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CLINICAL FEATURES OF MULTIPLE SCLEROSIS IN VARIOUS TYPES OF DISEASE COURSE

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Multiple sclerosis (MS) is an autoimmune demyelinating and neurodegenerative disease of the central nervous system. According to the clinical course of MS, the following phenotypes are distinguished: clinical isolated syndrome (CIS), relapsing MS (RMS) and progressive MS (PMS). The purpose of our study was to study the clinical manifestations of MS in various types of disease among residents of the city of Baku. A total of 559 patients were diagnosed with MS between 2013 and 2020. Of these, 392 (70.1%) patients were female and 167 (29.9%) were male. In 69,9% of patients the disease had the RMS type of course. The manifestation of the disease in the CIS and RMS groups began at almost the same age, with clinical manifestations of damage in one functional system, with a statistically significant difference in age with PRS, where the catastrophe was observed in several functional systems. Atrophic changes on MRI of the brain predominated in the group of patients with PMS type of course from the first symptoms of the disease. In patients treated with an interferon beta 1a, by the end of the year of treatment, EDSS in the RMS group there was a statistically significant improvement in clinical condition.

Key words: *multiple sclerosis, clinical features, clinical course.*

Connection of the publication with planned research works.

This work is a fragment of a dissertation for the degree of Doctor of Philosophy in medicine “Epidemiological and clinical features of multiple sclerosis in city of Baku”.

Introduction.

Multiple sclerosis (MS) is an autoimmune inflammatory demyelinating and neurodegenerative disease of the central nervous system, which is a leading cause of non-traumatic neurological disability in young people [1].

In 1996, the US National Multiple Sclerosis Society (NMSS) Advisory Committee on Clinical Trials in Multiple Sclerosis defined the clinical types of MS as relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS), and progressive relapsing MS (PRMS). These phenotypic descriptions were thought to reflect the full range of clinical subtypes of MS, but it was recognized that these descriptions may change over time [2].

Clinically, MS can occur in two ways: relapsing or progressive. Most often, the onset of the disease is a relapsing form of multiple sclerosis (MS), manifesting itself in the form of individual episodes of neurological dysfunction, followed by partial or complete remission, or its absence. Over time, the frequency of relapses usually decreases, and gradual deterioration occurs, leading to continuous progression. Despite these differences, all clinical forms of multiple sclerosis appear to reflect the same underlying disease process. Although inflammation is usually associated with relapse and neurodegeneration with progression, it is now recognized that both processes are present in virtually all patients throughout the disease course [1, 2].

In 2013, based on advances in biomarker technology, magnetic resonance imaging, and clinical symptoms, clinically isolated syndrome (CIS) and radiologically isolated syndrome (RIS) were added to the four traditionally recognized phenotypes (RRMS, SPMS, PPMS, PRMS) of MS. Subsequently, the International Advisory Committee on Clinical Trials of MS revised the disease phenotypes and MS was divided into the following clinical phenotypes: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), and progressive MS (PRS), consisting of two subtypes: secondary progressive (SPMS) and primary progressive (PPMS) [2, 3].

Almost 85-95% of MS patients are classified as relapsing-remitting MS (RRMS). About 15% of patients have a progressive course from the very beginning of the disease (primary progressive MS (PPMS). With RRMS, women are affected almost three times more often than men, and the average age of onset is 30 years, while with SPMS, the incidence rates for men and women are the same, and the average age of onset is 40 years [3, 4, 5, 6].

With RMS, there is a certain sequence of involvement of individual brain structures in the degenerative process, so atrophy of the gray matter (subcortical, then cortex) and, lastly, the white matter of the brain is initially detected. It is also noted that different types of MS are characterized by certain MRI images of brain atrophy: with SPMS, degenerative changes are more pronounced than with RMS [7].

The development of more effective treatments for MS represents a significant advance that has improved prospects for living without disability [1].

The aim of the study.

To study the clinical and radiological manifestations of multiple sclerosis in various types of disease among residents of the city of Baku.

Object and research methods.

