INTRODUCTION

The prevalence of ankylosing spondylitis (AS) reaches 0.3% among the population [1, 2], and one of the most common manifestations of the disease is the central and peripheral nervous system lesions (CNS, PNS) [3, 4], which is primarily caused by the pathology of the spine [5]. The main causes of severe neuropathy in patients with AS are subluxation and micro fracture of the vertebrae [6, 7, 8], as well as demyelinating pathology [9]. It should be noted that for such patients there are violations of the nervous system vegetative link [10], which, first of all, affect its parasympathetic component [11]. Almost always AS is accompanied by psychosomatic disorders [12, 13], which, eventually, further exacerbates the poor quality of patients’ life [14, 15]. Two forms of AS are identified – juvenile onset (JAC) and adult onset (AAC), depending on the age of the disease debut [16]. R. Conway and F. O’Shea [17] consider that these variants of the disease differ “like apples from oranges”. An increasing research interest in the disease over recent years has led to a number of significant insights in AS. The differences between juvenile and adult-onset AS represents an ongoing controversy. It is still uncertain whether these 2 entities are distinct disease processes or different manifestations of the same disease modulated by age of onset. A number of groups have looked at this aspect of the disease using a variety of methodologies and publishing a number of contrasting findings [18].

The aim of the study – to learn the frequency and nature of separate clinical signs of CNS and PNS lesions in patients with AS, to assess their special features in disease that began in childhood and adulthood.

MATERIALS AND METHODS

217 AS patients aged 16 to 57 years old (an average of (37.7±0.64) years were under observation. 88.9% of men and 11.1% of women among them. The disease duration averaged (10.5±0.39) years. A degree of AS activity was established in 21.2% of cases, II – in 56.7% and III – in 22.1%, 1 stage was noted in 18.4% of the surveyed patients’, II – in 50.7% and III – in 30.9%. Slowly progressive disease course occurred in 79.3% of cases, fast-progressing – in 20.7%. The so-called “central form” of AS was diagnosed in 33.6% of cases, “rhizomelic” – in 2.8%, “peripheral” – in 5.1%, “undifferentiated” – 58.5%. Ophthalmopathy (uveitis) and visceral changes are established in ¾ of the patients’ number. Peripherical arthritis was determined in 66.4% of the patients, sacroileitis – in 97.2%, manifested spondylopathy – in 94.9%. The parameters of the articular syndrome incidence were (5.4±0.25) r.u., its activity (DAS) – (4.0±0.10) r.u., the Lansbury index – (1.17±1.38) points, the index of arthritis progression – (1.3±0.15) r.u. The Barnett-Nordin meta-carpal index was (0.42±0.004) r.u., the bone mineral density index – (−1.49±0.055) SD. Enthesitis were noted in 38.7% of the surveyed, tendovaginitis – in 28.6%.

All patients were divided into two groups: the first (main) amounted to 35 (16.1%) patients with JAS (all males with onset of the disease under the age of 18), and the others 182 (83.9%), with AAS were included in the 2nd (control) group. The age of the main group representatives in the disease debut was (14.3±0.52) years, and at the time of the examination – (24.9±0.83) years, while in the control group it was (29.6±0.45) years and (40.2±0.58) years respectively. The duration of the disease in the 1st and 2nd groups did not differ. Both groups were approximately equal in the disease degree activity, but rapid progressive course of the disease in AAS was 2.7 times more common.

