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Original Scientific Article

ASSOCIATION OF RADIOGRAPHIC FINDINGS OF MUSCULOSKELETAL HAND INVOLVEMENT WITH CLINICAL AND SEROLOGICAL FEATURES OF SYSTEMIC SCLEROSIS

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Abstract. *Musculoskeletal manifestations (MSM) frequently occur in systemic sclerosis (SSc) and imply a variety of rheumatic symptoms and clinical features, from arthralgia to arthritis, contractures, tendon friction rubs, tenosynovitis, myalgia, muscle tenderness, and myositis. The objective of the study was to determine the prevalence of joint manifestations in clinical findings, as well as frequency and type of radiographic changes in 56 patients with the limited and diffuse form of SSc; to define the correlation between musculoskeletal hand changes in SSc and specific antibodies (antinuclear antibodies- ANA), as well as with antibodies specific for particular forms of SSc (anti-topoisomerase-1 antibodies- ATA, anticentromere antibodies- ACA); and to test the correlation between specific cardiopulmonary manifestations in SSc, and frequency and type of musculoskeletal changes. The obtained results indicated a high frequency of joint manifestations in SSc, which were estimated by clinical and radiographic examinations. Joint involvement in SSc was underestimated in clinical trials, as it occurred more frequently than expected. Radiographic hand findings in tested SSc patients indicated the presence of arthritis, erosions, joint space narrowing, radiological demineralization, acro-osteolysis, flexion contractures, and calcinosis. Hand involvement was an important cause of morbidity, which seriously affected the quality of life in patients with SSc. Various forms of joint and bone involvements could represent the base for introducing an innovative approach to treating musculoskeletal hand damage in SSc.*

Key words: *joint involvement, radiographic changes in hand, systemic sclerosis.*

Introduction

Systemic sclerosis (SSc), often known as scleroderma, is a chronic autoimmune disease of unknown cause, which is characterized by fibrosis of the skin and internal organs, followed by immune system activation and severe vascular disorders [1]. Two primary forms of the diseases are: limited (lSSc) and diffuse (dSSc). Limited subtype implies disease entities, such as morphea, linear scleroderma, "en coup de sabre", as well as other variants of the disease of different localization and degree of skin thickening, usually in the form of bands that affect specific parts of extremities, face, and forehead [2, 3].

Activation of endothelial cells and vascular disorders are the earliest symptoms of systemic sclerosis [4, 5]. Induction of endothelial cell (EC) damage may be activated by numerous triggers, such as infection, immune-mediated cytotoxicity, antiendothelial cell antibodies (AECA), and ischemia-reperfusion injury. As a primary feature of SSc, excessive fibrosis is the result of the complex sequence of mutually connected vascular injuries and activation of the immune system and represents a reparative process. Cell immunity plays a crucial role in the complex genesis of SSc, and is characterized by producing specific disease-related antibodies [6, 7]. Aside from cell immunity, scientists have noted activities of humoral immunity. Using the technique of indirect immunofluorescence (IIF), antinuclear antibodies (ANA)have been detected in > 95% of patients with SSc. Specific ANA, which are connected to specific disease manifestations, are found in > 80% SSc patients. The latest data have pointed out that more than 10 types of specific autoantibodies, especially anticentromere antibodies (ACA),antitopoisomerase antibodies (ATA), and anti-U1RNP antibodies, have been detected in patients with SSc or SSc overlap syndrome [8]. Clinical manifestations of SSc are heterogeneous and depend on the form of the disease (diffuse or limited) and organ involvement. Patients with the diffuse form of the disease are at risk of rapid development of severe skin fibrosis and internal organ involvement, while patients with limited SSc experience slowly progressive skin changes which do not affect the area above elbows, knees, proximal extremities, or trunk, but imply various degrees of internal organ involvement [9, 10].

