a urinalysis revealed moderate leukocyturia; electrocardiography showed chronic atrial fibrillation, which was detected for the first time. Prior to AChEI

treatment initiation, the patient underwent electromyography (EMG) with low-frequency (3 Hz) repetitive stimulation of the following muscles: m. orbicularis oculi, m. nasalis, m. digastricus, m. deltoid, and m. abductor digiti minimi. The EMG results were suggestive of abnormalities in postsynaptic neuromuscular transmission (muscle action potential (MAP) decrement 16–32%, post-activation depression and post-activation exhaustion, see Figure 1). Consequently, the diagnosis was revised to myasthenia gravis. Upon insertion of a nasogastric tube, the patient started AChEI (pyridostigmine bromide 180 mg daily) and glucocorticosteroid treatment (prednisolone 70 mg daily). General weakness, particularly in the legs, progressively increased with the treatment. Additionally, dyspnea developed, which may have been caused by the side effects of the ongoing treatment, also including fluctuations in blood pressure, progressive cardiac rhythm disturbances, and glycemia. The patient stopped walking without assistance.

To verify the diagnosis and modify the treatment, the patient was transferred to the Neurology Department of G.G. Kuvatov Republican Clinical Hospital.



A



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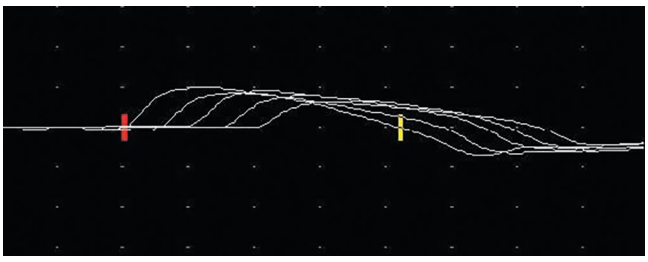

C

Fig. 1. Electromyogram of the patient N.
A – *m. deltoideus dextra,* primary amplitude decrement (1–5) 35%; *B* – post-activation depression; *C* – post-activation exhaustion.

At admission to the Neurology Department: height 180 cm, weight 67 kg (weight loss of 15 kg within 1.5 months), BMI 20.68 kg/m^2, respiration rate 19 breaths per min, chest expansion decreased. Lower legs are swollen. Blood oxygen saturation was 91%, with oxygen insufflation increased to 97%. Cardiac arrhythmia, tachycardia, heart rate 100 bpm. Nasogastric feeding. Other physical characteristics without visible changes.

Neurological examination: normal ranges of eye movement, no diplopia, the orbicularis oculi muscle strength grade 5; masticatory muscle hypotrophy with strength down to grade 3; the jaw jerk reflex not exaggerated, symmetric face, mimic muscle strength sufficient, hypophony, poor velar elevation, reduced swallowing reflex and palatal and pharyngeal reflexes, dysphagia, dysarthria, fibrillations on the tongue without hypotrophy, tongue movements and strength within normal range. The snout reflex and the nasolabial reflex were positive. The strength of the neck extensor muscles is at grade 1 and of the neck flexor muscles is at grade 2 (dropped head syndrome, DHS). The patient had a clinical picture of severe, predominantly flaccid, asymmetric tetraparesis. Active movements of the limbs are limited, predominantly on the right side: muscle strength in the proximal limbs decreased to grade 1 in the leg and grade 2 in the arm with plegia in the distal parts. Muscle strength in the left-side limbs decreased to grade 3, predominantly in the proximal parts. The muscle tone is decreased. Asymmetric diffuse upper and lower limb hypotrophy andingle fasciculations in the upper and lower limb muscles were observed. Tendon reflexes were symmetrically reduced, no pathological reflexes elicited. Moderate muscle fatigability was observed: a grade 0.5–1.0 muscle strength decrease during muscle strength re-assessments. Coordination in the left-side limbs within normal range. Gait assessment was impossible [due to the patient's immobility]. No sensory disturbances. The patient had urinary dysfunction associated with prostatic hyperplasia. After recommendation of the urologist, the patient was catheterized.

