World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-13, August 2022
ISSN: 2749-3644

INCIDENCE OF THYMUS GLAND PATHOLOGY IN PATIENTS WITH MYASTHENIA GRAVIS (LITERATURE REVIEW)

Khodzhieva Dilbar Tadjievna
D. in Medicine, Professor of Bukhara State Medical Institute
Ismailova Nigora Bakhtiyarova
basic doctoral candidate D. student at Bukhara State Medical Institute

Article history:

Received: June 24th 2022
Accepted: July 24th 2022
Published: August 30th 2022

Abstract:

Myasthenia gravis is a severe progressive disease with an unpredictable course. It is based on the production of autoantibodies that prevent normal neuromuscular transmission due to blockade of acetylcholine receptors [1, 2]. This pathology was first described at the end of the 17th century by the British neurologist Thomas Willis: "...a woman gradually and temporarily lost the strength and ability to speak, until she became silent like a fish". Wilhelm Erb (German neurologist) and Samuel Goldflam (Polish neurologist) made a major contribution to the study of myasthenia gravis, describing in detail the clinical manifestations of the disease, which contributed to the origin of another name for myasthenia gravis - "Erb-Goldflam disease".

Keywords: myasthenia gravis, Erb-Goldflam disease, Hashimoto's thyroiditis, acetylcholine receptors

INTRODUCTION. Myasthenia gravis is a rather rare neurological pathology, but its prevalence has increased in recent decades. In the 1970s, this disease occurred with a frequency of 3-5 people per 100 thousand population, and according to various modern observations, myasthenia gravis occurs in 1-30 cases per 100 thousand population [6]. In most cases, Erb-Goldflam disease manifests at a young age - 20-40 years old, and it is registered more often in women (female to male ratio as 3:1 - 4:1). After the age of 40, myasthenia gravis occurs with equal frequency in men and women, with the second peak of morbidity occurring at the age of 65-70 years. In childhood, the disease is rare, with children under 17 years of age accounting for up to 15% of all myasthenia gravis patients. Transient neonatal myasthenia gravis is found in less than a quarter of newborns whose mothers have been diagnosed with myasthenia gravis, and the risk of myasthenia gravis is increased if the pregnancy has a severe course of Erb-Goldflam disease [8]. Transient neonatal myasthenia gravis is characterized by impaired sucking and swallowing, masked face, silent cry, sagging lower jaw, and in severe cases - development of respiratory failure and death of the newborn due to acute hypoxia caused by respiratory muscle weakness [9]. It is observed in 10-20% of cases, and the risk of its occurrence depends to a greater degree not on the antibody titer in the mother's blood, but on their type. Adult and fetal antibodies to cholinoreceptors are distinguished [10]. Transient neonatal myasthenia gravis is caused by increased titers of fetal autoantibodies that penetrate through the blood-placental barrier from the pregnant woman. The first manifestations of muscle weakness in the newborn are registered after 2-4 days, the regression of symptoms with a favorable outcome is observed in a few weeks due to the destruction of circulating fetal antibodies that entered the body of the child [11]. The causes of myasthenia gravis have long been unknown. Before the XX century two theories were the most widespread: the theory of dysfunction and the theory of the lack of stimulating factors. According to the first, muscle weakness in patients was associated with the presence of non-normal fermentation products, which caused the similarity of the clinical picture in myasthenia gravis with curare poisoning. This theory was also confirmed by the development of muscle weakness in experimental animals during hemotransfusion from sick to healthy individuals. The theory of stimulating factors deficiency was based on increased cholinesterase activity, decreased tissue sensitivity to acetylcholine, or its insufficient synthesis [3]. According to modern concepts, this disease is caused by the production of specific autoantibodies to the transverse striated muscle tissue, which have been detected in the blood plasma of patients and on the motor endplates [10]. Myasthenia gravis has also been found to be associated with other autoimmune diseases (Hashimoto's thyroiditis, rheumatoid arthritis, systemic lupus erythematosus, type 1 diabetes) [4, 12]. The most predisposed phenotypes that are associated with changes in the genes responsible for the regulation of the immune system: HLA-B3, B8 and

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-13, August 2022
ISSN: 2749-3644