Musculoskeletal manifestations (MSM) are very frequent in SSc and implicate numerous rheumatic manifestations, from arthralgia to arthritis, contracture, tendon

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friction rubs, tenosynovitis, myalgia, muscle tenderness, and myositis. Joint involvement affects the quality of life of SSc patents and results in a significant decrease of work capacity or ability to perform everyday activities. According to various studies [11], the prevalence of arthralgia ranges from 23 to 81%. Moreover, synovial inflammation may cause diagnostic confusion. The assessment of arthritis in SSc is very complex due to the following disease features: skin edema, skin thickening and tethering, digital ulcer, subcutaneous calcinosis, and contractures. Physical examination is not sensitive enough to assess arthritis in SSc [12,13].

Tendon involvement in SSc primarily implies the presence of tenosynovitis and tendon friction rubs, which are often associated with the rapid progression of skin fibrosis. It usually occurs in the initial stage of the disease in patients with diffuse form, but it may be recorded in all stages and in all subtypes (lSSc and dSSc). Disease progression is accompanied by contractures of the involved joints, which affect movement and functions. Flexion contracture is characterized by permanent shortening of muscles and scar tissue, resulting in distortion and deformities which, based on numerous studies, may occur in 24 to 56% of patients.

Radiographic Changes in Bones and Joints

Conventional radiography is a method used to visualize late, destructive consequences of synovitis. However, this method cannot be used to visualize synovial membrane inflammation or early destruction of cartilage and bone. Radiographic changes in SSc include articular lesions with juxta-articular osteoporosis destruction and joint space narrowing, erosions in MCP, PIP and DIP joints, and wrists. Erosive arthropathycan look like erosive OA or psoriatic arthritis and cause changes that are similar to rheumatoid arthritis RA. The patients who meet classification criteria for SSc and RA have SSc- RA overlap syndrome [14, 15]. Prevalence of SSc -RA overlap is very hard to determine, as it occurs in 4.6–5.2% of patients.

In terms of radiographic findings, joint abnormalities may be associated with extra-articular involvements, skin atrophy, calcinosis cutis, and fingertip resorption, which differentiate SSc from other rheumatic diseases [16].

Study objectives are as follows: 1. to determine the prevalence of joint abnormalities in clinical findings, frequency, and types of radiographic changes in 56 patients with the limited diffuse form of SSc; 2. to define the correlation between musculoskeletal hand changes in SSc and antinuclear antibodies (ANA), as well as with antibodies specific for particular forms of SSc (ATA, ACA); and 3. to test the correlation between specific cardiopulmonary manifestations in SSc, and frequency and type of musculoskeletal changes.

Method: The study included a total of 56 patients (52 female and 4 male), median age 55.84±13.76 (age range: 33–79), who were treated at Rheumatology Clinic, Institute for Treatment and Rehabilitation Niška Banja. The average disease duration was 9.31±5.99 (range: 1–25) years. All patients met 2013 ACR/EULAR criteria for classifying SSc [17]. Disease duration was determined based on the first occurrence of Raynaud's phenomenon. Based on Le Roy et al. classification (2), a total of 33 patients suffered from lSSc, while 23 patients suffered from dSSc.

The functional status was defined based on Health Assessment Questionnaire (HAQ). The questionnaire was filled out by all SSc patients. HAQ contained twenty questions, classified into eight categories which referred to different activities: dressing and grooming, arising, eating, walking, object reaching, and gripping. The patients could select one of the four options for answering a particular question, while answers were scored 0-3, where: 0- can perform an activity without any difficulty, 1- with some difficulty, 2- with much difficulty, and 3- unable to perform an activity. The HAQ scores were classified into three grades: moderate disability (mild functional impairment) was graded from 0-1, severe disability (serious functional impairment) was graded from 1.01–2, while complete physical impairment and need of custodial care were graded from 2.01–3.

