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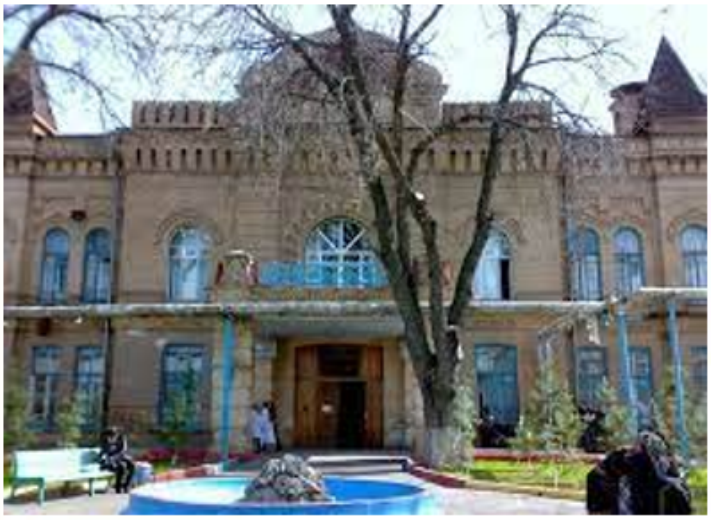

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Clinical-Neurological, Immunological Indicators & HLA Antigens in Rheumatoid Arthritis in the Uzbek Population

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ABSTRACT

Background. In rheumatoid arthritis, pathological changes in the joints affect the segment of the are apparatus of the spinal cord, its roots and peripheral nerves, as well as the segmental structures of the nervous system. Immunological, immunogenetic and neurophysiological changes due to the development of rheumatoid arthritis are not well understood, which complicates the development of criteria for early diagnosis. and methods of their complex therapy.

Material. 142 patients with rheumatoid arthritis, aged 16-70 years of the Uzbek population and other nationalities.

Conclusion. According to rheumatoid arthritis, diffuse damage to the nervous system with dysfunction of the autonomic departments, an early disorder of cerebral and peripheral hemodynamics, bioelectrical activity of the cerebral cortex, and a violation of higher cortical functions were observed. Timely complex therapy had a positive effect on the somatic, neurological, and immune statuses of the body and contributed to the regression of neurological symptoms.

Keywords: Rheumatoid arthritis, diseases of the central nervous system, early diagnosis, preventive therapy

INTRODUCTION

Rheumatoid arthritis is widespread, is one of the main causes of high disability and early disability and causes great material damage to the patient, this family and society [1,2,4,5,9,16,20,21].

In Russia, 8.5% of the population suffers from five rheumatic diseases, of which rheumatoid arthritis accounts for 0.42% or 84.6 patients per 10,000 people [7, 9]. In Uzbekistan, the rheumatoid arthritis rate is 49.9 per 10,000 population. The incidence of rheumatoid arthritis in Tashkent is 0.39% [19]. Thus, about Official statistics show that rheumatoid arthritis is a serious problem for public health.

In the literature, along with data on the defeat of the organs of movement and internal organs, the participation of the nervous system in the development of rheumatoid arthritis is described [3,4,5,8,10,11,13]. The authors argue that the nervous system in rheumatoid arthritis is involved in the pathological process. Also often indicated is the defeat of the peripheral and autonomic nervous system and the development of asthenic syndrome, pyramidal insufficiency syndrome in rheumatoid arthritis [7,12,14,15,18]. Despite the prevalence of

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rheumatoid arthritis in Uzbekistan, the pathology of the nervous system in this disease is almost not studied.

Those who have data on the violation of all parts of the immune system in rheumatoid arthritis have a genetic predisposition, in which the frequency of occurrence of his to compatibility antigen changes [6,7,15,20]. In rheumatoid arthritis, pathological changes in the joints affect the segment of the apparatus of the spinal cord, its roots and peripheral nerves, as well as the segmental structures of the nervous system.

Immunological, immunogenetic and neurophysiological changes due to the development of rheumatoid arthritis are not sufficiently studied, which complicates the development of criteria for early diagnosis and methods of their complex therapy.

The purpose of the work is to study the pathology of the nervous system in rheumatoid arthritis; to identify the features of the course of neurological syndromes depending on the activity of the prescription and sero-accessory of rheumatoid arthritis; to determine immunological, immunogenetic neurophysiological and psychological changes and to develop appropriate methods of therapy.

