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Osteophytes in the Joints of Patients with Ankylosing Spondylitis: Manifestation of Osteoarthritis or Underlying Disease?

Abstract

The aim is to study the frequency of peripheral joint damage and the incidence of osteophytes in patients with ankylosing spondylitis. **Materials and methods.** A total of 124 patients with ankylosing spondylitis meeting the 1984 New York criteria were examined; 84 (67.7%) were men. The patients were divided into two groups: patients below the age of 40 ($n = 61$, men – 44 (72.1%)) and aged over 40 ($n = 63$, men – 40 (63.5%)). In the first group, the median age was 34 [29; 38] years, in men – 34.5 [30; 37.5] years, in women — 31 [27; 38] years; in the second group – 50 [45; 56] years, in men – 51.5 [46; 54] years, in women — 48 [44; 59] years. The disease activity was determined, and X-ray examination results of the affected joints were evaluated. **Results.** Of the 124 ankylosing spondylitis patients, 82 (66.1%) had clinical and radiographic signs of arthritis at the time of the study or in their history. Among all of the examined patients, 111 (89.5%) had osteophytes in the peripheral joints, of whom 72 (64.9%) had signs of arthritis. In patients with ankylosing spondylitis, X-ray examination revealed the presence of both bone resorption and bone proliferation. **Conclusion.** Peripheral arthritis was found in more than half of patients with ankylosing spondylitis and was associated with higher disease activity. Asymmetric arthritis was more frequent in patients below the age of 40. Most patients showed signs of bone proliferation in the peripheral joints, with a predominant lesion of large joints of the lower extremities. In patients aged over 40, osteophytes are detected more often, more groups of joints are involved in the process, and joints of the hands and feet are affected.

Key words: *ankylosing spondylitis, osteoarthritis, bone resorption, bone proliferation*

Conflict of interests

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ASDAS — Ankylosing Spondylitis Disease Activity Score, BASDAI — The Bath Ankylosing Spondylitis Disease Activity Index, df — degrees of freedom, HLA-B27 — human leukocyte antigen-B27, AS — ankylosing spondylitis, IL — interleukin, OA — osteoarthritis, RA — rheumatoid arthritis, SI — sacroiliitis

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Introduction

Ankylosing spondylitis (AS) (M45.0) is a chronic inflammatory disease from the spondyloarthritis group, which is characterized by inevitable damage to the sacroiliac joints and/or spine and potentially leading to ankylosis, with frequent involvement of entheses and peripheral joints [1]. Arthritis is a frequent manifestation of AS. In particular, coxitis develops in a third of patients [2]. In patients with arthritis, periarticular osteoporosis, the narrowing of the joint space, and erosion are detected radiologically. Along with these changes or separately, osteophytes, which in routine clinical practice are usually interpreted as manifestations of secondary osteoarthritis (OA), are identified. The literature contains data on the incidence and pathogenesis of secondary OA in some autoimmune and immunoinflammatory diseases, especially rheumatoid arthritis (RA). OA in RA is believed to develop 1–5 years after the disease onset, with an incidence of up to 70.1% [3]. At the same time, there is practically no data on the features and time frame of the development of OA in patients with AS. RA incidence peaks at the age of 40–55 years, AS — at the age of 25–35 years, and OA — at an older age. Of interest are the presence, nature, and incidence of joint damage in patients with AS, especially at a young age, and the features and severity of bone resorption and bone proliferation processes.

The aim is to study the frequency of peripheral joint damage and the incidence of osteophytes in patients with ankylosing spondylitis.

Materials and Methods

We examined 124 patients with AS that met the 1984 New York criteria; 84 (67.7%) patients were men. The patients were divided into two groups: patients below the age of 40 ($n = 61$, men — 44 (72.1%)) and aged over 40 ($n = 63$, men — 40 (63.5%)). In the first group, the median age was 34 [29; 38] years, in men — 34.5 [30; 37.5] years, in women — 31 [27; 38] years; in the second group — 50 [45; 56] years, in men — 51.5 [46; 54] years, in women — 48 [44; 59] years. Patients of the two groups were comparable by sex and disease activity.