All patients with SSc were subjected to clinical examination, laboratory tests, standard hand radiography, and assessment of disease clinical manifestations. Internal organ involvement was defined in compliance with previously defined criteria [1]. Lung changes were defined based on the presence of bibasilar fibrosis at standard heart and lung radiography and/or at high-resolution computerized tomography, pulmonary function tests (FVC, DLCO/VA) and/or presence of pulmonary arterial hypertension detected at color Doppler echocardiography. Values of FVC< 75%, i.e. DLCO/VA< 75% compared to the normal values pointed to the presence of restrictive changes. Pulmonary arterial hypertension was defined as pulmonary pressure above 40mmHg at rest at Doppler echocardiography [18].

Heart involvement was recorded in the findings of pericarditis, complex arrhythmias, conduction disorders, diastolic dysfunction, and reduced left ventricular ejection fraction. Muscle involvement was assessed based on the presence of muscle tenderness and/or increased value of creatine phosphokinase (CPK).

The presence of synovitis, arthralgia, tendon friction rubs and flexion contracture was determined during a clinical examination. Additionally, the presence of active digital ulcers, indentations, and pitting scars from previous ulcers was analyzed.

Serology tests, which aimed at determining ANA and ACA were conducted by means of indirect immunofluorescence on HEP-2 cells (Immunoconcepts, Sacramento, California, USA). Titer 1:40, i.e. titer which was, in practice, recommended as "screening" was taken as limit ANA titer ("cut off" titer, i.e. titer representing the lowest value accepted as positive test result). Anti-topoisomerase antibodies were determined by the ELISA method (Imtec, Immunodiagnostics, Berlin, Germany).

All patients with SSc were tested for the presence of a rheumatoid factor (RF). Value of RF > 20 IU/L was

regarded as positive. ELISA (enzyme-linked immunosorbent assay) method (Imtec) was used to determine the presence of anti-CCP antibodies. The samples were classified as positive when values were >25 U/ml. The control group without CCP antibodies consisted of 28 healthy individuals of the same age and gender.

Standard hand and wrist radiography was conducted in all patients with SSc. The changes were evaluated by a radiologist who had no information on the clinical and serologic conditions of the patients (diagnosis). Radiographic joint changes in the tested SSc group included: erosions (cortical bony surface discontinuity) and joint space narrowing: focal or diffuse joint narrowing. Bone changes implied demineralization (juxta-articular or generalized osteoporosis) and bone resorption. Soft tissue changes included calcifications and flexion contractures. Joint space narrowing at proximal interphalangeal (PIP) joints and distal interphalangeal (DIP) joints were not analyzed if the presence of digital contractures was confirmed.

Student's t-test was used for comparing the mean values of age and disease duration. Chi-square test or Fisher exact test were used for comparing the frequency of categorical variables if one of the expected frequencies was less than 5.

Association of elevated values of ANA, ACA, and ATA with synovitis, erosions, flexion contracture, tendon friction rubs, cysts, joint space narrowing, resorption, osteoporosis, acro-osteolysis, calcinosis, and contracture was tested by calculating Phi (Fi) correlation coefficient. The threshold for defining statistical significance was less than 5% ($p<0.05$). The results of statistical analysis were shown in tables and graphs.

Quantitative analysis was carried out on a PC. Microsoft Office 2010 Excel was used for recording, ranking, and table and graphical presentation of the obtained data. Software package SPSS, Version 18.0, was used for statistical analysis and calculation.

Results

A total of 56 patients with SSc was included in the study, 4 (7.1%) of whom were male and 52 (92.9%) were female. The median age was 55.84±13.76, while the average disease duration was 9.31±5.99 years. Limited SSc was present in 33 (58.9%) patients, while diffuse SSc was identified in 23 (41.1%) patients.

Characteristics of patients with SSc are shown in Table 1.

Prevalence of synovitis in clinical findings of SSc patients was 12/56 (21.4%), arthralgia was identified in 45/56 (80.4%) patients, tendon friction rubs were recorded in 11/56 (19.7%) patients, while joint flexion was confirmed in 24/56 (42.9%) patients.

Radiographic changes in patients with SSc were divided into: 1. changes in joints, 2. changes in bones, and 3. changes in soft tissue.