The research work was carried out on the basis of the Department of Neurology and Clinical Neurophysiology of the Azerbaijan State Advanced Training Institute for of Doctors named after. A. Aliyev in two neurological departments of the Republican Clinical Hospital (RCH) named after academician M. M. Mirgasymov. The “State program for treatment, prevention and measures to combat multiple sclerosis”, existing in the Republic, made it possible to cover all residents of the city of Baku with multiple sclerosis. The study was conducted from July 1, 2013 to June 30, 2020 [8]. 559 patients with a definite diagnosis of MS were examined according to the McDonald criteria (modified 2010). Of these, 392 (70.1%) patients were female and 167 (29.9%) were male. In addition to the standard neurological examination, a special expanded scale for assessing the degree

of disability EDSS (Expanded Disability status Scale) was used, intended specifically for examining patients with MS [9]. MRI data was assessed using the standard MRI-RS protocol.

The data of all patients was included in an electronic database and calculations were carried out using the "Statistika for Windows 10" software package. Given the non-normal distribution of quantitative data, the median (Me), lower and upper quartiles (Q1-Q3) were used when comparing groups.

The study was conducted in accordance with the principles of the Helsinki Declaration on the Protection of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine. Written informed consent was obtained from all patients who participated in the study.

Research results.

Of the 559 patients with MS we examined, 390 (69.9%) had a relapsing (RMS) disease, 109 (19.5%) had a progressive (PMS) type of course, and 60 (10.6%) had a clinically isolated syndrome (CIS) **(table 1)**.

At the same time, the clinical type of RMS course prevailed in both women and men **(table 1)**. There were no statistically significant differences in the types of disease between the sexes.

The age of the patients we studied was 33.0 (27.0-41.0) years. In the CIS and RMS groups, the age was statistically significantly lower (28.0 (24.0-36.5) and 31.0 (26.0-38.0) years, respectively) than in the PMS group (44.0 (37.0-50.0) years) (p<0.05).

A study of the clinical types of MS by age group revealed that CIS is more common in the age group of 20-29 years, RMS in patients aged 30-39 years, and PMS is typical for the age groups 40-49 and 50-59 years **(table 2)**.

Analyzing the age of initial symptoms of the disease with the types of course, it was revealed that CIS and RMS begin at almost the same age (26.0 (24.0-34.0) and 27.0 (22.0-34.0)), with a statistically significant difference in age with PMS, in which manifestation had to be at 34.0 (25.0-41.0) years.

Considering that the clinical manifestation of MS can manifest itself as damage to one or several functional parts of the central nervous system, the patients we studied were divided into two groups: monosystem (mS) and multisystem (pS) manifestations of the disease. We found that in patients with CIS and RMS types of course, the disease manifests itself mainly with mS, while at the same time in RMS pS manifestations predominate (p<0.05) **(fig. 1)**.

As it is known, MS is not only a demyelinating disease, but also a neurodegenerative disease, manifested by atrophic changes on MRI. Our study examined the presence of atrophic changes on MRI examinations in 559 patients with MS at different stages of disease development: during manifestation (MRI1) and in the next two exacerbations (MRI2 and MRI3). Of these, 120 had atrophic changes in the brain. A study of MRI data showed that atrophic changes in the brain are most often detected in the PMS type of course than in CIS and RMS (p<0.05). At the same time, the prevalence of PMS type of course is observed already at manifestation, from the first symptoms of the disease. Thus, at manifestation (MRI1), moderate expansion of the subarachnoid spaces and ventricular systems were detected in PRS in 21.1% of cases, and with subsequent visualizations (MRI2 and MRI3), it tended to increase, reaching 57.4% **(fig. 2)**.