Human leukocyte antigen-B27 (HLA-B27) was determined in all patients. The BASDAI (the Bath Ankylosing Spondylitis Disease Activity Index) and ASDAS (Ankylosing Spondylitis Disease Activity Score) were used to assess disease activity. All patients underwent radiography of the affected joints. The stage of sacroiliitis (SI) was evaluated according to Kellgren (1966). Peripheral arthritis was considered at present or in history (inflammatory pain and swelling of the joints with impaired function, X-ray findings of periarticular osteoporosis, narrowing of the joint space and erosion, and synovitis according to ultrasound examination of the involved joints).

Statistical analysis was performed using STATISTICA 8 software. The data distribution was evaluated using the Shapiro—Wilk test; distribution at $p > 0.05$ was considered normal. The description of quantitative features with non-normal distribution was carried out with indication of the median, lower and upper quartiles. The Mann—Whitney test was used to determine the statistical significance of differences in the studied parameters. Pearson's chi-squared test was used to assess differences in the frequency of the features in two independent groups, with an indication of the number of degrees of freedom (df). Differences were considered significant at $p < 0.05$.

The study was carried out in accordance with the standards of good clinical practice (Good Clinical Practice) and the principles of the Helsinki Declaration. The study protocol was approved by the Ethics Committee. Prior to inclusion in the study, all participants received written informed consent.

Results

High disease activity was observed in 87 (70.2%) patients. Of the 82 patients examined, HLA-B27 was detected in 59 (72%). There were no significant differences in the frequency of HLA-B27 detection in patients of different gender. The age the disease onset and AS activity did not depend on the presence of HLA-B27. The incidence of signs of bone proliferation and peripheral arthritis was independent of HLA-B27 carriage.

Table 1 presents clinical features of patients with AS.

Table 1. Age-sex structure, symptom duration and disease activity

Feature	Total (n = 124)	Women (n = 40)	Men (n = 84)	ρ-value
Age at the time of the study, years	41 [34; 50]	42.5 [34.5; 53]	40 [34; 50]	0.43
Age of onset, years	25 [19; 32]	29 [22.5; 39.5]	23 [18.5; 30]	0.006 *
Duration of AS, years	15 [11; 20]	13.5 [9.5; 17]	16 [11; 22]	0.04 *
BASDAI	5.35 [3.72; 6.6]	5.65 [4.65; 7.0]	4.85 [3.35; 6.25]	0.02 *
ASDAS	3.41 [2.8; 4.0]	3.33 [2.7; 4.07]	3.46 [2.86; 3.93]	0.95

Note: AS — ankylosing spondylitis, ASDAS — Ankylosing Spondylitis Disease Activity Score, BASDAI — the Bath Ankylosing Spondylitis Disease Activity Index. The exact significance of the ρ-value is given. * ρ < 0.05

Table 2. The structure of the disease of the musculoskeletal system peripheral structures in patients with AS

Sign	Total (n = 124)	Group 1 ≤40 years old patients (n = 61)	Group 2 >40 years old patients (n = 63)	Pearson's chi- squared test	df	ρ-value
Arthritis	82 (66.1%)	43 (70.5%)	39 (61.9%)	1.02	1	0.3
Synovitis	7 (5.6%)	5 (8.2%)	2 (3.2%)	-	-	-
Dactylitis	10 (8.1%)	7 (11.5%)	3 (4.8%)	-	-	-
Bursitis	8 (6.5%)	5 (8.2%)	3 (4.8%)	-	-	-
Symphysitis	5 (4%)	4 (6.6%)	1 (1.6%)	-	-	-
Tendonitis	12 (9.7%)	4 (6.6%)	8 (12.7%)	-	-	-
Enthesitis / enthesopathy	25 (20.2%)	14 (23%)	11 (17.5%)	0.6	1	0.4

Note: the exact significance of the ρ-value is given. Pearson's chi-squared test was not used if the expected frequency was less than 5