DW3, which can be determined by specific primers, specific oligonucleotides and by genome sequencing, have been found [12]. Mutations in the COLQ gene, which encodes a protein that binds the acetylcholinesterase tetramer, have been found to lead to the development of hereditary myasthenia gravis [13]. One of the most common causes of this disease is mutations in the genes responsible for coding for H-cholinoreceptor subunits (mainly α-subunits). Infectious and inflammatory processes, surgical interventions, injuries, psycho-emotional stress, overheating, taking antihypertensive drugs (nifedipine, verapamil), antiarrhythmic drugs (procainamide, quinine) may provoke the occurrence of Erb-Goldflam disease [14]. The effect of the thymus on myasthenia gravis is still not fully understood. It is believed that B-lymphocytes are produced in the thymus gland, producing autoantibodies to nicotinic cholinoreceptors, blocking them and destroying the structure of the postsynaptic membrane. Thymic hyperplasia is found in almost all patients with myasthenia gravis, in 15-40% - neoplasms, atrophic processes are less often observed, and in 3-10% of patients no pathology of thymus gland is revealed [15]. However, more than half of patients (up to 75%) with benign tumors of thymus do not have clinical manifestations of myasthenia gravis. Also this pathology can develop after thymectomy, which is explained by the initiating role of the thymus in the development of the disease, and further progression of Erb-Goldflam disease is caused by hyperactivation of reticuloendothelial system [3, 4]. Thus, it is obvious that thymus dysfunction is directly related to the pathogenesis of myasthenia gravis.

The mechanism of this disease is due to the loss of function of neuromuscular acetylcholine receptors due to the production of polyclonal IgG antibodies against all subunits of acetylcholine receptors - "seropositive myasthenia gravis" [5]. In Erb-Goldflam disease there is activation of complement components, which have a direct damaging effect on the postsynaptic membrane structures. This is due to the formation of the membrane attack complex (MAK), which is a bond of four effector proteins of the immune system, creating pores or transmembrane channels, which leads to cell damage and death due to disruption of the osmotic balance [6]. However, the breakdown of cholinergic receptors increases, and they bind to acetylcholine molecules and pass into the cell by endocytosis; one molecule of auto-IgG has been found to bind two cholinoreceptors. The autoantibodies also block nicotine-sensitive acetylcholine receptors, acting as a steric hindrance to receptor binding to acetylcholine, thereby disrupting neuromuscular transmission at the synapse [10]. It was found that in the early stages of the disease patients have an increased titer of antibodies of class IgM, and as myasthenia gravis progresses, they are replaced by IgG. Although autoantibodies directed against skeletal muscle cholinoreceptors have been proved to play a leading role in myasthenia gravis, no exact correlation between antibody concentration and symptom severity has been found [15]. Studies of this issue have led to the conclusion that there are at least two types of autoantibodies. The first type leads to increased degradation of cholinoreceptors, while the second type blocks them. However, most auto-IgG affects postsynaptic structures [16]. Antibodies of the first type are detected in 80-95% of patients and cause receptor deficiency, while antibodies of the second type disrupt the functions of the receptor ion channels and are detected quite rarely, but even low concentrations of these autoantibodies can lead to the development of severe myasthenic crises [5]. Antibodies to type 2 acetylcholine receptors are detected in most patients with severe myasthenia gravis. In addition, the fixation of autoantibodies on the postsynaptic membrane leads to structural changes in the synapse and synaptic gap. The seropositive variant of Erb-Goldflam disease occurs in 90-97% of patients. Modern studies have shown that the largest number of autoantibodies binds precisely to the α-subunit of acetylcholine receptors, but the reason for its selection as a dominant antigenic target in this pathology has not yet been elucidated [17].

Myasthenia gravis seronegative variant is observed in 3-10% of patients, i.e. no autoantibodies to acetylcholine receptors are detected in blood serum. For a long time, the pathogenesis of myasthenia gravis in this group of patients remained unclear, since no decrease in the number of cholinoreceptors was detected [3]. The autoimmune genesis of the disease in the seronegative variant was confirmed by experiments with animals transfused with immunized serum from patients, which led to the development of experimental myasthenia gravis, as well as the positive result of treatment with immunosuppressive drugs and plasmapheresis [17]. Current studies have revealed that 50% of seronegative myasthenia gravis patients have antibodies to muscle-specific tyrosine kinase, an enzyme involved in the formation of the neuromuscular plate [18]. This transmembrane protein ensures acetylcholine receptor clustering and normal synaptogenesis through interaction with the protein agrin synthesized in motoneurons, which leads to phosphorylation of the receptor subunit bound to