MATERIAL AND METHODS OF RESEARCH

Neurophysiological (EEG, REG, RVG, EchoES, PFI), immunological, immunogenetic, and psychophysiological research methods are conducted.

There were 142 patients under observation, aged 16-70 years (average age was 42.3±1.1 years);; 75 (52.8%) patients were of young and working age (16-44 years). Men were 19 (13.4%), women 123 (86.6%). Women fell ill 5.5 times more often than men.

120 (84.5%) patients were persons of the Uzbek population and 22 people (15.5%) of other nationalities.

RESULTS

The articular form of rheumatoid arthritis was detected in 110 (77.5%) patients, and rheumatoid arthritis with vicariates - in 32 (22.5%). The duration of the disease ranged from 2 months of eggs to 28 years (average 6.8±0.5 years).

Depending on the rheumatoid factor (RF), patients were divided into seropositive - 95 (66.9%), and seronegative - 47 (33.1%).

I degree of activity of rheumatoid arthritis (RA) was diagnosed in 31 (21.8%), II degree - in 104 (73.3%), III degree in 7 (4.9%) patients.

Functional insufficiency of the joints (FTS) of the I degree was detected in 25 (17.6%), II degree - in 96 (67.6%), III degree - in 18 (12.7%) people. In 126 (88.7%) patients, a slowly progressive course was noted, in 6 (21.6%), little progressive, in 10 (7.1%) - a rapidly progressive course. I X-ray stage was detected in 10 (13.9%) patients; II - in 40 (54%), III - in 16 (21.6%), stage IV - in 7 (9.4%) of the 74 examined.

Clinical and neurophysiological studies of RA with damage to the joints and internal organs revealed syndromes of damage to the central, and peripheral nervous systems with dysfunction of the autonomic departments and changes in higher nervous activity. In 3 (2.1%) patients, acute cerebral circulation disorder (ONMK) was established against the background of rheumatoid vasculitis of cerebral vessels, in 23 (16.2%) - encephalopolineuropathy (EPN), in 36 (25.3%) - myelopolineuropathy (MPN), in 60 (42.3%) - vegetative-sensory polyneuropathy (VSP), in 20 (14.1% - asthenovegetative syndrome (ABC).

VSP and MPN were more common than other forms of lesions of the NS. Cerebral symptoms were moderately pronounced: patients complained of headaches, nausea, vomiting, dizziness, noise in the head, in the ears, memory loss, weakness and restriction of movement in the distal part of the arms and legs, weight loss of the hands, feet, their cooling and asthenic complaints.

The neurological status was characterized by the defeat of I, V, VII, X, and XII pairs of cranial nerves (more often of the V pair) manifested by soreness of the Valle points (10 people 7%), a decrease or absence of conjunctival and corneal reflexes (37 people 26.1%),, an increase in the mandibular reflex (72 people 50.1%), central paresis of the facial (52 people 36.6%) and sublingual (15 people 10.6%) nerves. A positive symptom of Marinesko-Rodovich was detected in 27 (19%) patients, and proboscis in 12 (8.5%). Patients

In the motor sphere, hemiparesis occurred in only 3 patients with ONMK, in 92 (64.8%) patients in the distal parts of the hands and in 50 (35.2%) mild tetra- or paraparesis were observed. In 62 (43.7%) patients, there was an increase in tendon reflexes from the hands and in 82 (57.7%) - legs with an expanded reflexogenic zone and the presence of pathological symptoms of Babinski - in 28 (19.7%), Rossolimo - in 14 (9.8%), Op p Enheim in 6 (4.2%), Zhukovsky - in 5 (3.5%), Bekhterev - in 6 (4.2%), clonus of the foot - in 15 (10.6%), carpal analogues - in 35 (24.6%) patients. These symptoms indicate damage to the central neuron of the motor pathway.

According to the reflex theory, irritation of the receptors of the affected joints is reflexively redirected to motor neurons, which in turn causes the development of muscle atrophy.