Patients underwent X-ray (“Multix-Compact-Siemens”, Germany) and ultrasound (“Envisor-Philips”, the Netherlands and “ATL3500-Siemens”, Germany) with a study of peripherical arthritis, spondylopathy and sacroileitis, and performed...
Dual-energy X-ray absorptiometry of the proximal femur ("QDR-4500-Delphi-Hologic", USA), echocardiography (Acuson-Aspen-Siemens, Germany, Envisor-C-Philips, the Netherlands) and ultrasound doppler examination of vessels (angiographer "Aplia-XG-Toshiba", Japan). In the part of patients, electromyography (Neuro-MVP-4, Russia) was performed with the estimation of the pulse velocity and potential amplitude, computerized (Somazom-Emotion-6-Siemens, Germany) and magnetic resonance ("Gygoscan-Intera-Philips", The Netherlands) tomography of the sacroiliac joints, spine and brain. The serum levels of antibodies to cyclic citrullinated peptide (aCCP), the concentration of interleukin (IL) 1β and tumor necrosis factor (TNF) α were studied using the enzyme immunoassay (PR2100 Sanofi Diagnostic Pasteur, France), and the immunobiochemical analyzer "Olympus-AU-640" (Japan), concentrations of C-reactive protein (CRP), fibrinogen (FG), circulating immune complexes (CIC), immunoglobulins (Ig) A, G and M were determined in blood serum.

RESULTS AND DISCUSSION

The CNS lesion was diagnosed in 74.7% of the patients with AS, PNS – 33.2%, in patients with AAS twice as likely, and changes in PNS is 5 times less. It should be noted that PNS lesion occurred in all JAS patients. Among the patients with AS, dyscircular encephalopathy was detected in 54.4% of cases, asthenic vegetative syndrome – in 39.2%, corticonuclear syndrome – in 22.6%, cortical ataxia – 19.4%, peripheral polyneuropathy and pyramidal syndrome – 18.0%, cerebellar ataxia – 17.5%, radiculopathy – 16.6%, pseudobulbar syndrome – 14.3%, cervicocranialgia – 13.8%, Morton’s metatarsalgia – 12.9%, peripheral mononeuropathy – 10.6%, metacarpal canal syndrome – 9.2%, transient cerebrovascular disorders – 8.3%, epileptiform syndrome – 7.8%, neuralgia of the trigeminal nerve – 4.6%, facial nerve neuritis – 3.7%.

The pathology of the central nervous system (CNS) in the case of AAS is manifested with dyscircular encephalopathy in 72.8% of cases, with asthenic vegetative syndrome – in 52.5%, with corticonuclear syndrome – in 30.3%, with cortical ataxia – in 25.9%, with pyramidal syndrome – in 24.1%, with cerebellar ataxia – in 23.5%, with pseudobulbar syndrome – in 19.1%, with transient ischemic attack – in 11.1%, with epileptiform syndrome – in 10.5%, and the PNS lesion is revealed in 54.2% of observations like peripheral polyneuropathy, in 50.0% – radiculopathy, in 41.7% – cervicocranialgia, in 38.9% – Morton’s metatarsalgia, in 32.0% – peripheral mononeuropathy, in 27.8% – metacarpal canal syndrome, in 13.9% – neuralgia of the trigeminal nerve, in 11.1% – facial nerve neuritis.
Such signs of nervous system lesion as peripheral mononeuropathy, corticofugal syndrome, cortical ataxia, pseudobulbar syndrome, and transient ischemic attack were not observed in JAS, and dyscirculatory encephalopathy was observed significantly less frequently by 70 %, and asthenic vegetative syndrome – by 85 %. Meanwhile, disease beginning in childhood is marked by peripheral polyneuropathy, radiculopathy, cervicocranialgia, Morton’s metatarsalgia, metacarpal canal syndrome, neuralgia of the trigeminal nerve, facial nerve neuritis, and epileptiform syndrome, which were observed more often than in AAS, respectively, in 15.1; 3.3; 2.2; 2.9; 90.5; 7.8; 5.2 and 3.6 times, as shown by McNe- mar-Fisher’s analysis and reflected in Fig. 1 and 2.

According to Wilcoxon-Rao’s multivariate dispersion analysis, the age of patients in the disease debut is influenced on integral signs of CNS changes. We selected those signs of AS clinical course that simultaneously had Brown-Forsythe dispersion relations and Kendall’s correlation with the severity of the nervous system lesion. It turned out to have existed a direct relationship between the severity of the cervical spine lesion and the prevalence of spondylopathy in cases of JAS, and with the DAS parameter and the involvement of the “root” (shoulder, hip) joints in cases of AAS.