Table 1 – Clinical phenotypes of MS

Sick	RMS	PMS	CIS	General group
General group	391 (69,9%)	109 (19,5%)	59 (10,6%)	559
Women	271 (69,1%)	77 (19,6%)	44 (11,2%)	392
Men	120 (71,9%)	32 (19,2%)	15 (9,0%)	167

Table 2 – Representation of clinical phenotypes of MS by age groups

Phenotype of the course / age	<19	20-29	30-39	40-49	50-59	>60	General group
CIS	2 (3,3%)	34 (56,7%)	14 (23,3%)	7 (11,7%)	3 (5%)	0	60
RMS	28 (7,2%)	141 (36,2%)	137 (35,1%)	62 (15,9%)	22 (5,6%)	0	390
PMS	1 (0,9%)	10 (9,2%)	25 (22,9%)	37 (33,9%)	35 (32,1%)	1 (0,9%)	109
General group	31	185	176	106	60	1	559

In our study, EDSS in the general group of patients was 3.5±0.07 points. When studying this indicator for course variants, the following trend was revealed: in the CIS and RMS groups, EDSS was statistically significantly lower (2.0 (1.5-3.0) and 3.0 (2.0-4.0), respectively) than in the PMS group, where the degree of disability was rough and equal to 6.0 (5.0-7.0) points. Of the 559 patients with MS, 284 were treated with a course-modifying drug for MS, interferon beta 1a (Avonex), according to a standard regimen. Before treatment with interferon beta, EDSS in the PMS group corresponded to the moderate severity of MS (5.5 (4.5-6.0)), while in the CIS and RMS groups it corresponded to a mild degree (4.0 (3.0-4. 5) and 3.0 (2.0-4.0), respectively). A year later, during treatment, the condition of patients in the CIS and PMS groups remained stable (3.0 (2.0-4.0) and 4.25 (4.0-5.5),

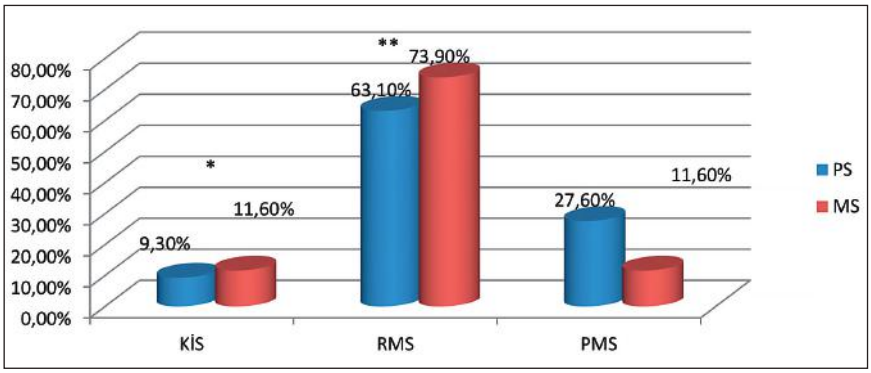

Figure 1 – Involvement of functional parts of the central nervous system during manifestation depending on the type of MS.

Notes: *- statistically significant difference (p=0.009) between CIS and PRS; * * – statistical significant difference (p=0.002) between RRS and PRS.

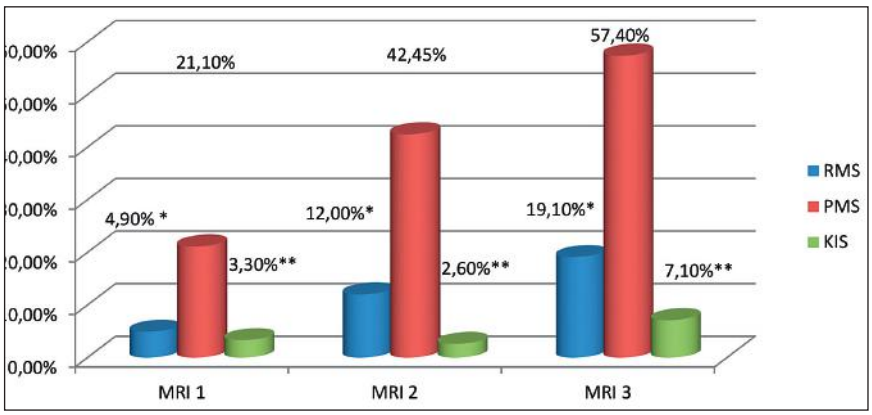

Figure 2 – Atrophic changes in the brain on MRI depending on the type of MS.
Notes: *- statistically significant difference (p<0.05) between PMS and RMS; ** – statistically significant difference (p<0.05) between PMS and CIS