Table 1. Immunological parameters of patients with RA, M±m

Parameter Control	Control, n=50	RA, n=137
Leukocytes 109 g/l	6,15±0,15	6,4±,014*
Lymphocytes %	27,5±0,08	24,6±0,5
chl/μlz	1677±20	1426±39
T cells %	63,5±0,20	47,2±0,35
chl/μl	1064±22	684±14
T-helpers %	48,7±1,21	36,2±0,35
chl/μl	815±32	526±12
T-suppressor %	14,7±1,2	9,4±0,22
chl/μl	245±13	158±6
Tx/Ts	3,30±0,15	3,8±0,19
B cells %	17,5±0,60	12,9±0,09
chl/μl	295±15	189±3
O-cells %	19,0±0,11	39,9±0,6
chl/μl	318±28	574±17
FAN %	54,8±1,8	43,8±0,04
A	1,4±0,10	2,51±0,12
M	1,3±0,14	1,39±0,07*
G	7,2±0,31	12,5±0,35
CEC st.	12,0±0,3	49,4±0,7

Note: *- not a reliable difference from control. In all other cases, the validity of p<0.001-0.05

A characteristic and early symptom of the defeat of the NS in RA impaired sensitivity, hemihypesthesia occurred in 3 (2.1%) patients with ONMK, hypoesthesia or anesthesia in the form of "bracelets" or "cuffs" over the affected joints - in 120 (84.5%), polyneurous type - in 118 (83.1%), hypoesthesia in the form of "gloves" and socks - in 75 (52.8%), forearms - in 28 (19.7%), lower legs - in 25 (15.5%), hyperesthesia of the hands in 13 (9.2%) and legs in 10 (7%) (16.2%), combined with symptoms of polyneurgia in 82 (57.7%).

Violation of deep sensitivity decrease in joint-muscular feeling in the fingers of the feet - 22 (15.5%) and the fingers of the hands - in 13 (9.2%).

Vegetative disorder was observed in all patients (hyperhidrosis of the palms, feet, dry skin, changes in the skin, nails, acrocyanosis, lability of the pulse, red or white dermographism, etc.).

All forms were characterized by the following features:

ONMK (15 years of age) ischemic type of stroke in the basin of the middle cerebral artery on the right, with central lesions of the facial and sublingual nerves and hemiparesis on the left.

EPN (10 years or more) damage to the cranial nerves (decrease in corneal and conjunctival reflexes, central paresis of the facial nerve, horizontal nystagmus when looking in both directions), Marinescu-Radovic's symptom, mild predominantly distal para- or tetraparesis, increased tendon reflexes, distal hyperesthesia or hypoesthesia, pathological reflexes, and muscle atrophy.

MPH is a mild tetra- or paraparesis, severe atrophy of the muscles of the hands, feet, forearm, lower legs, increased tendon reflexes and the appearance of pathological signs (Babinsky, Oppenheim, Rosolimo, Wechterew, clonusoid of the feet), which indicates damage to the central neuron of the motor pathway and the myelitic component. Myelitic syndrome occurred within 5 years, less often after 10 years or more.

VSP - distal peripheral tetra- or paraparesis with atrophy of the interosseous muscles, tenar, hypotenar of the hands, feet, forearm, lower legs, less often, shoulders and thighs, pain in the limbs, paresthesia, distal violation of sensitivity of the polyneurotic type in the form of "gloves" and "socks" with pronounced hyperhidrosis or dryness of the hands and feet.

ABC-changes in the psycho-emotional sphere and dysfunction of the ANS are mainly of a sympathetic nature; functional disorders: asthenia and changes in the volitional sphere. According to our data, changes in the emotional sphere occurred with the prescription of RA from several months to 2-3 years; more than 3-5 years, changes in the volitional sphere were observed, which indicates changes in the cerebral cortex confirmed by EEG and psychophysiological studies. Functional disorders of the nervous system arose as a result of constant pain in the joints, reflex flow of pathological pain impulse from the tissues of damaged joints along the intra and proprioceptive pathways to the cerebral cortex,

which can be attributed to the phenomenon of maladaptation in RA.

It should be noted that organic neurological symptoms were more pronounced in patients with a seropositive form, activity of II - III degree, II - IV stages and systemic manifestations, with frequent attachments of myelitic and encephalitic components. Often in the early stages of RA, the ANS was involved in the pathological process (asthenic syndrome developed), then peripheral NS, and after it myelytic and encephalitic components.

When conducting a general blood test in 102 (71.8%) patients with RA, leukocytosis, lymphocytosis, neutrophilia, acceleration of ESR were detected - indirectly indicate the activity of the inflammatory process of this disease. Immunobiochemical mechanisms play an important role in the diagnosis and determination of the activity of the inflammatory process. High ASLO-O titers were characteristic of RA patients 102 (71.8%). Positive C-reactive protein (99.69%) also indicated the activity of the inflammatory process. Rheumafactor (RF) was identified in 95 (66.9%) ra patients. In cases where the disease began with a lesion of the NS and had a protracted course and minimal activity, clinical and immunobiochemical indicators were not always informative enough. Therefore, we examined the immune status of 137 (96.5%) – RA. In 48 (33.8%) patients, the immune status was studied before and after treatment with immunomodulators - thymogen and trental. The control group consisted of 25 (7.1%) patients who did not receive immunomodulators.

