Anterior Chest Wall Pain in Recent Inflammatory Back Pain Suggestive of Spondyloarthritis. Data from the DESIR Cohort

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ABSTRACT. Objective. To determine the prevalence of anterior chest wall (ACW) pain in patients with recent inflammatory back pain (IBP) suggestive of spondyloarthritis (SpA), and to investigate the influence of ACW pain on the overall features of these patients.

Methods. The DESIR cohort is a prospective, multicenter French cohort of patients with early IBP suggestive of SpA, including 708 patients (mean age 33.8 yrs, 53.8% females, 57.3% HLA-B27-positive). ACW pain was defined by at least 1 episode of chest wall pain attributed to SpA by the rheumatologist, after ruling out other causes of chest pain. Data on the baseline demographic characteristics, functional status and quality of life, imaging features, bone mineral density, and blood tests were compared in patients with and those without ACW pain. Factors associated with ACW pain were identified by univariate and multivariate analysis (logistic regression).

Results. The prevalence of ACW pain in the DESIR cohort ($n = 316/708$ patients) was 44.6% (95% CI 40.9–48.3). ACW pain occurred after the first symptoms of IBP in 62%. Localization was diffuse in 41% of the positive cases. A stepwise multivariate analysis found an association between ACW pain and the enthesitis score, involvement of thoracic spine, diagnosis of ankylosing spondylitis (AS), and radiographic abnormalities of sacroiliac joints.

Conclusion. In recent IBP suggestive of SpA, presence of ACW pain is associated with enthesitis, thoracic spine involvement, radiographic sacroiliitis, diagnosis of AS, and with a more severe disease. ACW pain could be interpreted as a diagnostic feature for AS. (First Release May 15 2013; J Rheumatol 2013;40:1148–52; doi:10.3899/jrheum.121460)

Key Indexing Terms:

ANTERIOR CHEST WALL
STERNOCOSTAL JOINT

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Anterior chest wall (ACW) involvement is a classic feature in defined and advanced spondyloarthritis (SpA), but it is not included in classification or diagnostic criteria¹. In a

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series describing a population with established ankylosing spondylitis (AS; 50 patients fulfilling the Amor criteria, mean disease duration 12 yrs), Fournié, *et al*² found a prevalence of ACW (sternocostoclavicular) involvement of 58% by clinical examination and 50% by bone scintigraphy. Using radiographic material from a 10-year retrospective study of 268 patients with seronegative arthritis, Jurik³ found changes in sternoclavicular joints in 17% of patients with AS, and in manubriosternal joints in 51% of patients with AS. In AS, the presence of ACW involvement was significantly related with duration of the disease, advanced sacroiliitis, and involvement of the spine and root joints. In a retrospective single-center study of 275 patients with established SpA, ACW pain was reported in 37.1%⁴, in relation with duration of disease.

Little is known about ACW involvement in early SpA or inflammatory back pain (IBP) suggestive of SpA and the patients' characteristics associated with this condition. The main objective of our study was to determine the prevalence of ACW pain and its characteristics in patients with recent IBP. The secondary objectives were to evaluate the influence of ACW pain on clinical, laboratory, and imaging

findings [standard radiographs, magnetic resonance imaging (MRI) of the entire spine, ultrasound], bone mineral density (BMD), and body composition features (fat mass, lean mass), and fulfillment of classification criteria.

MATERIALS AND METHODS

This was a cross-sectional study evaluating all patients enrolled in the DESIR cohort and for whom data were available at baseline. The DESIR cohort is a prospective, multicenter French cohort of patients with early IBP (classified according to Calin⁵ or Berlin⁶ criteria, taking into account for the latter 2 out of 4 items) of more than 3 months' and less than 3 years' duration, with symptoms suggestive of SpA according to the local investigator's assessment (score ≥ 5 on a 0 to 10 numerical rating scale in which 0 = not suggestive and 10 = very suggestive of SpA), and planned to be followed up for least 5 years. The method of assembly of the cohort and the main characteristics of patients at baseline have been reported⁷. This cohort included 708 patients: mean age 33.8 years, 53.8% women, 57.3% HLA-B27-positive. Presence or history of ACW pain was assessed by the investigators for all patients at baseline, and recorded by interview. ACW pain was defined by at least 1 episode of at least 1 day duration of inflammatory chest wall pain, as spontaneous symptoms, attributed to SpA by the rheumatologist, after other causes of chest pain were ruled out. The baseline characteristics included age, ethnicity, date at onset of IBP and peripheral arthritis, nature of IBP, presence of SpA features, relevant family history, and medication including use of nonsteroidal antiinflammatory drugs and disease-modifying antirheumatic drugs. Duration of axial symptoms was defined as the time between the first axial symptom and the initial interview. Examination was also performed to determine the Ritchie Articular Index (53 joints) and swollen joint count (28 joints), spinal mobility as measured by the Bath Ankylosing Spondylitis Metrology Index (BASMI) and chest expansion, and enthesitis index (Maastricht AS Enthesitis Score). Extraarticular features were also evaluated, particularly uveitis, psoriasis, and inflammatory bowel disease (IBD; presence or history with medical diagnosis).

