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Comparative Analysis of the Clinical Presentation of Reactive Arthritis

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Abstract This article presents the results of studies on the features of the clinical course of reactive arthritis of post-enterocolitic and urogenital forms. The study was carried out in 120 patients with an established diagnosis of reactive arthritis.

Keywords Reactive arthritis, Secondary osteoarthritis, Articular syndrome

1. Introduction

Reactive arthritis (RA) is one of the diseases of spondyloarthritis group, which is characterized by inflammatory lesion of joints, associated with trigger infection, as a rule, in genetically predisposed subjects. The pathology affects people from 20 to 40 years old, and mostly men [3]. About 85% of patients with RA are carriers of HLA-B27 antigen [4]. For a long time the term "Reuter's disease" was used for the definition of RA associated with urogenital infection. Recently the terms of RA and Reuter's disease are under discussion [2].

It is known, that etiological structure of RA is heterogeneous. At the same time the greater spectrum of the agents responsible for the development of arthritis revealed annually. The most often determined is the interrelation of the disease with previous intestinal infections such as intestinal (postenyerocolitic RA: Yersinia enterocolitica, Yersinia pseudotuberculosis, Salmonella, Shigella, Klebsiella, Clostridium difficile, Campylobacter jejuni); urogenital (mostly linked with the infection conditioned by Chlamydia trachomatis, Ureaplasma) [8]. Pathogenetical aspects of RA are not studied well. Though the role of the infection in the development of the disease is commonly accepted, not only the agent but also the state of the macro organism is important. Immune pathological processes associated with the development of hyper immune response to infectious agent located inside a joint or extraarticulatory play a basic role in the RA pathogenesis [6]. Trigger factors can initiate cytotoxic T-cellular response leading to proliferation and activation of CD8+T-lymphocytes, causing lesion of synovial membrane and, consequently, development of arthritis.

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There is pathogenetic hypothesis of "antigen mimicry" of bacteria possessing common antigen determinants with HLA-system, providing cross-sectional reaction of produced antibodies not only with alien, but also with proper antigens. The role of HLA-B27 antigen in the development of RA can be also explained by the theory of "arthritogenic peptide", the point of which is that HLA-B27 is arthritis-inducing peptide (a component of a cellular membrane of trigger micro organisms) cytotoxic to CD8+ population T-lymphocytes, triggering immune inflammatory response [8]. That is why in the modern time the possibility of autoimmune processes in the formation of articulate syndrome in RA, promoting chronization of the pathology, is under discussion. Due to heterogeneity of etiological structure and pathogenetic peculiarities RA diagnostics is associated with significant difficulties, conditioning the necessity of application of complex virologic, bacteriological, immunological, and sometimes morphological studies. Nevertheless, the basis of the diagnosis is a complex of clinical and history data, while the set of laboratory tests is often additional for the confirmation of the clinical diagnosis [4].

RA, the clinical presentation of which is very heterogeneous and first of serves to be the reflection of etiological infectious factor, in some cases have complicated diagnosis. Existing clinical recommendations and clinical-laboratory approaches do not provide objective early diagnostics of the pathology. Only dynamic follow-up and testing provide correct verification of the diagnosis [1,4].

Many problems of this pathology stay unsolved and that, first of all, is linked to the specificity of the disease, non-specific clinical manifestations [5,7], which are often similar to other rheumatic pathologies accompanied by arthritis with more unfavorable progression and prognosis.

The objective of the work was to assess the peculiarities of modern progression of reactive arthritis.

2. Material and Research Methods

One hundred and twenty patients aged from 18 to 50 years old (36.9±8.3) diagnosed with RA (70 men and 50 women) and term of the disease 3.8 ±1.7 years were enrolled in the study.

The age structure of the RA patients in the study was as follows: 12.5% were 18-20 years old, 16.7% were 21-30 years old, 45.8% were 31-40 years old, and 25% of the patients were 41-50 years old.

In all patients we studied parameters characterizing inflammatory process (number of leukocytes, ESR, cialic acids, seromucoid, C-reactive protein). For the identification of "trigger" factors we used blood enzyme immunoassay, providing definition of IgM and IgG antibodies.

Statistical processing of the results was performed with the help of Microsoft Office and Statgraphics Plus 5.0 software packages. For the assessment of reliability of differences we applied Student's t-criterion. Critical level of significance for checking of statistical hypotheses in the comparison of the groups was considered to be equal to 0.05.