Table 1 Patients with SSc

Characteristics	Patients with SSc (n=56)
Age	55.84±13.76
Male/female	4 (7.1%) / 52 (92.9%)
Disease duration (in years)	9.31±5.99
Cutaneous subtype	
limited	33 (58.9%)
diffuse	23 (41.1%)
Raynaud's phenomenon	54 (96.4%)
Digital ulcer	22 (39.3%)
HAQ>1,5	31 (55.4%)
Lung fibrosis	34 (60.7%)
Elevated pulmonary artery systolic pressure (SPRV>40mmHg)	3 (5.4%)
Positive antinuclear antibodies (ANA)	42 (76.4%)
Positive anti-topoisomerase-1 antibodies (anti-Scl 70)	14 (25.0%)
Positive anticentromere antibodies (ACA)	11 (20.4%)
Elevated creatine phosphokinase and/or muscle tenderness	3 (5.4%)
Increased acute phase reactants	15 (26.8%)
Positive RF	10 (17.9%)
Positive anti-CCP antibodies	10 (17.9%)

Joint space narrowing was observed in 34 (60.7%) SSc patients, erosions were identified in 21 (37.5%) patients, while arthritis (confirmed by radiography, in case of the detected presence of erosions and joint space narrowing) was found in 14 (25%) patients with SSc.

Changes in bones implied the presence of bone resorption, acro-osteolysis, and radiological demineralization. The frequency of occurrence of each of the stated changes in the SSc group was shown in Table 2.

Table 2 Radiographic changes in patients with SSc

Radiographic changes	Patients with SSc (n=56)
Changes in joints	
Erosions	21 (37.5%)
wrist	9 (16.1%)
MCP	7 (12.5%)
PIP	9 (16.1%)
DIP	15 (26.8%)
Joint space narrowing	34 (60.7%)
wrist	19 (33.9%)
MCP	27 (48.2%)
PIP	27 (48.2%)
DIP	24 (42.9%)
Arthritis (erosions + joint space narrowing)	14 (25.0%)
Changes in bones	
Demineralization	22 (39.3%)
Bone resorption	19 (33.9%)
Acro-osteolysis	17 (30.4%)
Changes in soft tissue	
Calcinosis	20 (35.7%)
Flexion contracture	23 (41.1%)

Finally, changes in soft tissue included calcinosis, which was observed in 20/56 (35.7%) patients, and flex-

ion contracture, which was identified in 23/56 (41.1%) patients with SSc.

The presence of calcinosis (57.1:22.9%; p=0.010) and positive ANA (95.2:64.7%; p=0.010) was more frequent in 21 patients with erosive arthropathy than in 35 patients without erosive arthropathy.

Table 3 Comparison of clinical and serological features in SSc patients with and without erosive changes

Characteristics	Erosive arthropathy (n=21; 37.5%)	No erosive changes (n=35; 62.5%)	p
SSc subtype			
diffuse SSc	10 (47.6%)	13 (37.1%)	0.440
limited SSc	11 (52.4%)	22 (62.9%)	
Digital ulcer	10 (47.6%)	12 (34.3%)	0.323
Calcinosis	12 (57.1%)	8 (22.9%)	**0.010**
Organ involvement			
Lungs	14 (66.7%)	20 (57.1%)	0.480
Heart	11 (52.4%)	18 (51.4%)	0.945
Positive RF	4 (19.0%)	6 (17.1%)	0.857
Positive anti-CCP	4 (19.0%)	6 (17.1%)	0.857
Positive ANA	20 (95.2%)	22 (64.7%)	**0.010**
Positive ACA	5 (23.8%)	6 (17.1%)	0.617
Positive anti-topoI antibodies	8 (38.1%)	6 (17.1%)	0.080
HAQ >1,5	14 (66.7%)	17 (48.6%)	0.187

Association of Clinical Joint Findings and Musculoskeletal Manifestations with Total and Specific Antibodies in Patients with SSc

Significant positive correlation between arthralgia and ANA (Fi=0.293 and p=0.030) was confirmed in all tested patients. Additionally, substantial positive correlation between the presence of arthralgia and elevated values of ANA(Fi=0.357 and p=0.045), as well as between the presence of flexion contracture and elevated values of anti-Scl 70 (Fi=0.418 and p=0.015) was determined in patients with lSSc. On the other hand, significant negative correlation between the presence of flexion contracture and elevated values of ACA(Fi=-0.435 and p=0.043) (Table 4) was identified in patients with dSSc.