Patients were asked to complete the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Global index (BAS-G), Health Assessment Questionnaire (HAQ), Medical Outcomes Study Short Form-36 (SF-36), and AS Quality of Life score questionnaires.

Blood tests were performed in the regional rheumatology centers. These included C-reactive protein (CRP), erythrocyte sedimentation rate, and HLA-B27 antigen, and the usual biological measures. The Ankylosing Spondylitis Disease Activity Score (ASDAS)⁸ was calculated using CRP (ASDAS-CRP).

All imaging modalities (radiographs and MRI) were evaluated by the local radiologist or rheumatologist. Radiographs of the sacroiliac (SI) and hip joints were graded according to the following scale: 0 = normal, 1 = doubtful (grade 1), 2 = obvious (grade 2 or 3), and 3 = fusion. Lateral radiographs of the cervical and lumbar spine were used to calculate the modified Stoke AS Spine Score (mSASSS)⁹.

T1-weighted fast spin-echo (T1-FSE) and short-tau inversion recovery (STIR) 1–1.5 Tesla MRI of the spine and the SI joints were performed to assess inflammatory and structural lesions. The MRI scans were classified by the local radiologist or rheumatologist as having definite, doubtful, or absent inflammatory or structural lesions at the spinal and sacroiliac level.

Data on baseline demographic characteristics, functional status and quality of life, imaging features (standard radiographs, MRI, ultrasound), BMD, and blood tests were compared in patients with and those without ACW pain. These data allowed determination of European Spondylarthropathy Study Group (ESSG) score, Amor criteria, and Assessment of Spondyloarthritis International Society (ASAS) classification criteria¹ for each patient. Both the date of the first symptom of IBP and the symptoms of ACW pain were recorded, as well as the date of the visit. Factors associated with the presence of ACW pain were identified by both

univariate and then multivariate analysis (logistic regression with the variables significant in univariate analysis); *p* values < 0.05 were considered significant. Data were extracted from the DESIR database locked at December 12, 2011.

Our study was approved by the French Departmental Directorate of Health and Social Affairs (Directeur Départemental des Affaires Sanitaires et Sociales) and received approval from the ethics committees. It was conducted in accord with the Declaration of Helsinki and the guidance for good clinical practice. All participants gave written informed consent to enter the study.

RESULTS

Prevalence. Three hundred sixteen cases of ACW pain were reported at baseline: the prevalence of ACW pain in the DESIR cohort (*n* = 316/708 patients) was 44.6% (95% CI 40.9–48.3). ACW pain occurred after the first symptoms of IBP in 62%, before appearance of symptoms in 14%, and simultaneously (± 1 month) in 24% of cases. Localization was diffuse in 41% of the positive cases, sternocostal in 35%, manubriosternal in 29%, or sternoclavicular in 26%, with the possibility of several simultaneous localizations.

Univariate analysis. Presence of ACW pain was significantly associated in univariate analysis (Table 1) with pain in cervical and thoracic spine, buttock, peripheral arthritis and enthesitis, fulfillment of ASAS modified New York criteria and ESSG criteria, associated reactive arthritis and SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome, increased BASDAI, ASDAS, BASFI, BASG, BASMI and articular index, increased CRP, reduced SF-36 (physical and mental components), radiographic SI involvement, and reduced BMD (data not shown for BMD). ACW pain was not associated with body mass index, HLA-B27, chest expansion, dactylitis, uveitis, psoriasis, smoking, age, age at onset, or ultrasound and MRI findings (inflammatory or chronic changes, SI and spine; data not shown).

Multivariate analysis. A stepwise multivariate analysis found a statistically significant association between ACW pain and the enthesitis score, involvement of the thoracic spine, and radiographic abnormality of the SI joints (Table 2). Because of the relation between the 2 variables “diagnosis of AS” and “radiographic sacroiliitis,” the former was deleted from the multivariate analysis (Table 2).