In RA with NS lesions, an immunological study was conducted in 137 (96.5%) patients with a relative and absolute number of T-lymphocytes was 1.3 and 1.6 times, B-lymphocytes in 1.4 and 1.6 times, T-helper cells in 1.3 and 1.6, T-suppressors in 1.6, FAN in 1.3 times lower than normal.

There was an increase in the content of "zero" lymphocytes twice. In IgA and IgG serums - 1.8 and 1.7 times. Deeper immunodeficiency was noted in patients with a high degree of activity with a rapidly progressive course, with myelitic and encephalitic. GSP with a process of up to 5 years. (Table 1)

Immunogenetic studies in 32 patients with RA of the Uzbek population revealed a predisposition to RA associated with HLA antigens A28, B14, B18, B22, B27. B27 was detected in 53%, which is 10 times higher than normal (5.3%); in these patients, immunological changes were more pronounced. In the locus, HLA - A 28 was more common (9.4% versus 4.1%, RR - 2.43). In group B, the greatest risk of developing RA was established. in the presence of antigens B14 (9.4% vs. 4.1%, RR – 2.43), B18 (15.6% vs. 7.84%, RR – 2.18), B22 (6.3% vs. 1.2% RR – 5.53), B27 (53.1% vs. 5.3%, RR – 20.22).

EEG - studies were conducted in 84 (59.2%) RA patients with NS lesions. EEG showed a decrease in inhibitory processes in patients. In the cerebral cortex, an increase in the activating influences of subcortical-stem structures was observed. It was characterized by irregularity (23 people), deformation (10 people), disorganization (13 people), smoothness of regulatory differences (15 people). A small rhythm, a decrease in its amplitude do oppression and absence (15 people), a "flat" type of curve (6 people), the predominance of beta rhythm (22 people), the presence of slow waves, more often theta, less often delta range (20 and 5 people), acute high-amplitude oscillations and "peaks" (8 and 6 people).

Functional load exacerbated background activity (10 people). Dysfunction of the median-stem structures of the brain was detected in 15 patients.

A direct correlation was established between the clinical form, the severity of the disease and the degree of damage to the central nervous system and EEG manifestations.

So, the EEG revealed diffuse changes in the lung (13 people . - 15.5%), moderate (33 people. 39.3%) and significant (38 people). – 45.2%) of the degree of severity. More common III (43%), IV (42%), I (7%), II (6%) types of EEG. EEG data are due to dysfunctions of the central nervous system, its autonomic parts of the EEG to correctly assess the degree of CNS damage in RA.

EchoES examined 128 (90%) RA patients. When comparing the EchoEG and the degree of activity of RA, an increase in phenomena was established, and intracranial hypertension and additional echo signals.

Thus, Echo-ES studies revealed intracranial hypertension and expansion of the cerebrospinal fluid system with concomitant, displacement of M-echo, due to edema and swelling of the brain, especially with localization of ONMK in the basin of the middle cerebral artery.

The main manifestations of RA are generalized lesions of the vascular system, rheumatoid vascular, characterized by lesions of small and medium arteries and impaired capillary circulation.

REG studies were conducted in 130 (91.5%) patients with RA with NS lesions. REG study showed that RA is accompanied by a change in the state of the tone of the cerebral vessels (mainly an increase, less often a decrease) and dystonia of blood vessels with venous circulation. A certain dependence of the indicators of hemodins of the brain on the degree of damage to the NS, with ONMK, EPN and severe form of RA was revealed.

Table 2. Frequency of detection of HLA antigens in RA patients, %

HLA	Control n=245	RA patients n=32	X2	RR
A1	15.1	21.9	0.97	1.58
A2	35.1	18.8	3.41	0.43
A3	23.7	15.6	1.04	0.59
A9	22.0	25.0	0.14	1.18
A10	20.4	25.0	0.36	1.3
A11	12.0	6.25	1.00	0.48
A19	4.9	6.25	0.11	1.29
A28	4.1	9.4	1.77	2.43*
B5	13.3	9.4	0.50	0.64
B7	6.3	3.1	0.68	0.43
B8	6.3	6.25	0.02	0.90
B12	11.0	3.13	1.94	0.26
B13	20.0	18.8	0.03	0.93
B14	4.1	9.4	1.77	2.43*
B15	8.2	3.1	1.03	0.36
B16	6.9	3.1	0.68	0.43
B17	6.5	9.4	0.36	1.49
B18	7.8	15.6	2.22	2.18*
B21	9.0	9.4	0.06	1.04
B22	1.2	6.3	4.03*	5.53*
B27	5.3	53.1	67.0*	20.22*
B35	13.1	15.6	0.16	1.23
B40	5.7	6.3	0.02	1.11

Note: * - significant difference from control.