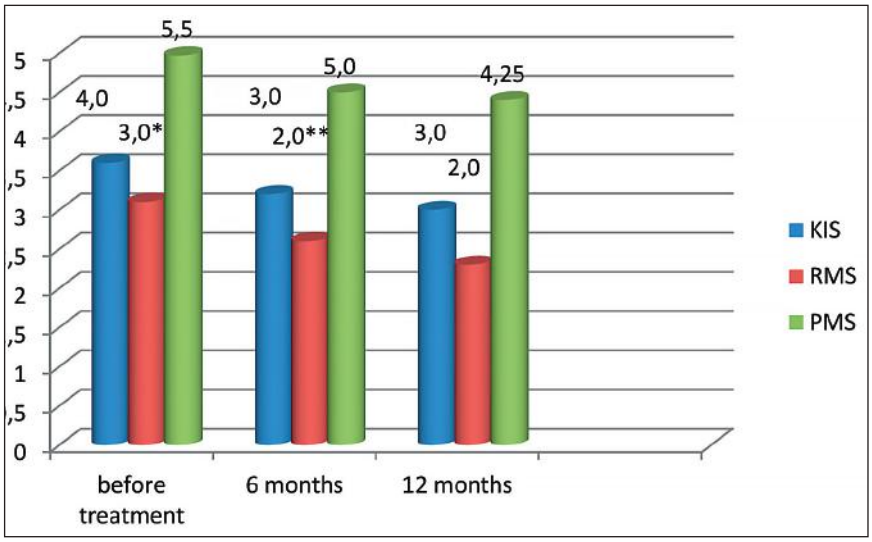

Figure 3 – EDSS results before and after interferon beta treatment.
Notes: * – statistically significant difference (p<0.05) between EDSS before treatment and 6 months; ** – statistically significant difference (p<0.05) between EDSS 6 and 12 months.

respectively), whereas in the RMS group there was a statistically significant improvement in clinical condition (2.0 (1.0-4.0)) **(fig. 3)**.

Discussion of research results.

According to the clinical course of MS, the following phenotypes are distinguished: clinical isolated syndrome (CIS), relapsing MS (RMS) and progressive MS (PMS) [2].

According to the 2020 MS atlas all over the world, regardless of the region, the relapsing-remitting type of MS prevailed over the progressive type of course [10]. The same difference between the types of course was found in our study, where remitting-remitting was recorded in 69.9% of patients, in 19.5% had a progressive type of course and 10.6% had a clinically isolated syndrome. In a study conducted in the Iranian Islamic Republic, a region territorially close to Azerbaijan, similar results were also obtained (RMS – 81.0%, PMS – 19.0%) [11]. Given the significant difference in percentage representation, the purpose of this analysis was to study the clinical features of different types of MS. In our study of RMS, the clinical type of course prevailed in both sexes, while no statistical difference was found between women and men. We found that patients in the CIS and RMS groups were significantly younger than patients in the PMS group ($p<0.05$). Accordingly, patients with the CIS type of course were more often found in the age group of 20-29 years, RMS – in 30-39 years, and PMS – 40-49 and 50-59 years. Similar results can be found in other studies, which indicate that patients with the RMS type of course have a younger age compared to patients from the PMS group [11, 12]. The first symptoms of MS in the CIS and RMS groups appear at a younger age than in the PMS group. An interesting fact is that in these groups the disease, as a rule, manifests itself as monosymptomatics. Whereas, in patients with PMS, already at manifestation, a combination of symptoms of damage to several parts of the nervous system is detected (polysymptomatic manifestation).