According to Wilcoxon-Rao analysis, the age of AS patients at the onset of the disease affects the integral clinical signs of PNS. In the main group, there is a direct correlation between the severity of changes in PNS with tendovaginitis and involvement the thoracic spine, and in the control group – with the AS stage, the presence of the coxitis and the severity of sacroileitis.

The age of the disease debut in the main group correlates inversely with the severity of the dyscirculatory encephalopathy, asthenic vegetative and epileptiform syndrome, and it is observed a direct correlation with the stage of the pathological process, peripheral polyneuropathy – by the prevalence of tendovaginitis in patients, cervicocranialgia – by the cervical spine lesion, metacarpal canal syndrome – by the degree of disease activity. In cases of AAS, the development of dyscirculatory encephalopathy is closely related to enthesitis, pseudobulbar syndrome – with the “root” joints lesion, pyramidal syndrome – with changes in the cervical spine, cortical ataxia and metacarpal canal syndrome – with DAS indices, radiculopathy – with AS stage.

Regardless of the AS variant and the nature of the nervous system lesion, there is a dispersion relation between the severity of the CNS, PNS pathology and IgA, CIC levels in blood. In addition, the severity of the central nervous system lesion in the patients of the main and control groups is closely related to aCCP serum level, and in the case of AAS, as is also to fibrinogenemia level. The severity of CNS lesion in patients with JAS is directly correlated with level of IgA and TNFα in blood, and PNS – with IL1β. In cases of AAS, there are inverse correlations between the severity of CNS changes and immunoglobulinemia, CIC and IL1β parameters, and it is observed a direct correlation with TNFα values. It should be emphasized that the severity of PNS lesion in patients with AAS is inverse correlated with the concentration of CIC in blood and directly from IL1β.

Taking into account the performed statistical data results of the survey, the prognostic positive sign in regard to the severity of the CNS damage is the level of IgA <2 mmol / L

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<td>r=0.5268, p=0.0011; R2=0.52672670.0028111012</td>
<td>r=0.1544, p=0.0374; R2=0.06427860.01136542</td>
<td>r=0.7061, p=0.00002; R2=0.715129910.012059087</td>
<td>r=0.1388, p=0.0074; R2=0.1930644470.010813934</td>
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Correlation-regression Pearson’s relations of patients’ age in the disease debut with clinical manifestations of the nervous system lesion.

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<td>Fig.3. Relation with asthenic vegetative syndrome in JAS</td>
<td>Fig. 4. Relation with corticofugal syndrome in AAS</td>
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<td>Fig. 5. Relation with cervicocranialgia in JAS</td>
<td>Fig. 6. Relation with radiculopathy in AAS</td>
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<M-SD of this main group) in patients with JAS and the serum level of IgA &lt; 3 mmol/l in AAS ( &gt; M + SD control group).

The next stage of our research was an assessment of the immune disorders role in the pathogenetic constructions of CNS and PNS lesion in patients with JAS and AAS. For this purpose, we selected those indicators that simultaneously had significant Brown-Forsythe dispersion relations and Kendall correlation. It turned out that the development of dyscirculatory encephalopathy directly depends on the level of CIC, pyramidal syndrome – on CRP, peripheral polyneuropathy – on IL1β, cervicocranialgia – on IgA, the metacarpal canal syndrome – on TNFα, Morton’s metatarsalgia – on FG. There were no such dependencies in patients with AAS, but there were completely different ones. Thus, corticonuclear syndrome and the development of mono- and polyneuropathy were associated with the level of CIC, pseudobulbar syndrome – with IgM, the severity of radiculopathy – with CRP, Morton’s metatarsalgia – with IL1β. These data once again point to the completely polysemantic manifestations of the AS with the debut of the disease in childhood and adulthood.