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-13, August 2022
ISSN: 2749-3644

rapsin. Antibodies to muscle-specific tyrosine kinase are detected more frequently in women. The seronegative variant is also characterized by the development of cranial and bulbar abnormalities, manifestation at an earlier age, and a tendency to myasthenic crises. The severity of the seronegative variant correlates with the titer of antibodies to muscle-specific tyrosine kinase [17]. Myasthenia gravis mostly affects young women of reproductive age. This pathology is characterized by a subacute onset with the appearance of eye symptoms: ptosis, diplopia, lagophthalmus, gaze palsy [15]. Then paresis of facial muscles, pharynx, palate join, which leads to the development of aspiration complications (such as aspiration pneumonia, bronchospasm, acute asphyxia due to airway obstruction, vomiting, regurgitation of gastric contents), reflex changes in pulse rate and blood pressure, heart rate, and possible seizures and collapse. Dangling of the jaw, dysarthria, and drooping of the head can be observed [2, 5]. When the extremities, abdomen and thorax are involved, there is a picture of generalized myasthenia gravis, which is dangerous with involvement of intercostal muscles and diaphragm and development of respiratory disorders [5].

The issue of pregnancy management in patients with myasthenia gravis is poorly studied. At the present stage, it has been established that myasthenia gravis is not a disease in which pregnancy and childbirth are impossible. However, during this period, due to endocrine restructuring, increased stress on a woman's body, psycho-emotional changes, myasthenia gravis gets an unpredictable course. And it is impossible to predict the course of the disease on the basis of its duration and the condition of a woman before pregnancy. According to some studies, the risk of complications during pregnancy is minimal, and the severity of the disease may decrease [19, 20]. Other observations suggest that pregnancy is a trigger factor for myasthenia gravis progression [2,12]. The main complications of myasthenia gravis during labor are abdominal muscle weakness, weak labor, premature delivery, prenatal effusion of amniotic fluid, leading to a prolonged waterless period, chorioamnionitis, fetal retinal damage, intraventricular hemorrhage, respiratory distress syndrome, which in 50-70% of cases leads to fetal death [23, 24]. Hypo- and atonic bleeding in the early postpartum period are more frequent than in healthy women, which is dangerous in the development of hemorrhagic shock, and in case of wavy blood loss by a woman in labor - gradual and unnoticeable deterioration of the woman's condition due to activation of compensatory-adaptive reactions [2, 5]. Pregnancy in stable remission provides an opportunity to minimize the risk of complications. According to current observations, prior therapy for myasthenia gravis, such as thymectomy or thymic radiotherapy, increases the likelihood of a favorable pregnancy and delivery [6]. The possibility of prolongation of pregnancy in the first trimester should be decided together with the neurologist. If the pregnancy is continued, the patient should be informed that she should avoid muscular and psycho-emotional overexertion, and prevent upper respiratory and urinary tract infections, as these may provoke a myasthenic crisis [2,6]. Also, women with Erb-Goldflam disease are more likely to develop gestosis, in which potassium-eluting diuretics should not be prescribed and may worsen the course of myasthenia gravis. The tactics of delivery depend on the condition of the patient. Natural delivery through the natural birth canal is preferable, and if the condition worsens, a cesarean section is performed. Indications for termination of pregnancy are: progressive worsening of myasthenia gravis, resistant to therapy with anticholinesterase and immunosuppressive drugs, decompensation, involvement of vital functions [7].

CONCLUSION. Thus, based on the above, we can conclude that myasthenia gravis is a risk factor in pregnancy. This is due to the more frequent occurrence of the disease in women of reproductive age, an increased likelihood of complications during this period, the unpredictable nature of the course of the disease, and the difficulty of conservative treatment because of the negative effects of drugs on the fetus. The tactics of pregnancy and childbirth should be chosen individually by obstetrician-gynecologist, neurologist, and anesthesiologist, which will improve the prognosis for the life and health of the mother and child.