We studied the presence of atrophic changes on MRI in patients with MS depending on the type of disease at different stages of MS development: during manifestation and in the subsequent two exacerbations. It is generally accepted that brain tissue loss may result from acute focal neuroinflammatory events as well as from more diffuse primary or secondary neurodegenerative processes that occur regardless of lesion activity [13]. In the general group of patients, already at the manifestation of the disease, approximately 10% of patients had atrophic changes detected on MRI of the brain, which in subsequent exacerbations were found in almost 1/3 (28.7%) of those examined. At the same time, when studying MRI of the brain of patients, depending on the clinical course of the disease, it was shown that the PMS group statistically significantly prevails over the CIS and RMS groups, and in which the percentage of degenerative changes increases to 57.4%. Treatment of MS is the most discussed topic in the literature dedicated to this disease. In our study, 284 patients were prescribed beta interferon 1a (Avonex), according to the standard regimen. In all patients, the clinical condition before and after treatment was assessed by EDSS. The study showed that by the end of the first year of treatment with interferon beta, EDSS in the CIS and PMS groups remained stable, while in the RRS group there was a statistically significant improvement in clinical condition.

Conclusions:

1. The majority of patients had the RMS type of disease (69.9%).

2. RMS type of course prevailed in the age group under 40 years, and PMS – over 40 years.

3. In patients with the RMS type of course, the disease manifested itself mainly in one part of the nervous

system; in patients with PMS, clinical manifestations were observed in several functional systems.

4. Starting from the manifestation of the disease, atrophic changes on MRI of the brain tended to progress in all types of MS, with a predominance in PMS.

5. The use of beta interferon-1a by the end of the first year of treatment leads to an improvement in the neurological status of MS patients in the RMS group.

Prospects for further research.

The development of more effective methods of treating multiple sclerosis in various types of the disease among the residents of Azerbaijan, which would improve the quality of life without disability.

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КЛІНІЧНІ ОСОБЛИВОСТІ РОЗСІЯНОГО СКЛЕРОЗУ ПРИ РІЗНИХ ТИПАХ ПЕРЕБІГУ ЗАХВОРЮВАННЯ

Гулієва А. І.

Резюме. Розсіяний склероз (РС) є однією з провідних причин інвалідності нетравматичного характеру серед молодого працездатного населення. Найчастіше маніфестація захворювання розпочинається з рецидивуючої форми РС, яка клінічно проявляється одним або кількома неврологічними симптомами, що мають тенденцію до часткового або повного відновлення. Згодом, частота рецидивів зменшується, нейродегенеративні процеси збільшуються і захворювання прогресує. Метою нашого дослідження було вивчення клінічних проявів РС за різних типів перебігу хвороби серед жителів міста Баку. За семирічний період дослідження (2013-2020 рр.) діагноз РС було поставлено 559 пацієнтам. З них 392 (70,1%) пацієнтів жіночої та 167 (29,9%) чоловічої статі. При цьому, у 390 (69,9%) пацієнтів захворювання мало рецидивуючий (РРС), у 109 (19,5%) – прогресуючий (ПРС) тип перебігу і у 60 (10,6%) спостерігався клінічно ізольований синдром (КІС). КІС частіше зустрічався у віковій групі 20-29 років, РРС – у групі 30-39 років, а для ПРС були характерні групи 40-49 і 50-59 років. Маніфестація захворювання в групах КІС і РРС розпочиналася практично в однаковому віці (26,0 (24,0-34,0) і 27,0 (22,0-34,0)), із клінічними проявами ураження в одній функціональній системі, зі статистично значущою різницею за віком із ПРС (34,0 (25,0-41,0)), де катастрофа спостерігалася в декількох функціональних системах. Атрофічні зміни на МРТ головного мозку переважали в групі пацієнтів з ПРС типом перебігу з перших симптомів захворювання (21,1% випадках), а маючи тенденцію до зростання при наступних візуалізаціях, досягнувши 57,4%. У пацієнтів, які отримали лікування препаратом, що змінює перебіг РС, – бета-інтерферон 1а, на кінець року лікування, ЕДСС у групах КІС і ПРС залишався стабільним (3,0 (2,0-4,0) та 4,25 (4,0-5,5), відповідно), тоді як у групі РРС було статистично значуще поліпшення клінічного стану (2,0 (1,0-4,0)).