DISCUSSION

In this prospective cohort of patients with IBP suggestive of early SpA, ACW pain was found with a prevalence of 44.6%. This is in the range of previous studies in established SpA and with smaller sample sizes. Among 45 patients with definite AS with a mean disease duration > 10 years, Dawes, *et al*¹⁰ found chest pain in 63% of patients (and 7% of controls matched for sex and age). In a retrospective single-center cohort of established SpA⁴ at Cochin Hospital, Paris, ACW pain was reported in 37.1% of 275 patients, with a mean disease duration of 16 years. In 110 patients

Table 1. Comparison of baseline characteristics between patients with and those without anterior chest wall (ACW) pain (univariate analysis).

Characteristics	Patients with ACW, n = 316	Patients Without ACW, n = 392	p
Male sex, %	45	47	0.6
Mean age, yrs	33.6 ± 8.5	33.8 ± 8.7	0.8
Location of axial involvement since beginning			
Cervical spine, %	45	33	0.001
Thoracic spine, %	67	49	0.000001
Gluteal, %	78	72	0.048
Peripheral articular involvement, %	63	52	0.003
Entheses involvement, %	54	45	0.009
Diagnosis of ankylosing spondylitis at inclusion, %	47	38	0.009
ASAS criteria fulfillment at inclusion, %	72	65	0.04
ESSG criteria fulfillment at inclusion, %	82	75	0.02
Duration between SpA diagnosis and inclusion, days	272	226	0.4
Age at IBP onset, yrs	31.9	32.4	0.5
Associated conditions at inclusion			
Reactive arthritis, %	1.9	0.26	0.006
SAPHO syndrome, %	6	2.6	0.02
Inflammatory bowel disease, %	5.9	2.3	0.05
Activity, quality of life			
Patient-acceptable symptom state, %	37	45	0.04
BAS-G (0–10)	5.40 ± 2.59	4.84 ± 2.51	0.005
BASDAI (0–100)	47.4 ± 20.2	42.4 ± 18.5	0.001
ASDAS-CRP	2.63 ± 1.09	2.39 ± 0.97	0.003
BASFI (0–100)	33.5 ± 23.3	27.9 ± 21.9	0.001
Short Form-36			
Physical	38.64 ± 8.95	41.04 ± 9.45	0.001
Mental	38.93 ± 11.24	41.30 ± 11.15	0.005
Health Assessment Questionnaire (0–3)	0.66 ± 0.52	0.54 ± 0.49	0.001
ASQoL	10.11 ± 4.71	8.57 ± 5.07	0.001
Clinical findings			
Enthesis index (0–13)	3.65 ± 3.57	1.91 ± 2.53	0.001
Articular index	5.84 ± 10.05	3.04 ± 6.82	0.001
BASMI (0–10)	2.47 ± 1.04	2.32 ± 0.97	0.04
Laboratory tests			
HLA-B27, %	61	55	0.15
CRP, mg/l	10.3 ± 16.8	7.8 ± 12.0	0.02
Hemoglobin, g/dl	15.3 ± 18.8	16.1 ± 17.4	0.05
Imaging			
Radiographic sacroiliitis*, %	54	45	0.003
mSASSS	1.17 ± 3.11	1.0 ± 2.7	0.3

* Score ≥ 1 (see text for details). CRP: C-reactive protein; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score (CRP based); BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score; IBP: inflammatory back pain; ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; BAS-G: Bath Ankylosing Spondylitis Global Score; ASAS: Assessment of Spondyloarthritis International Society; ESSG: European Spondyloarthropathy Study Group; SpA: spondyloarthritis; SAPHO: synovitis, acne, pustulosis, hyperostosis, osteitis.

with early SpA evaluated by Ramonda, *et al*¹¹, 36% complained of pain and/or tenderness of ACW. In the study by Weber, *et al*¹² of 122 SpA patients, ACW pain or tenderness was present in 26%.

ACW pain occurred before IBP and represented the first rheumatologic symptom of SpA in 14% of patients with ACW pain and 6% of the whole cohort; this can be compared with 9.8% of patients with ACW pain and 3.6% of the whole cohort (with mean delay before diagnosis of

4.2 years) in the series from Elhai, *et al*⁴. Elhai, *et al*⁴ demonstrated a clear relationship of chest pain with duration of the disease.

In our cohort, ACW pain was distributed between several localizations of the ACW, diffuse in 41% of the positive cases, sternocostal in 35%, manubriosternal in 29%, or sternoclavicular in 26%, with the possibility of several simultaneous localizations. In the Cochin experience⁴, the joints involved were sternocostal joints > 60%, manubrio-

Table 2. Stepwise multivariate analysis (the item “diagnosis of ankylosing spondylitis before inclusion in the study” not included in the analysis, because of its relationship with radiological sacroiliitis); significant results.