Asociation of Radiographic Findings of Musculoskeletal Manifestations in Patients with SSc With Total and Specific Antibodies

A significant positive correlation between erosions and elevated values of ANA (Fi=0.349 and p=0.009), as well as between calcinosis and elevated values of ACA (Fi=0.279 and p=0.041) was recorded in all SSc patients. Furthermore, a substantial positive correlation between erosions and elevated values of ANA (Fi=0.488 and p=0.005), as well as between the presence of demineralization (osteoporosis) and elevated values of anti-topo I antibodies (Fi=0.368 and p=0.035) (Table 5) was confirmed in patients with SSc.

Table 4 Correlation between synovitis, erosions, flexion contracture and tendon friction rubs in clinical finding and total ANA, ACA and anti-topo I antibodies in all patients with SSc and in subtypes

Patients	Finding		ANA	ACA	Anti-Scl 70
All SSc patients	Synovitis	Fi	0.190	-0.160	0.201
		p	0.164	0.249	0.137
	Arthralgia	Fi	**0.293**	-0.021	0.182
		p	**0.030**	0.883	0.180
	Flexion contracture	Fi	-0.028	-0.267	0.250
		p	0.838	0.051	0.063
	Tendon friction rubs	Fi	0.064	-0.027	0.234
		p	0.641	0.844	0.083
Patients with lSSc	Synovitis	Fi	0.217	-0.186	-0.100
		p	0.233	0.309	0.580
	Arthralgia	Fi	**0.357**	0.218	0.134
		p	**0.045**	0.230	0.458
	Flexion contracture	Fi	-0.035	-0.149	**0.418**
		p	0.850	0.415	**0.015**
	Tendon friction rubs	Fi	0.078	0.000	0.313
		p	0.672	0.999	0.076
Patients with dSSc	Synovitis	Fi	0.046	-0.061	0.124
		p	0.835	0.787	0.573
	Arthralgia	Fi	0.358	-0.417	0.371
		p	0.094	0.054	0.082
	Flexion contracture	Fi	-0.112	**-0.435**	0.045
		p	0.610	**0.043**	0.837
	Tendon friction rubs	Fi	0.150	-0.158	0.405
		p	0.495	0.483	0.056

Table 5 Correlation between radiographic musculoskeletal changes and total ANA, ACA and anti-topo I antibodies in all patients with SSc and in subtypes

Patients	Finding		ANA	ACA	Anti-Scl 70
All SScpatients	Cysts	Fi	0.046	-0.130	-0.109
		p	0.740	0.349	0.424
	Erosions	Fi	**0.349**	0.068	0.234
		p	**0.009**	0.625	0.082
	Joint space narrowing	Fi	-0.017	0.121	-0.211
		p	0.899	0.385	0.118
	Demineralization (OP)	Fi	0.192	0.142	0.127
		p	0.160	0.305	0.352
	Resorption	Fi	0.224	0.109	0.109
		p	0.100	0.434	0.424
	Acro-osteolysis	Fi	0.187	0.053	0.157
		p	0.172	0.703	0.248
	Calcinosis	Fi	0.243	**0.279**	0.086
		p	0.074	**0.041**	0.528
	Contracture	Fi	-0.049	0.029	0.105
		p	0.723	0.834	0.442