Thus, REG - studies of patients with RA with lesions of the NS indicate changes in the vascular system of the brain, characteristic of rheumatoid vasculitis.

RVG - studies of the upper and lower extremities were carried out in 94 (66.2%) patients with RA. Pronounced changes in peripheral hemodynamics in patients, hypotension, hypertension, and dystonia of blood vessels with venous congestion in the upper and lower extremities, more often with VSP.

PFI - studies in RA were conducted in 84 (59.2%) patients. In RA, along with polyneuropathy, there was a pronounced asthenic syndrome. In patients with RA, memory impairment was aggravated depending on the degree of activity of the inflammatory process, with II, III degree of activity, especially with EPN. In RA, a decrease in short-term memory attention took place with all degrees of activity. The ability to mathematically count was significantly reduced.

Therefore, in patients with RA, in connection with the defeat of cerebral vessels in the form of vasculitis, with subsequent hypoxia of brain tissue and secondary metabolic changes in higher cortical functions, degeneration of neurons of the cerebral cortex may occur. Studies of higher cortical functions can identify these changes at an early preclinical stage of patients with RA.

Thus, the EEG revealed changes in mild (27 people) moderate (41 people) and significant (26 people) degree of severity; REG changes in cerebral hemodynamics by hyper- (62 people) or hypotonic (18 people) type with signs of venous discirculation (25 people) and asymmetry of blood filling (20 people); REG increase (20 people) or decrease (32 people) peripheral vascular tone, in 21 (16.2x) patient Echoes revealed the presence of intracranial hypertension with an expansion of 111 ventricles by 8.5-9 mm, which indicates the defeat (with Ra) of the choroid plexuses, ventricular ependyma. Psychophysiological studies of 56 (39.4%) patients showed a violation of short-term memory, reaction speed, attention and ability to mathematical counting.

DISCUSSION

Complex therapy of PA with damage to the nervous system includes non-steroidal anti-inflammatory drugs: indomethacin, voltaren, orthofen (75-150 mg / day), remoxicam (7.5 mg), naproxen (500-750 mg / day), ibuprofen (1-2 g / day); they were used for a longtime. Simultaneously, a corticosteroid drug kenalog (40 mg) was injected into the most inflamed joints. Of the basic agents for 6 months, the following were used: crisanol (5%, 2 ml, 1 time per week intramuscularly), D-penicillamine (250 mg / day inside), cuprinil (300-750 mg / day), delagil (0.25 g / day).

Depending on the neurological manifestations, patients received appropriate therapy. the treatment tactics were individual.

In the treatment of ONMK, EPN, MPN, and VSP, drugs that improve blood microcirculation in the brain and spinal cord, vascular drugs were prescribed: pentoxifylline Trental (2%, 5 ml in 200 ml of isotonic sodium chloride solution intravenously, drip. N 5-10) or caventone (0.5%, 2 ml in 200 ml of isotonic sodium chloride solution intravenously, drip, N 5-10), then trental, cavinton and cinnari (one of the drugs 1 tablet. 3 times a day, for a month), nicotinic acid (17th. 2 ml intramuscularly, N 20). To increase metabolism and stimulate the brain and spinal cord, neurometabolic drugs were prescribed: piracetam (20%, 5 ml) or cerebrolysin (5 ml intramuscularly or intravenously).

With polyneuropathies, the course of treatment included stimulating drugs: proserine (0.05%, 1 ml intramuscularly. N 20), gliatilin 4 ml-1000mgna 200.saline solution intravenously drip No. 3-6, neuromidin 10-20 mg 2-3 times a day for up to 6 months, dibazole (inside). vitamins of group "B" (B1, B6, B12). ATP: with asthenic syndromes tranquilizers: tamelan 1 cap 2-3 times, novo-Pasit, palora, atarax 12.5-25 mg, sonopax 10 mg in the evening , phenovelamus, diazepam (1-3 times a day, depending on the severity of asthenia), immunomodulatory drug thymogen (0.01%, 1 ml, intramuscularly, every other day. N 5), physiotherapy, massage, acupuncture and exercise therapy.