The patient was differentially diagnosed between motor neuron disease and neuromuscular junction disorder. A neostigmine test was performed twice with no apparent positive effect.

MAP decrement assessment by needle electromyography (EMG) in m. trapezius, *m. abducens digiti minimi dextr.* performed 12 h after AChEI withdrawal detected no neurophysiological signs of disturbance in neuromuscular transmission. No significant changes in M-response or decremental response were observed during post-tetanic depression and exhaustion. Needle EMG results showed a pattern of neurogenic changes in motor action potentials with greater average duration and amplitude in *m. rectus femoris, m. tibialis anterior, m. deltoideus*, and *m. interosseous* I (Fig. 2). Detection of single spontaneous fibrillation potentials and fasciculations confirms generalized damage to motor neurons in the spinal

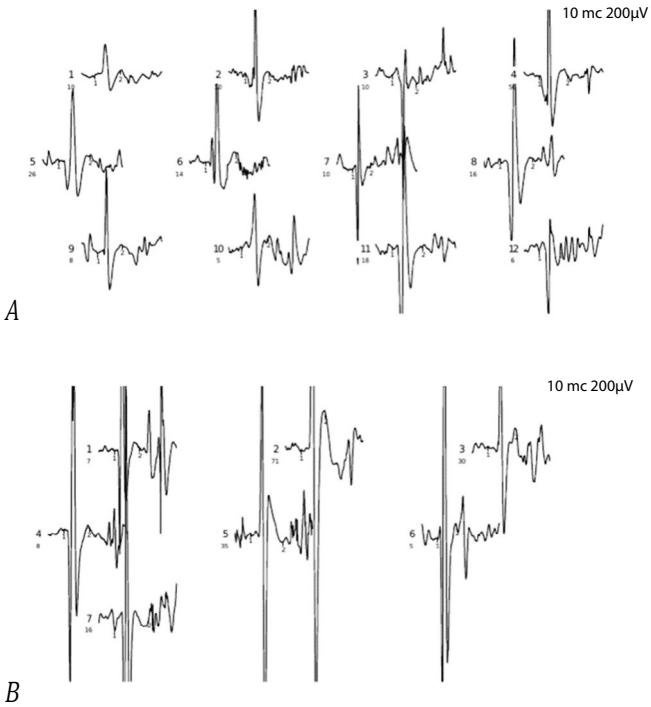

Fig. 2. Needle electromyogram of patient N.
A – m. deltoideus dextra, average duration 13.3 ms (8.9–16.3 ms, ref. values < 12 ms), average amplitude 1408 μV (459–2164 μV, ref. values < 550 μV), spontaneous activity (single fibrillation and fasciculation potentials); *B – m. interosseous I dextra*, average duration 14 ms (9.9–17.8 ms, ref. values < 10.3 ms), average amplitude 4863 μV (2125–8427 μV, ref. values < 750 μV), and moderate spontaneous activity (fasciculation potentials).

cord. The EMG assessment of the tongue muscles detected a single spontaneous fibrillation potentials and an increased average amplitude of motor action potentials without any changes in duration.

To rule out focal lesions in the brainstem area, a brain MRI was conducted, which revealed the signs of chronic cerebrovascular insufficiency (Fig. 3).

Complete work-up of the patientrevealed left kidney cyst, moderate right kidney pyelectasia, diverticula and pseudo-diverticula in the urine bladder, and diffuse pulmonary sclerosis.

The complete blood count results were within normal range; urinalysis detected transitory macrohematuria and leukocyturia caused by uroinfection due to insertion of urinary catheter; comprehensive metabolic panel results indicated hypoproteinemia (51.0 g/L against ref. values of 66–83 g/L) and hypoalbuminemia (31.6 g/L against ref. values of 35–52 g/L), elevated urine acid levels up to 440.9 μM/L (ref. values: 208.3–428.3 μM/L), and other parameters within a range of reference values. Prostate-specific antigen: 2.450 ng/mL (ref. value < 6.5 ng/mL). Elevated anti-AChR antibody titers: > 20 nM/L (ref. values < 0.5 nM/L).