Patients	Finding		ANA	ACA	Anti-Scl 70
Patients with lSSc	Cysts	Fi	0.078	-0.333	-0.313
		p	0.672	0.062	0.076
	Erosions	Fi	**0.488**	0.190	0.224
		p	**0.005**	0.298	0.211
	Joint space narrowing	Fi	-0.031	-0.044	-0.094
		p	0.868	0.813	0.604
	OP	Fi	0.187	0.073	**0.368**
		p	0.306	0.692	**0.035**
	Resorption	Fi	0.164	0.234	0.250
		p	0.371	0.198	0.160
	Acro-osteolysis	Fi	0.078	0.000	0.313
		p	0.672	0.999	0.076
	Calcinosis	Fi	0.244	0.298	0.199
		p	0.179	0.097	0.266
	Contracture	Fi	0.009	0.110	0.177
		p	0.963	0.548	0.326
Patients with dSSc	Cysts	Fi	0.146	0.097	0.220
		p	0.506	0.668	0.314
	Erosions	Fi	0.079	-0.097	0.214
		p	0.719	0.668	0.327
	Joint space narrowing	Fi	0.283	0.250	0.032
		p	0.191	0.261	0.886
	OP	Fi	0.283	0.250	0.032
		p	0.191	0.261	0.886
	Resorption	Fi	0.311	-0.061	-0.054
		p	0.149	0.787	0.806
	Acro-osteolysis	Fi	0.311	0.208	-0.054
		p	0.149	0.353	0.806
	Calcinosis	Fi	0.283	0.250	0.032
		p	0.191	0.261	0.886
	Contracture	Fi	-0.181	-0.097	0.038
		p	0.408	0.668	0.863

Discussion

Hand involvement is prevalent in patients with SSc and is the result of late detection of disease manifestations, as well as lack of ideal treatment which would provide adequate mobility, preserve hand strength and contribute to maintaining hand activity in various aspects of life. Inflammatory arthritis, tendon friction rubs, tendinitis/tendinosis, diffuse swelling, skin sclerosis and calcinosis, acro-osteolysis, Raynaud phenomenon and digital ulcers represent various manifestations of hand involvement. Such manifestations are clear signs of the disease and its duration, and depend on the form of the disease- diffuse or limited SSc [17, 19]

According to the data available in the literature, joint involvement is present in 46% to 97% of SSc patients. Even though the symptoms are usually detected after the occurrence of Raynaud phenomena, they may sometimes be identified even before Raynaud. One of the most frequent initial signs is arthralgia. In rare cases, arthritis may be detected, as well as the combination of arthralgia and arthritis. During the later stages, arthralgia may be the result of synovial fibrosis without previous synovitis. Symmetric, polyarticular arthritis affects metacarpophalangeal (MCP) and proximal interphalangeal(PIP) joints, which is almost identical as with rheumatoid arthritis (RA), with a slight difference that SSc may affect distal interphalangeal (DIP) joints. The published research has indicated thathandjoint involvement strongly correlates with functional disability and poor quality of life. Therefore, early assessment and treatment of the above changes in patients with SScare of crucial importance.

The European Scleroderma Trials and Research Group (EUSTAR) analyzed the presence of joint manifestations in 7286 patients with SSc and confirmed that synovitis was prevalent in 16% of SSc patients. Synovitis was more often associated with a diffuse form of the disease and presented a predictive factor for dSSc, the occurrence of pulmonary hypertension, muscle tenderness, new digital ulcers, and reduced left ventricular ejection fraction.

Our research demonstrated a high frequency of joint involvement in SSc, which was in compliance with the findings of other authors.

Moreover, the prevalence of synovitis in clinical findings of our patients with SSc was 12/56 (21.4%). Arthralgia was detected in 45/56 (80.4%) patients, tendon friction rubs were found in 11/56 (19.7%) patients, while flexion contractures were identified in 24/56 (42.8%) patients.