3. Results and Discussion

Among the patients with RA enrolled in the study more often there were people of 30-40 years old, and there were more men (23.3%) in this age group, while in the group of patients of 40-50 years old there were more women (55.8% of the total number of the age group). In the structure of RA there were reliably more ($p<0.05$) cases with long-lasting progression of the pathology, which was equal to 55.8% of all cases; acute progression was observed in 26.7% and chronic one in 17.5% of the examined patients (Table 1). Long-lasting progression of RA among the patients of 40-50 years old was observed in 46.7% of the cases, which allows to classify that age group as a group of RA relapse risk.

Table 1. Distribution of RA patients according to etiological factor of reactive arthritis development (%)

Etiologic factors	Progression of arthritis n=120					
	Acute n=32 (26.7%)		Long-lasting n=67 (55.8%)		Chronic n=21 (17.5%)	
	M %	F %	M %	F %	M %	F %
Urogenital form (n=82) 68.3%						
Chlamydia trachomatis	7.5	10.8	23.3	14.1	10.8	1.7
Postenterocolytic form (n=38) 31.7%						
Sinia enterocolitica	1.7	4.2	0.8	4.2	1.7	0.8
Campylobacter jejune	1.7	0.8	10	3.3	0.8	1.7
Total	10.9	15.8	34.1	21.6	13.3	4.2

As it is seen from Table 1, dependently on the trigger factor, the most often revealed one was Chlamydia trachomatis (68.3%). It should be noted, that men more often had urogenital arthritis (41.6%). At the same among postenteric forms of the disease we more often isolated Sinia enterocolitica (13.4%) and Campylobacter jejune (18.3%). Analysis of patients' distribution according to the trigger factor allowed us to reveal reliable differences in the prevalence of RA. Thus, it could be noted, that the prevalence of RA, caused by Campylobacter jejune among postenteric forms with acute progression is twice higher that with chronic one.

Primary examination in cases of classic progression with arthritis lesions of eyes and urogenital tract were noted in 36.7% of the patients. Abortive form of RA with fast unnoticeable lesion of eyes and urogenital tract was noted in 69.2%. Obliterated clinical presentation like that certainly makes RA diagnosis complicated in the conditions of family polyclinic.

We performed dynamic follow-up of the patients for two years, which provided clarification of the character of articulate pathology. There were more patients with I–II activity stage of the process and II stage (55.8%) of articulate functional failure.

Articulate dysfunction was more often conditioned by periarticular lesions, which caused pain syndrome, limitation of articulate mobility, and secondary osteoarthrosis (OA). As it is seen from Table 2, articulate syndrome was mostly observed in the joints of legs, prevailingly in ankle (85.8%) and knee joints (81.7%).

Table 2. Articulate syndrome in patients with reactive arthritis

Parameter	Absolute number (n=120)	%
Prevalence of the lesion		
Monoarthritis	35	29.2
Oligoarthritis	57	47.5
Polyarthritis	28	23.3
Location		
I toe	30	25
Hip joint	49	40.8
Knee joint	98	81.7
Ankle joint	103	85.8
Metatarsophalangeal joint	19	15.8
Interphalangeal joint	17	14.2
Shoulder joint	9	7.5
Wrist joint	43	35.8
Interphalangeal joints of hand	57	47.5

Oligoarthritis (47.5%) was noted a little bit more often than polyarthritis. A quarter (23.3%) of patients had lesion of 3-4 joints. Polyartthritis often proceeded with asymmetric lesion of lower limbs with "spiral staircase" type and characteristic extra articulate manifestations. Patients with monoarthritis also in more than a half of the cases had involvement of ankle (69.3%), and less often knee joint (29.2%) into inflammatory process. In single cases there was notable pain in wrist and shoulder joints. In cases of mono and oligoarthritis all patients had swelling of joints and

expressed limitation of their mobility. In cases of polyarthritis there was swelling of several joints, while others were just painful. The number of painful joints in the examined patients corresponded to 5.5±0.6, the number of swelling joints was 4.24±0.8, pain according to VAS in centimeters was equal to 8.1±0.7. Besides that, 90.8% of the patients with RA had clinical manifestations of enthesitis, most often pain in heel and metatarsal bones. As it is seen in the Figure 1, in 18.3% of the cases there were periostitis of calcaneal tubercle ("loose" heel spurs). It should be noted, that arthritis was asymmetric, seronegative, ADC negative, combined with urethritis and conjunctivitis. Clinical manifestations of sacroiliitis were noted in 25% of the patients, with I-II stage on x-ray. It should be noted, that in 66.7% of the cases there were x-ray symptoms of OA of hip joints (35.8%) and knee joints (64.2%). At the same time there was decrease in the height of articulate cartilage in arthrosonography with diminishing of the thickness of the cartilage in joints from 1.6±0.8 mm different from the group of patients (p>0.05), who had no OA.