Ключові слова: розсіяний склероз, клінічні особливості, тип перебігу.

CLINICAL FEATURES OF MULTIPLE SCLEROSIS IN VARIOUS TYPES OF DISEASE COURSE

Guliyeva A. I.

Abstract. Multiple sclerosis (MS) is one of the leading causes of non-traumatic disability among the young working population. Most often, the manifestation of the disease begins with a relapsing form of MS, which is clinically manifested by one or more neurological symptoms that tend to partial or complete recovery. Subsequently, the frequency of relapses decreases, neurodegenerative processes increase and the disease progresses. The purpose of our study was to study the clinical manifestations of MS in various types of disease among residents of the city

of Baku. During the seven-year study period (2013-2020), 559 patients were diagnosed with MS. Of these, 392 (70.1%) patients were female and 167 (29.9%) were male. At the same time, in 390 (69.9%) patients the disease had recurrent (RMS), 109 (19.5%) had progressive (PMS) types of course, and 60 (10.6%) had a clinically isolated syndrome (CIS). CIS was more common in the age group of 20-29 years, RMS in the group of 30-39 years, and PMS was typical in the groups of 40-49 and 50-59 years. The manifestation of the disease in the CIS and RMS groups began at almost the same age (26.0 (24.0-34.0) and 27.0 (22.0-34.0)), with clinical manifestations of damage in one functional system, with a statistically significant difference in age with PRS (34.0 (25.0-41.0)), where the catastrophe was observed in several functional systems. Atrophic changes on MRI of the brain predominated in the group of patients with PMS type of course from the first symptoms of the disease (21.1% of cases), and with subsequent visualizations it tended to increase, reaching 57.4%. In patients treated with a drug that modifies the course of MS – beta interferon 1a, by the end of the year of treatment, EDSS in the CIS and PMS groups remained stable (3.0 (2.0-4.0) and 4.25 (4.0-5.5), respectively), while in the RMS group there was a statistically significant improvement in clinical condition (2.0 (1.0-4.0)).

Key words: multiple sclerosis, clinical features, clinical course.

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A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article.

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FEATURES OF THE FUNCTIONAL STATE OF THE LIVER AND INDICATORS OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CORONARY HEART DISEASE COMBINED WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Long-term CHD comorbid with NAFLD leads to acceleration of atherogenesis, imbalance of ED and adipocytokines. To compare indicators of the liver functional state, levels of adipocytokines, C-reactive protein and marker of endothelial dysfunction in patients with CHD comorbid with and without NAFLD was the aim of research. 145 patients with CHD comorbid with NAFLD and 100 patients with CHD were examined. When analyzing the obtained laboratory parameters characterizing the liver functional state, it was established that in patients with CHD comorbid with NAFLD, a significant moderate elevation in the levels of ALT and AST was registered, which characterizes the presence of cytolysis syndrome. An imbalance of adipocytokines was also found in these patients: a decline in the concentration of adiponectin, an elevation in the level of resistin, and a decline in the ratio of adiponectin to resistin. A substantive increase in the serum level of ADMA and CRP in patients with combined pathology indicates the presence of ED against the background of activation of systemic inflammation, which may have pathogenetic significance in the growing of CHD comorbid with NAFLD.

Key words: *CHD, NALFD, adipocytokines, resistin, endothelial dysfunction.*

Connection of the publication with planned research works.

The scientific research was conducted according of the plan of the departmental topic of the Department of Therapy and Family Medicine of UzhNU “Innovative methods of the diagnostic and the treatment of pathology of internal organs in obese patients” state registration No. 0121U111773.

Introduction.

Coronary heart disease (CHD) is the common disorder of the cardiovascular system (CVD) and has dangerous consequences that cause disability and premature death. In Ukraine, the incidence of CHD has doubled over the last decade and is 68.8% [1]. Modern data on the pathogenesis of CHD prove that atherosclerosis is the result of a process of chronic inflammation of low intensity and, thanks to lipoperoxidation, causes the transformation of low-density lipoproteins (LDL) with