The study included 56 patients, 45 of whom were diagnosed with arthralgia- 24 (72.7%) patients with lSSc and 21 (91.3%) with dSSc. Arthritis was detected in 12 patients (21.4%), i.e. 3 (9.1%) patients with lSSc and 9 (39.1%) patients with dSSc, tendon friction rubs were identified in 11 (19.7%) patients, i.e. 8 (24.2%) lSSc patients and 3 (13%) dSSc patients. Flexion contractures were confirmed in 24(42.8%) patients, i.e. 12 (36.4%) patients with lSSc and 12 (52.2%) patients with dSSc. Thus, arthritis and flexion contractures were much frequent in patients with dSSc, which was in compliance with available literature data.

According to EUSTAR registry [11], tendon friction rubs were confirmed in 11% of SSc patients. Tendon friction rubs were described as skin crepitus on joint palpation during movement, most probably due to the presence of fibrin deposits on the surface of the tendon and fascia sheath. EUSTAR patient registry confirmed the association of tendon friction rubs with digital ulcers, muscle tenderness, pulmonary fibrosis, and proteinuria. Furthermore, tendon friction was associated with severe functional disability (high HAQ index), while reduced tendon friction and improved clinical results were associated with lower values of HAQ index.

This research focused on testing the frequency of tendon friction rubs in a cohort of 56 patients suffering from different forms of SSc (dSSc and lSSc), as well as on determining the association of tendon friction rubs with other clinical features of SSc patients. Tendon friction rubs were identified in 11/56 (19.6%) patients with SSc, which corresponded to the study conducted by the French authors [11]. Clinically proved tendon friction rubs were predominantly recorded in older patients with longer disease duration and significant functional disability (HAQ > 1.5). Additionally, this entity was associated with the presence of anti-topoisomerase antibodies.

EUSTAR registry confirmed the association of tendon friction rubs with digital ulcers, muscle tenderness, pulmonary fibrosis, and proteinuria. Flexion contracture is a severe

disorder that often occurs in the later stage of the disease, primarily in wrists, small hand joints, and elbow joints, and occurs in 31% of SSc patients registered in EUSTAR. Small joint contractures usually occur in MCP and interphalangeal (IP) joints, and are associated with difficulties in performing everyday activities. Due to increased skin pressure in the bony prominence area and SSc vasculopathy, skin ulcers appear on contractures. Our research confirmed the presence of flexion contracture in 24/56 (42.9%) SSc patients, more often in diffuse form than in limited form (52.2% vs. 36.4%). The research indicated that SSc patients with flexion contractures often suffered from a diffuse form of the disease, pulmonary fibrosis, and had topoisomerase antibodies. Additionally, our research pointed out the association between the presence of flexion contracture in SSc and severe functional disability expressed by HAQ score of > 1.5.

Antinuclear antibodies were detected in 76.4% of SSc patients who took part in our research, which was less than the percentage recorded in the study conducted by the French authors (91%)(39), while the percentage that we recorded was much closer to the percentage stated in the studies of Allali et al. (62%) and Admou et al. (70%) [21, 22].

Radiographic Changes

Standard conventional radiography has remained the primary diagnostic method for monitoring disease progression and efficiency of treating patients with SSc. Radiographic changes are classified as follows: 1. changes in soft tissue, 2. changes in bones, 3. changes in joints, and 4. changes in muscle [23].

Skin changes are characterized by progressive thickening of subcutaneous tissue, its resorption, and subcutaneous calcifications (calcinosis cutis).

Subcutaneous calcifications occur quite often, i.e. in 10–30% of SSc patients, and are usually accompanied by extrusion of calcified material from the skin. The results of research conducted by the French researchers recorded the presence of calcinosis in 28/120 (23%) of SSc patients [15], which was partially confirmed by the results of our study that recorded the presence of Calcinosis in 20/56 (35.7%) of SSc patients. Digital calcifications were usually detected in SSc patients with CREST form of limited SSc. The majority of SSc patients who participated in our study suffered from CREST form of SSc, which explained the percentage of calcifications detected in our group of SSc patients.