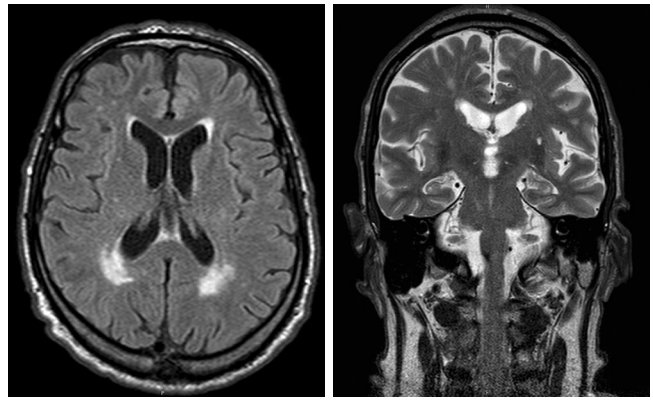

Fig. 3. Periventricular hyperintensity of vascular origin on T2 (*A*) and FLAIR (*B*) MRI scans of the patient's brain.

Based on progressive asymmetric paresis, the absence of any other symptoms since its onset in the upper right limb, electrophysiological signs of neuronal damage present on threelevels of central nervous system, and the absence of positive response to AChEI administration, the diagnosis was established as motor neuron disease (MND). Amyotrophic lateral sclerosis, spinal onset with asymmetric tetraparesis to the degree of plegia in the distal parts of the upper right limbs, neck muscles involvement, bulbar-pseudobulbar syndrome, and respiratory disturbances. Insignificant anti-AchR positivity. Concominant diagnosis: coronary artery disease associated with arrhythmia. Chronic atrial fibrillation and congestive heart failure (ACC/AHA Stage B, NYHA Class II). Stage III arterial hypertension. Stage I prostatic hyperplasia.

Following the gradual withdrawal of prednisolone and pyridostigmine bromide, the patient exhibited a slight improvement in blood oxygen saturation levels and respiratory function.

Discussion

At the district hospital (Level II of healthcare system), the initial diagnosis for patient N was myasthenia gravis, which was subsequently revised to amyotrophic lateral sclerosis (ALS). However, the presence of anti-AChR antibodies raised doubts about the absence of myasthenia gravis.

The potential association between ALS and myasthenia gravis is manifold. The most straightforward explanation is that they are capable of mimicking each other, as previously stated. Nevertheless, clinical cases with combination of these two diseases are particularly intriguing. In the majority of MG-ALS comorbidity cases documented in the literature, classical myasthenia gravis preceded the symptoms indicative of upper and lower motor neuron damage, which may be considered a transformation of MG into ALS. Few cases of

patients with MG followed by ALS have also been previously described. Epidemiological data analysis showed that MG patients, who further developed ALS, were of older age, had two times more frequently a bulbar onset, and a more severe course of disease [2].

The majority of authors consider MG and ALS coexistence to be far beyond coincidence. Based on western countries incidence rates the co-occurrence of both diseases is a really exceptional event ($7.5/10^9$), while S. de Pasqua et al. reported higher incidence rates based on their studies ($1.87/10^7$) [2]. In terms of pathogenesis, the immunological dysfunctions in patients with MG may trigger the ALS development, especially if there is genetic predisposition. Antibodies to lipoprotein–related receptor protein 4 (LRP4) can be found both in some MG subtypes and in ALS, as this protein plays an important role in the neuromuscular synapse and motor neuron functioning. This mechanism is uncommon and is unlikely in the present case, as the patient was anti-AChR antibody positive with elevated anti-AChR antibody titers. On the other hand, dysfunction of the regulatory T-cells (Tregs) typical for MG may be considered a trigger to motor neuron damage. Tregs are shown to suppress proinflammatory cytokine production, stimulate production of antiinflammatory cytokines and neurotrophic factors, as well as mediate microglia activation, etc. [3]. In MG, suppressive function of Tregs is compromised [4], whereas in ALS, Tregs are thought to suppress microglial activation and production of free radicals [5]. Experimental studies suggest that decreased blood levels of Tregs are associated with rapid disease progression [6].