	ACW Pain, n = 316	No ACW Pain, n = 392	Adjusted OR (95% CI)	p
Global enthesitis score (0–13)	3.65 ± 3.57	1.91 ± 2.53	1.206 (1.142–1.274)	< 0.0001
			For an increase of 1 unit	
Involvement of thoracic spine (pain), yes vs no (%)	212 (67)	192 (49)	2.204 (1.590–3.054)	< 0.0001
Radiographic sacroiliac score (%)				
0: normal	142 (46)	209 (55)		
1: doubtful	81 (26)	75 (20)	1.7474 (1.168–2.611)	0.0066
2: established or fusion	88 (27.9)	99 (25.78)	1.648 (0.122–2.420)	0.0108

ACW: anterior chest wall.

sternal 48%, and sternoclavicular joint 33%. In the series from Fournié, *et al*², in 50 patients with AS and 50 with psoriatic arthritis, ACW involvement was found in half the patients, the most common sites being manubriosternal symphysis and sternoclavicular joints. In the study from Ramonda, *et al*¹¹, at clinical examination, sternocostoclavicular joints were involved in about 80% of the cases and the sternum in 35%.

Our results clearly suggest ACW involvement as a marker of disease activity and severity. Patients with ACW pain showed lower percentage of patient-acceptable symptom state, increased disease activity (BAS-G, BASDAI, ASDAS, CRP), and reduced functional capacities and quality of life (increased BASFI, BASMI, HAQ scores, reduced SF-36 physical and mental component scores); all were statistically significantly different from patients without ACW pain. This was noted by Dawes, *et al*¹⁰, who found significantly longer duration of morning stiffness and reduced spinal mobility in AS patients with chest pain compared to those without. In contrast, Elhai, *et al* reported that patients with ACW pain in established SpA did not have more severe disease⁴, without giving more details.

ACW pain was associated in our population with thoracic spine and peripheral involvement (joint scores and enthesitis scores), but not with dactylitis. This was not the case in the study from Elhai, *et al*⁴ in established SpA, which found an association only between ACW pain and heel pain. In univariate analysis in our study, an association was found with reactive arthritis and SAPHO syndrome (and a trend to association with IBD), but not with psoriasis or uveitis. In multivariate analysis, the relation with enthesitis remained significant.

ACW pain was associated with fulfillment of the ASAS and ESSG criteria and with diagnosis of AS in the univariate analysis, and with radiographic sacroiliitis in the univariate and multivariate analyses. Diagnosis of AS was more frequent in patients with chest pain in the study by Elhai, *et al*⁴; in a 10-year retrospective study of 268 patients with seronegative arthritis, radiographic ACW involvement was

significantly related in the AS patients to advanced sacroiliitis and spine involvement (and disease duration)³; and ACW lesions found by MRI occurred more frequently in AS patients than in those with nonradiographic SpA, out of 122 patients with SpA¹².

Specific imaging procedures for ACW involvement were not planned as part of the protocol of the DESIR cohort, and this represents the main limitation of our study. Some data on this are available in the literature. Jurik³ found radiographic involvement of the sternoclavicular joint in 17% and of the manubriosternal joint in 51% of patients with AS studied. In the 110 patients with early SpA described by Ramonda, *et al*¹¹, a bone scan was positive in 100% and an MRI scan in 62.5% of those with clinical involvement. Weber, *et al*¹² assessed whole-body MRI in 122 patients with SpA (95 AS, median disease duration 11 yrs; and 27 nonradiographic SpA, median disease duration 1.2 yrs) and 75 healthy controls. Bone marrow edema was recorded in 44.3% of patients with SpA, in 25% of the patients with IBP, and in 9.3% of controls. That study demonstrated the lack of association between clinical and imaging findings indicative of inflammation in ACW involvement in SpA: the agreement between patient self-report of pain and ACW tenderness on clinical examination was moderate (kappa value 0.5); kappa values between clinical and MRI inflammation ranged from –0.18 to 0.25 for all patients with SpA.

Together, our results confirm the high prevalence of ACW pain in early SpA. ACW pain in these patients with recent IBP suggestive of SpA was associated with higher disease activity and severity, and with higher rates of radiographic changes of SI joints and diagnosis of AS. This association was not related to a longer duration of symptoms (because age and symptom duration were similar in patients with and those without ACW pain), so ACW pain might be regarded as a diagnostic (classification) feature of axial SpA.

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