The prevalence of skeletal myopathy in SSc varied from 5 to even 96%, due to the lack of consensus over diagnostic criteria. The published studies predominantly implied the combination of clinical, biological, electromyography (EMG), MRI, and/or histological evidence of muscle abnormality. During the research on the frequency of myopathy and/or myositis, Avouac et al. confirmed muscle tenderness in 27% of SSc patients and CPK increase in 8% of SScpatients. Furthermore, the researchers demonstrated that, in terms of statistical significance, an increase of CPK in the SSc group with synovitis occurred more often, $p<0.005$ [11].

As for our group of SSc patients, muscle tenderness was confirmed in 8.9% of patients, primarily with clinically proved synovitis. Increased value of creatine phosphokinase (CPK) was determined in 5.4% of SSc patients. Flexion contracture was the most frequent form of joint abnormality at hand radiography and it was detected in approximately 90% of patients with SSc [24]. Prevalence of finger flexion contracture was significantly higher in patients with dSSc compared to patients with lSSc.

During our research and radiological examination, the presence of flexion contracture was confirmed in 23/56 (41.1%) of SSc patients. The percentage was much higher compared to the results obtained by Avouac et al., who detected the presence of this entity in 23% of SSc patients. The probable reason for this discrepancy could be the median age of the patients and frequency of dSSc in our population (41.1%) of SSc patients, compared to the percentage (33%) of dSSc patients who took part in the study of the French authors.

Acro-osteolysis is characterized by resorption of distal phalanges and is primarily associated with atrophy of hand fingertips. Resorption of distal phalange occurs in 20 to 25% of SSc patients and usually affects hand fingers, while resorption of proximal phalange occurs very rarely. Our study recorded the presence of hand bone resorption in 19 (33.9%) SSc patients, while acro-osteolysis was confirmed in 30.4% of the patients, which was in compliance with the results of other studies. After conducting the radiological examination, Avouac et al. identified the presence of acro-osteolysis in 19/103 (18%) patients with SSc. Additionally, Allali et al. confirmed the presence of this phenomenon in 18% of SSc patients [14, 21].

Raynaud phenomenon is regarded as the most frequent manifestation of SSc which occurs in 95% of patients. If accompanied by digital ulcer (DU), Raynaud phenomenon becomes even more complex. The research of Young et al. confirmed that 44 to 60% of SSc patients had DU at some stage of the disease [19]. The frequency of DU in our research was completely in line with the published research results of other authors, as DU was detected in 22/56 of our patients with SSc (39.3%). The presence of digital ulcer is identified as an independent predictor for radiographic progression of acro-osteolysis, which is confirmed bya strong association between acro-osteolysis and digital vascular and systemic complications. Bone demineralization is a periarticular sign of chronic joint inflammation. Various research studies [25–28] recorded 4–42% prevalence of juxta-articular osteoporosis at hand radiography, while our research results indicated that the above prevalence was 39.3%, which was in agreement with the results of previously mentioned studies.

SSc erosions are predominantly identified in PIP and MCP joints but could be present in DIP hand joints. Research conducted by Avouac et al. confirmed the pres-

ence of erosion at hand DIP [15] in 72% of SSc patients. The majority of the patients who took part in the above study were postmenopausal women, so the occurrence of arthropathy which was not associated with SSc was quite possible. The results of our study were consistent with the study of the French authors who depicted a high frequency of erosions on hand DIP and PIP identified by radiography.

Conclusion

The results obtained in this study indicated a high frequency of joint manifestations in SSc, which was confirmed by clinical and radiographic examination. Joint involvement in SSc was underestimated in clinical trials, as it occurred more frequently than expected. Radiographic hand findings in tested SSc patients indicated the presence of arthritis, erosions, joint space narrowing, radiological demineralization, acro-osteolysis, flexion contractures, and calcinosis. Hand involvement was an important cause of morbidity, which seriously affected the quality of life in patients with SSc. Various forms of joint and bone involvements presented in this paper, from arthralgia to arthritis and deformities, point out the need of applying innovative approaches and options for treating patients with systemic sclerosis.

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