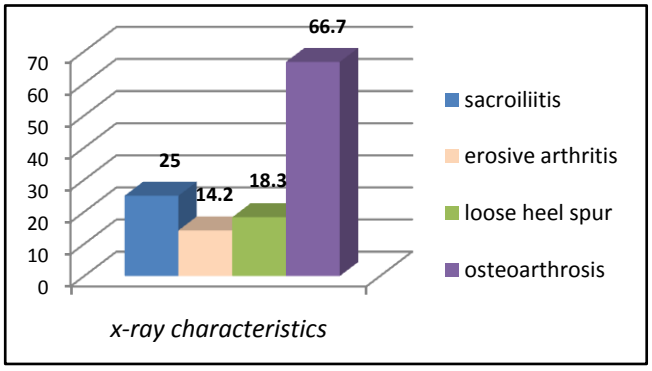

Figure 1. X-ray manifestations in patients with reactive arthritis

It is notable that, in 33.3% of the cases secondary OA developed in patients with RA within initial years (6-12 months) of the disease (fig. 2). Moreover, as it is seen from Figure 2, in 8.75% of the patients had III and IV stages of OA within the first year, and 13.5% within the second year, proving the necessity of endoprosthetics. In its turn from Table 3 it is seen, that OA was seen almost five times more often among the patients with RA with isolated Chlamydia trachomatis (72.5%), than with other trigger factors (p<0.05).

Table 3. Distribution of patients with RA dependently on etiological factor of secondary osteoarthrosis development

Trigger factors	n=80	
	Absolute number	%
Chlamydia trachomatis	58	72.5
Sinia enterocolitica	13	16.25
Campylobacter jejune	9	11.25

Symptoms of synovitis were identified in 100% of the patients; it was isolated and combined with periarthritis in the form of bursitis or tendinitis. Particularly, lesions of Achilles tendon such as ligamentitis and bursitis were noted in 27.5% of the patients.

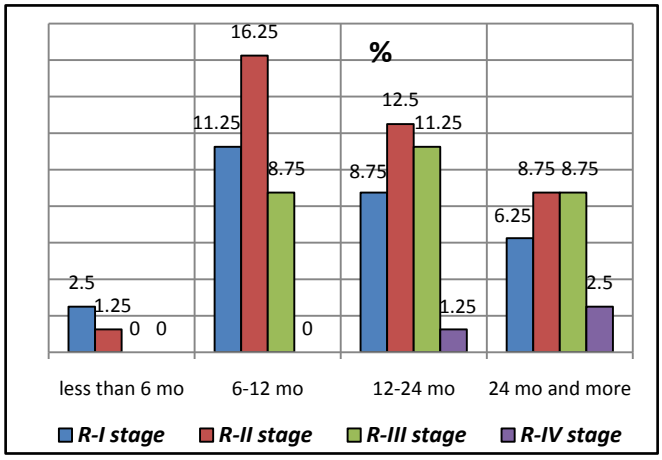

Figure 2. X-ray symptoms of secondary osteoarthrosis dependently on the term of disease in patients with reactive arthritis

Besides articulate syndrome there were lesions of urogenital tract such as urethritis, prostatitis, balanoposthitis in men, and colpitis, adnexitis, urethritis, and oophoritis in women. Urethritis was registered both in men and women. There was often combination of various pathologies of urogenital tract. Dysuria was noted in 73 patients with RA (60.8%). At the same time cystitis was diagnosed in 13 of them (10.8%) and pyelonephritis in 38 (31.7%). Acute conjunctivitis was observed in 29 patients (24.2%). Fever, intoxication in the debut of the disease were observed in 1/3 of the cases. Dermal lesions included keratodermia in 32 patients (26.7%), dermatitis in 29 (24.2%), and onychodystrophy in 20 (16.7%). Iron deficiency anemia mild degree was noted in 21 patients (37.5%). Four patients had RA together with phenotypic signs of connective tissue dysplasia, fifteen patients with arterial hypertension, 43 with pathologies of thyroid gland, and 20 of them had hypothyroids, while four suffered autoimmune thyroiditis with euthyroiditis.

4. Conclusions

Thus, on the basis of the performed study of the patients with RA we determined, that most often the pathology had long-lasting character. Prevalence of urogenital arthritis (caused by Chlamydia trachomatis) was twice higher that in case of postenterocolytic. Patients with urogenital RA more often had characteristic development of secondary osteoarthrosis, developing within initial years of the disease progression, requiring further studies.

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