Neuromuscular synapse dysfunction plays a role in the pathogenesis of ALS due to a "dying back" phenomenon, i. e. progressive degeneration of motor axons, muscle denervation and decreased neuromuscular transmission [7]. The pathogenetic similarities between ALS and MG are supported by electrophysiological studies. In their compound muscle action potential (CMAP) decrement study, D. Zhang et al. demonstrated a decrease in M-response amplitude in m. abductor pollicis brevis in ALS patients — the so-called neurogenic decrement [8]. Nowadays, neuromuscular junction dysfunction is considered to play a special role in the pathogenesis of ALS [9].

The patient's history of basal cell skin carcinoma does not exclude paraneoplastic ALS [10]. However, in the presented case, cancer was highly differentiated with low immunogenicity, which resulted in a low risk of paraneoplastic response. The tumor as a source of antigenic stimulation was removed two years prior to disease onset, and the patient did not respond to immunosuppressive therapy.

The patient with predominantly flaccid tetraparesis was diagnosed with late-onset MG and presumptive therapy (AChEI + glucocorticosteroids) at the district l hospital failed to yield any positive results. Moreover, administration of glucocorticosteroids had a transient negative effect that leveled off after their withdrawal. Results of follow-up examination ruled out MG and were suggestive of ALS. At the same time, the anti-AChR ab test was positive. A comprehensive analysis of clinical and electrophysiological data, and review of the patient's family medical history revealed no signs of neuromuscular synapse dysfunction, and the patient was diagnosed with ALS. The presence of autoantibodies was regarded clinically insignificant. In the presented case, positive anti-AChR ab test result may indicate an immune response to the AChR degeneration in the neuromuscular synapse [11, 12]. Several authors suggested that pathogenesis of certain ALS subtypes includes autoimmune traits [11], but failure of the glucocorticosteroid therapy is inconsistent with this hypothesis.

Thus, MG-ALS co-morbidity is a rare but explainable phenomenon in terms of pathogenesis [13–17]. A case report presented in this article highlights the importance of a comprehensive analysis of the clinical picture in the diagnosis of neuromuscular diseases. Even the presence of disease-specific autoimmune antibodies is not sufficient to diagnose MD. The diagnosis must be supported by other typical manifestations, such as oculomotor muscle involvement, pronounced muscle fatigability, response to AchRI therapy, cold pressure test, and muscle action potential decrement by low-frequency repetitive nerve stimulation.