Compared to men, AS in women was diagnosed significantly more often at an older age ($p = 0.006$), and BASDAI activity was higher ($p = 0.02$). All patients had various stages of sacroiliitis (SI): stage 3 (on the right — in 41 (41.1%), on the left — in 44 (35.5%) patients) and stage 4 (on the right — in 54 (43.5%), on the left — in 51 (40%) patients) were detected more often. The structure of the disease of the musculoskeletal system peripheral structures in patients with AS is presented in Table 2. Clinical and/or radiographic signs of peripheral arthritis and coxitis were found in 82 (66.1%) patients; their median BASDAI was 5.7 [4.2; 6.8]. The median BASDAI in patients without arthritis was 4.3 [2.6; 5.8]. AS activity in patients with arthritis was significantly higher ($p = 0.005$). The incidence of arthritis in different groups of joints is presented in Table 3. Bone proliferation in the joints was more often determined in patients with a longer duration of AS ($p = 0.02$); no connection with the activity of the process was detected ($p = 0.8$). The duration of the disease in patients below the age of 40 was 12 [8; 16] years; BASDAI — 4.9 [3.4; 6.2], and ASDAS — 3.4 [2.5; 4.0]. Stage 3 SI was detected

in 22 (36.1%) patients, and stage 4 SI in 23 (37.7%) patients. Signs of peripheral arthritis were observed in 43 (70.5%) patients. In this group, asymmetric joint damage was observed more often compared with patients aged over 40 ($\chi^2 = 7.8, p = 0.005$). The duration of the disease in patients aged over 40 was 18 [13; 24] years; BASDAI — 5.4 [3.9; 6.7], ASDAS — 3.42 [2.9; 4.0]. The most common was SI of the 3rd (22; 35% of patients) and 4th (31; 49.2% of patients) radiographic stages. Peripheral arthritis was detected in 39 (61.9%) patients. It was statistically significant that in patients of this group, osteophytes were more often detected on radiographs of peripheral joints, more groups of joints were affected, and lesions of the hip joints, hands and feet were observed more often compared with patients below the age of 40 (Table 4). Based on X-ray imaging, bone proliferation in peripheral joints was detected in 111 (89.5%) of the examined patients, of whom 72 (64.9%) showed signs of bone resorption on the radiographs. Hip (92; 74.2% of patients) and knee (72; 58.1% of patients) joints were mainly affected in patients of both age groups.

Table 3. Peripheral arthritis and coxitis in patients with AS

Groups of affected joints	Total (n = 124)	Group 1 ≤40 years old patients (n = 61)	Group 2 >40 years old patients (n = 63)	Pearson's chi- squared test	df	p-value
Asymmetric arthritis	31 (25.0%)	22 (36.1%)	9 (14.3%)	7.8	1	0.005 *
Hip joints	32 (25.8%)	15 (24.6%)	17 (27.0%)	0.09	1	0.7
Knee joints	50 (40.3%)	25 (41.0%)	25 (39.7%)	0.02	1	0.9
Ankle joints	35 (28.2%)	18 (29.5%)	17 (27.0%)	0.1	1	0.8
Joints of the feet	34 (27.4%)	16 (26.2%)	18 (28.6%)	0.09	1	0.8
Hand and wrist joints	41 (33.1%)	19 (31.1%)	22 (34.9%)	0.2	1	0.7
Elbow joints	12 (9.7%)	6 (9.8%)	6 (9.5%)	0.003	1	0.95
Shoulder joints	10 (8.1%)	4 (6.6%)	6 (9.5%)	-	-	-
Temporomandibular joints	4 (3.2%)	2 (3.3%)	2 (3.2%)	-	-	-

Note: the exact significance of the p-value is given. * $p < 0.05$ Pearson's chi-squared test was not used if the expected frequency was less than 5

Table 4. Signs of bone proliferation, aseptic necrosis and total arthroplasty in patients with AS