LITERATURE:

1. Khodjieva D. T., Khaydarova D. K. Clinical and neuroph clinical and neurophysiological ch ogical characteristics of teristics of post-insular cognitive disorders and issues of therapy optimization. Central Asian Journal of Pediatrics. Dec.2019. P 82-86
2. Ходжаева Д.Т., Хайдарова Д.К. Хайдаров Н.К. Совершенствование диагностической тактики постинсультных когнитивных расстройств. Журнал Биомедицина. – 2019. - №5. С. 80-86.
3. Ходжиева Д.Т. Клинико-неврологическая и параклиническая характеристика больных с

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-13, August 2022
ISSN: 2749-3644

ишемическим инсультом в зависимости от наличия когнитивного дефицита. Неврология журнали – 2019. - № 4. С.29-33
4. Kamalova Malika Ilkhomovna, Islamov Shavkat Eriyigitovich, Khaidarov Nodir Kadyrovich. Morphological Features Of Microvascular Tissue Of The Brain At Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 2020. 2(10), 53-59
5. Khodjieva D. T., Khaydarova D. K., Khaydarov N. K. Complex evaluation of clinical and instrumental data for justification of optive treatment activites in patients with resistant forms of epilepsy. American Journal of Research. USA. № 11-12, 2018. С.186-193.
6. Sadriddin Sayfullaevich Pulatov. (2022). Efficacy of ipidacrine in the recovery period of ischaemic stroke. World Bulletin of Public Health, 7, 28-32.
7. Хайдарова Д.К., Ходжиева Д.Т., Самадов А.У. Оптимизация терапии сосудистой деменции в раннем восстановительном периоде
8. инсульта. Медицинский журнал Узбекистана. №5 (80) 2019, 23-27.
9. Хайдарова Д.К., Ходжиева Д.Т., Хайдаров Н.К. Показатели нейропсихологических исследований у больных с умеренными когнитивными расстройствами на фоне хронической ишемии мозга. Неврология журнали – 2020. - № 1. С. 34-37.
10. Ходжиева Д.Т., Самадов А.У. Джунаидова А.Х. Совершенствование диагностической тактики и особенности когнитивного дефицита у постинсультных больных. Неврология журнали – 2020. - № 1. С.49-51
11. Ходжаева Д.Т. Low-dose neuroprotection in case of cognitive disorders in patients with ischemic stroke. International Journal of Pharmaceutical Research | July – 2019. С.1167-1170.3.
12. M. I. Kamalova, N.K.Khaidarov, Sh.E.Islamov,Pathomorphological Features of hemorrhagic brain strokes, Journal of Biomedicine and Practice 2020, Special issue, pp. 101-105
13. Kamalova M., Khaidarov N., Shomurodov K. Microscopic examination of brain tissue in hemorrhagic stroke in uzbekistan //Матеріали конференцій МЦНД. – 2021.
14. Khaidarov Nodir Kadyrovich, Shomurodov Kahramon Erkinovich, &Kamalova Malika Ilhomovna. (2021). Microscopic Examination OfPostcapillary Cerebral Venues In Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 3(08), 69–73.
15. Ходжиева Д.Т., Джунаидова А.Х. Rehabilitation of patients with acute disorders of cerebral circulation and improvement. Журнал клинической психологии и психиатрии. №1.2020.С 13-19.
16. Хайдарова Д.К., Хайдаров Н.К., Маджидова Ё.Н., Ходжаева Д.Т. Влияние различных типов лечения на холинергическую и FAS – опосредованную систему у больных хронической ишемии мозга с умеренными когнитивными расстройствами. Научно практический журнал, Неврология. – Ташкент, 2015. – №2. – С. 46-47.
17. Хайдарова Д.К., Маджидова Ё.Н., Ходжаева Д.Т. Влияние хронической ишемии головного мозга на когнитивные вызванные потенциалы. Научно практический журнал, Неврология. – Ташкент, 2015. – №2. – С. 56.
18. Khaydarova Dildora Kadirovna, Samadov Alibek Uktamovich. Optimization of neuroprotective therapy for ischemic stroke in the acute period. Журнал неврологии и нейрохирургических исследований. №3. 2020 С. 13-15.
19. Khaydarova Dildora Kadirovna, Samadov Alibek Uktamovich. Current issues in the development of neuroprotective therapy in ischemic stroke. Web of Scientist: International Scientific Research Journal 2021. P. 6-10
20. Khodjieva D. T., Khaydarova D. K., Khaydarov N. K. Clinical and euroimaging diagnostics of syringomyelia associated with Chiari malformation. International Journal of Pharmaceutical Research. 2021. P. 2418-2415.
21. Xaydarov Nodirjon Kadirovich, Khaydarova Dildora Kadirovna. Clinical And Etiological Factors Of Atopic Stroke (Literature Review). NVEO - Natural Volatiles & Essential Oils. 2021.P. 12049-12058