References / Список источников

1. Rodolico C., Bonanno C., Toscano A. et al. MuSK-associated myasthenia gravis: clinical features and management. *Front. Neurol.* 2020;11:660. DOI: 10.3389/fneur.2020.00660
2. De Pasqua S., Cavallieri F., D'Angelo R. et al. Amyotrophic lateral sclerosis and myasthenia gravis: association or chance occurrence? *Neurol. Sci.* 2017;38(3):441–444. DOI: 10.1007/s10072-016-2787-3
3. Tiemessen M.M., Jagger A.L, Evans H.G. et al. CD4+CD25+Foxp3+ regulatory T cells induce alternative activation of human monocytes/macrophages. *Proc. Natl. Acad. Sci. U S A.* 2007;104(49):19446–19451. DOI: 10.1073/pnas.0706832104
4. Berrih-Aknin S., Le Panse R. Myasthenia gravis: a comprehensive review of immune dysregulation and etiological mechanisms. *J. Autoimmun.* 2014;52:90–100. DOI: 10.1016/j.jaut.2013.12.011
5. Zhao W., Xie W., Xiao Q. et al. Protective effects of an anti-inflammatory cytokine, interleukin-4, on motoneuron toxicity induced by activated microglia. J. Neurochem. 2006;99(4):1176–1187. DOI: 10.1111/j.1471-4159.2006.04172.x
6. Beers D.R., Henkel J.S., Zhao W. et al. Endogenous regulatory T lymphocytes ameliorate amyotrophic lateral sclerosis in mice and correlate with disease progression in patients with amyotrophic lateral sclerosis. *Brain.* 2011;134(Pt 5):1293–1314. DOI: 10.1093/brain/awr074
7. Fischer L.R., Culver D.G., Tennant P. et al. Amyotrophic lateral sclerosis is a distal axonopathy: evidence in mice and man. Exp. Neurol. 2004;185(2):232–240. DOI: 10.1016/j.expneurol.2003.10.004
8. Zhang D., Zhao Y., Yan C. et al. CMAP decrement by low-frequency repetitive nerve stimulation in different hand muscles of ALS patients. *Neurol. Sci.* 2019; 40(12):2609–2615. DOI: 10.1007/s10072-019-04027-7
9. Щербакова Н.И., Касаткина Л.Ф., Гуркина Г.Т и др. Развитие бокового амиотрофического склероза у больного с миастенией: случайное сочетание или патогенетически взаимосвязанные состояния? *Неврологический журнал.* 2013;18(6):9–16.
Shcherbakova N.I., Kasatkina L.F., Gurkina G.T. et al. An unusual case of amyotrophic lateral sclerosis in a patient with myasthenia gravis: random combination or pathogenesis related conditions? *Nevrologicheskii zhurnal.* 2013;18(6):9–16.
10. Verma S., Khurana S., Vats A. et al. Neuromuscular junction dysfunction in amyotrophic lateral sclerosis. *Mol. Neurobiol.* 2022;59(3):1502–1527. DOI: 10.1007/s12035-021-02658-6
11. Yang Z., He L., Ren M. et al. Paraneoplastic amyotrophic lateral sclerosis: case series and literature review. *Brain Sci.* 2022;12(8):1053. DOI: 10.3390/brainsci12081053
12. Mehanna R., Patton E.L. Jr., Phan C.L. et al. Amyotrophic lateral sclerosis with positive anti-acetylcholine receptor antibodies. Case report and review of the literature. *J. Clin. Neuromuscul. Dis.* 2012;14(2):82–85. DOI: 10.1097/CND.0b013e31824db163
13. Ashizawa T. False positive anti-acetylcholine receptor antibodies in motor-neurone disease. *Lancet.* 1986;1(8492):1272. DOI: 10.1016/s0140-6736(86)91408-x
14. Longinetti E., Sveinsson O., Press R. et al. ALS patients with concurrent neuroinflammatory disorders; a nationwide clinical records study. *Amyotroph. Lateral Scler. Frontotemporal. Degener.* 2022;23(3–4):209–219. DOI: 10.1080/21678421.2021.1946084
15. Ковражкина Е.А., Сердюк А.В., Разинская О.Д. и др. Миастенический синдром у пациента с терминальной стадией бокового амиотрофического склероза. *Журнал неврологии и психиатрии им. С.С. Корсакова.* 2023;123(7):102–107.
Kovrazhkina E.A., Serdyuk A.V., Razinskaya O.D. et al. Myasthenic syndrome in a patient with end-stage amyotrophic lateral sclerosis. *S.S. Korsakov Journal of Neurology and Psychiatry.* 2023;123(7):102–107. DOI: 10.17116/jnevro2023123071102
16. Tai H., Cui L., Guan Y. et al. Amyotrophic lateral sclerosis and myasthenia gravis overlap syndrome: a review of two cases and the associated literature. *Front. Neurol.* 2017;8:218. DOI: 10.3389/fneur.2017.00218
17. Санадзе А.Г., Касаткина Л.Ф. Два случая трансформации миастении в боковой амиотрофический склероз. *Нервно-мышечные болезни.* 2012;(4):53–58.
Sanadze A.G., Kasatkina L.F. Two cases transformation myasthenia gravis to amyotrophic lateral sclerosis. *Neuromuscular Diseases.* 2012;(4):53–58. DOI: 10.17650/2222-8721-2012-0-4-53-58

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