For headaches and polyneuralgia, analgesics, painkillers were prescribed, with intracranial hypertension, dehydrating agents: furosemide or hypothiazide, diacarb against the background of potassium preparations, L-lysine escénate 5 ml - 100 ml phys. award.

CONCLUSION

Thus, in RA, diffuse damage to the nervous system with dysfunction of the autonomic departments, an early disorder of cerebral and peripheral hemodynamics, bioelectric activity of the cerebral cortex, a violation of higher cortical functions, a decrease in the T- and B-link of immunity, an increase in immunoglobulins A, G, a change in blood parameters Timely complex therapy had a positive effect on the somatic, neurological and immune statuses of the body and contributed to the regression of neurological symptoms. Genetic markers of predisposition to RA in persons of the Uzbek population HLA A28, B14, B18, B22, B27, which is important for determining risk groups, early diagnosis and prevention of RA.

Ethics approval and consent to participate - All patients gave written informed consent to participate in the study.

Consent for publication - The study is valid, and recognition by the organization is not required. The author agrees to open the publication

Availability of data and material - Available

Competing interests - No

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Conflict of interests-The authors declare that there is no conflict of interest.

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O'ZBEK POPULYATSIYASIDA RATSIONDA KLINIK-NEVROLOGIK, IMMUNOLOGIK PARAMETRLAR VA HLA ANTIGENLAR

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Toshkent tibbiyot akademiyasi

ABSTRAKT

Mavzuliligi. Revmatizmda bo'g'imlardagi patologik o'zgarishlar bo'g'imlarning ar apparati segmentiga, uning ildizlari va periferik nervlariga, shuningdek, nerv sistemasining segmental tuzilmalariga ta'sir qiladi. Revmatizm rivojlanishi tufayli immunologik, immunogenetik va neyrofiziologik o'zgarishlar yaxshi tushunilmaydi, bu esa erta diagnostika mezonlarining rivojlanishini murakkablashtiradi. va ularning kompleks terapiyasi usullari.

Material. 142 nafar revmatizm bilan og'rigan bemorlar, o'zbek millatiga mansub 16-70 yosh.

Xulosa. Revmatizmga ko'ra, avtonom bo'limlarning disfunksiyasi bilan asab tizimining diffuz shikastlanishi, bosh miya va periferik gemodinamikaning erta buzilishi, bosh miyaning bioelektrik faoliyati, yuqori kortikal funktsiyalarning buzilishi kuzatildi. O'z vaqtida kompleks terapiya tananing somatik, nevrologik va immun holatiga salbiy ta'sir ko'rsatdi va nevrologik alomatlarning regressiyasiga sabab bo'ldi.

Tayanch iboralar: Revmatizm, markaziy asab tizimi kasalliklari, erta diagnostika, profilaktik terapiya

КЛИНИКО-НЕВРОЛОГИЧЕСКИЕ, ИММУНОЛОГИЧЕСКИЕ ПОКАЗАТЕЛИ И АНТИГЕНЫ HLA ПРИ РЕВМАТОИДНОМ АРТРИТЕ В УЗБЕКСКОЙ ПОПУЛЯЦИИ

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АБСТРАКТ

Актуальность. При ревматоидном артрите патологические изменения в суставах влияют на сегментарный аппарат спинного мозга, его корешков и периферические нервы, а также на сегментарные структуры нервной системы. Иммунологические, иммуногенетические и нейрофизиологические сдвиги вследствие развития ревматоидного артрита недостаточно изучены, что затрудняет разработку критериев ранней диагностики и методов их комплексной терапии.

Материал. 142 больных с ревматоидным артритом, в возрасте 16-70 лет узбекской популяции и других национальностей.

Заключение. При ревматоидном артрите наблюдались диффузное поражение нервной системы с дисфункцией вегетативных отделов, раннее расстройство церебральной и периферической гемодинамики, биоэлектрической активности коры головного мозга, нарушение высших корковых функций. Своевременная комплексное терапия оказала положительный эффект на соматический, неврологический и иммунный статусы организма и способствовала регрессу неврологической симптоматики.

Ключевые слова: Ревматоидный артрит, заболевания центральной нервной системы, ранняя диагностика, превентивная терап