Groups of affected joints	Total (n = 124)	Group 1 ≤40 years old patients (n = 61)	Group 2 >40 years old patients (n = 63)	Pearson's chi- squared test	df	p-value
Osteophytes in at least 1 group of joints	111 (89.5%)	49 (80.3%)	62 (98.4%)	10.8	1	0.001 *
Hip joints	92 (74.2%)	40 (65.6%)	52 (82.5%)	4.7	1	0.03 *
Knee joints	72 (58.1%)	32 (52.5%)	40 (63.5%)	1.5	1	0.21
Ankle joints	9 (7.3%)	2 (3.3%)	7 (11.1%)	-	-	-
Joints of the feet	16 (12.9%)	3 (4.9%)	13 (20.6%)	6.8	1	0.01 *
Joints of the hands	20 (16.1%)	5 (8.2%)	15 (23.8%)	5.6	1	0.02 *
Elbow joints	7 (5.6%)	2 (3.3%)	5 (7.9%)	-	-	-
Shoulder joints	16 (12.9%)	6 (9.8%)	10 (15.9%)	1.0	1	0.3
Scapulohumeral periarthritis	9 (7.3%)	4 (6.6%)	5 (7.9%)	-	-	-
Temporomandibular joints	2 (1.6%)	0	2 (3.2%)	-	-	-
Total arthroplasty	11 (8.9%)	6 (9.8%)	5 (7.9%)	1.4	1	0.7
Aseptic necrosis	17 (13.7%)	8 (13.1%)	9 (14.3%)	0.04	1	0.9

Note: the exact significance of the p-value is given. * $p < 0.05$ Pearson's chi-squared test was not used if the expected frequency was less than 5

In 17 (13.7%) patients, aseptic necrosis of various bone structures (acetabular roof, the head of the femur or humerus, tibia, and talus) was detected. Eleven (8.9%) patients underwent total joint replacement (TJR): 3 of them underwent total replacement of both joints, in 7 — one hip joint; in 1 patient, TJR of the hip, shoulder and both knee joints was performed. In the majority of cases (8; 72.7%), the reason for surgery was osteoarthritis, in 2 (18.2%) cases — fractures, in 1 (9.1%) — aseptic necrosis.

Discussion

AS in all its forms of clinical manifestations and complications can lead to early disability of patients (often at a young age), reduced quality of life and the need for surgical intervention, including due to the development of secondary OA [4–8]. Our data are consistent with the results of a cohort population study conducted by M.C. Lu et al. (2017), who demonstrated early development of OA in patients below the age of 40, which required TJR [9].

In patients with AS aged over 40, the increase in the incidence of bone proliferation may be associated with the development of OA with existing peripheral joint damage. Radiography of peripheral joints in patients with AS, often detects osteophytes along with erosion. Signs of bone proliferation in the joints are often interpreted as osteoarthritis, rather than the manifestation of an underlying disease [8]. The obtained data indicate that bone resorption and bone proliferation are likely a manifestation of an underlying disease, as well as its activity. This assumption is supported by the high AS activity in patients of this group and the development of large joint arthritis in young patients. Early OA in people below the age of 45 is extremely rare, and, in contrast, AS makes its debut at a young age [10]. It is known that AS is characterized by both resorption and excessive proliferation of bone tissue under the influence of proinflammatory cytokines, primarily interleukin-17 (IL17) [11–13]. It has been proven that this cytokine leads to the development of osteophytes between the vertebrae. The high incidence of osteophytes in patients with AS may be associated with the level of IL17, not only in the systemic circulation but primarily locally — at the sites of tendon attachment. Koo B. S. et al. (2020) showed a comparable level of IL17, IL23 and a lower level of tumor necrosis factor- α in the synovial membrane of the joints of patients with AS compared with RA [14]. Therefore, it cannot be ruled out that osteophytes in the peripheral joints and spine are a single manifestation of the underlying disease. To confirm this hypothesis, special prospective studies are required.

Conclusion

Most of the patients included in the study had a high activity of the disease, and the 3rd and 4th radiographic stages of sacroiliitis. Peripheral arthritis was found in more than half of the patients with AS and was associated with higher disease activity. Asymmetric arthritis with a predominant lesion of large joints of the lower extremities was detected more often in patients below the age of 40. In patients with AS in peripheral joints, signs of bone proliferation are often found along with signs of bone resorption. The obtained data demonstrate the need for further study of the features of peripheral joint damage in AS.

Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication.

K.D. Dorogoykina (ORCID: 0000-0003-1765-2737): Research concept and design, obtaining data, analyzing and interpreting data, writing articles, approving the final version of the publication.

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