CONCLUSIONS Changes in PNS are observed 4.9 times more often in patients with JAS, and CNS lesion is 2 times less likely than in cases of the disease debut in adulthood, while in patients with JAS the severity of CNS damage is associated with the involvement of the cervical spine and the abundance of spondylopathy, PNS – with the presence of tendovaginitis, arthritis of the “root joints” (shoulder, pelvic) and changes in the thoracic spine, whereas in the case of AAS, CNS lesion depends on DAS parameters, the X-ray stage of the disease, the involvement of the sacroiliac joints, and the age of the disease onset affects the development of asthenic vegetative and corticonuclear syndromes, the occurrence of radiculopathy, cervicocranialgia and metacarpal canal syndrome. And IgA level is more involved in the pathogenetic constructions of the CNS pathology, and the level of IL1β in blood – in PNS, moreover, IL1β and IgA levels determine the occurrence of cervicocranialgia and Morton’s metatarsalgia in other observations of the AS.

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LITERATURE
УРАЖЕННЯ НЕРВОВОЇ СИСТЕМИ ПРИ АНКІЛОЗИВНОМУ СПОНДІЛІТИ, ЩО ПОЧАВСЯ У ДИТЯЧОМУ ТА ДОРОСЛОМУ ВІЦІ

Резюме. Поширеність анкілозивного спонділіту (АС) серед населення складає 0,3 %, що значно частіше розвивається у віці 20–30 років. Виділяють дві форми АС – дитячу і дорослу, залежно від віку дебюту захворювання. Проблема діагностики ювіле́ньного АС (ЮАС) належить до найактуальніших у педіатричній ревматології, при цьому еволюції такого захворювання в дорослому віці залишається невивченою. Існує віковий диморфізм ураження центральної нервової системи (ЦНС) та перифері́йної (ПНС), але у хворих на ЮАС та в решти випадків він не з’ясований.

Мета дослідження – вивчити у хворих на АС частоту й характер окремих клінічних ознак ураження ЦНС та ПНС, оцінити їх особливості при захворюванні, що почалося в дитячому й дорослому віці.

Матеріали і методи. Обстежено 217 хворих на АС (193 чоловіки і 24 дівчинки) середнім віком – 38 років. Швидкість прогресування переважно констатається в 21 % спостережень, помірний і високий ступені активності – в 79 %, II–III стадії – у 82 %, поліартрит – у 65 %. ЮАС діагностовано в 15 % випадків (усі хлопчики), в яких III стадія мала місце у дітей, а в інших пацієнтів.

Результати дослідження та їх обговорення. Зміни ПНС спостерігаються у 4,9 раза частіше у хворих на ЮАС, а ЦНС – в 2 рази рідше, ніж у випадках дебюту захворювання в дорослому віці. При цьому в цьому випадку перша група тяжкість ураження ЦНС пов’язана із залученням до процесу шийного відрізку хребта і з поширенням спондилопатії, ПНС – з наявністю тендиніту, артриту кореневих суглобів (плечових, кульшових) і змін грудного відрізку хребта, тоді як в другій групі – з параметрами інтегрального індексу активності артриту та рентгенологічної стадії хвороби.

Целль исследования – изучить у больных ас частоту и характер отдельных клинических признаков поражений цнс и пнс, оценить их особенности при заболевании, начавшемся в детском и взрослом возрасте.

Материалы и методы. Обследовано 217 больных ас (193 мужчин и 24 женщин) среднего возраста – 38 лет. Быстропрогрессирующее течение констатировано в 21 % наблюдений, умеренная и высокая степень активности – в 79 %, II–III стадии – в 82 %, полиартрит – в 65 %. ЮАС отмечен в 16 % случаев (все мальчики), у которых III стадия имела место вдвоє чаще, чем в остальных пациентов.

Результаты исследований и их обсуждение. Изменения ПНС наблюдаются в 4,9 раза чаще у больных ЮАС, а ЦНС – в 2 раза реже, чем в случаях дебюта заболевания в этом возрасте. При этом у пациентов первой группы тяжесть поражений центральной нервной системы (ЦНС) и периферической (ПНС), но у больных ЮАС и в остальных случаях он не выяснен.

Выводы. АС с разным возрастом дебютом заболевания – это типичное вveneZровическое заболевание, которое риску развития отдельных признаков поражений ЦНС и ПНС, которые в этих группах имеют свои патогенетические особенности.

Ключевые слова: спондилит анкілозивний; діти; доросли; нерва система; поражение; течение.