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Psoriasis and phenotype of patients with early inflammatory back pain

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ABSTRACT

Background Psoriasis is an important clinical feature in spondyloarthritis. However, the influence of psoriasis on the clinical, functional and imaging features of patients with inflammatory back pain (IBP) related to spondyloarthritis is not known.

Objectives To determine the prevalence of psoriasis and its impact in patients with recent IBP suggestive of spondyloarthritis.

Methods The prevalence of psoriasis was determined in 692 patients (mean age 33.3±8.5 years, 53.8% female, 58.3% human leucocyte antigen B27 positive) included in the DESIR cohort. Demographic characteristics, imaging features and blood tests of patients with and without psoriasis were compared.

Results The prevalence of psoriasis was 16.6%. Patients with rather than without psoriasis more often presented with enthesitis (59.1% vs 47.5%; p=0.02) and had more active disease (BASDAI 4.8±1.8 vs 4.4±2.0; p=0.05) and poorer functional status (BASFI 3.6±2.2 vs 3.0±2.3; p=0.006; SF-36 (physical function) 61.9±24.4 vs 66.9±24.9; p=0.04). Patients with psoriasis showed higher levels of C-reactive protein (p=0.02), total cholesterol (p=0.01) and triglycerides (p=0.02). The two groups did not differ in structural changes as assessed by standard x-rays or MRI at the spinal and sacroiliac levels. However, ultrasonography of the Achilles tendon revealed psoriasis associated with bone erosions (p=0.0003) and abnormal vascularisation (p=0.04). Multivariate regression analysis revealed BASFI score (p=0.03), cholesterol level (p=0.02), dactylitis (p=0.0006) and family history of psoriasis (p<0.0001) as independent predictors of psoriasis.

Conclusions In patients with recent IBP suggestive of spondyloarthritis, psoriasis is associated with active axial disease and frequent concomitant enthesopathy and dactylitis.

Psoriasis is a common chronic, recurrent, immune-mediated condition of the skin, with variable clinical presentation, distribution and severity. Its prevalence is estimated to be between 1.5% and 3% in Europe and North America.[1 2] Patients with severe psoriasis have impaired quality of life and are more likely to have comorbidities such as obesity, diabetes, metabolic syndrome and ischaemic heart disease. A preferential association with other inflammatory diseases such as Crohn's disease has been reported.[3 4] These epidemiological data raised the issue of the impact of psoriatic inflammation on dysfunction of other organs, although this hypothesis is still debated.

Beyond the skin, psoriasis is an important clinical feature in spondyloarthritis, a group of related but phenotypically distinct disorders comprising ankylosing spondylitis (AS), inflammatory bowel disease-associated arthritis, reactive arthritis and psoriatic arthritis (PsA).[5] PsA is an inflammatory arthritis that affects approximately 15% of patients with psoriasis.[6–8] Patients with PsA typically present with asymmetrical oligo/polyarthritis, dactylitis and the absence of positive serological test results for rheumatoid arthritis.[9–11] As compared with the attention paid to peripheral involvement, less attention has been paid to spinal involvement in these patients,[12 13] although inflammatory spinal disease might develop in 5–25% of psoriasis cases.[14–16]

Studies assessing the association of psoriasis per se and a particular phenotype of peripheral arthritis yielded conflicting results. Two studies reported that psoriasis, without classifying patients as having PsA or not, was not related to the short or long-term outcome in patients with peripheral arthritis.[17 18] By contrast, in another study, patients with psoriasis had a more aggressive clinical course with a poorer functional and radiological outcome.[19] We have only few data about the association of psoriasis and spondyloarthritis pattern in patients with predominantly inflammatory symptoms in the spine or established AS.

In this study, we investigated the prevalence of psoriasis in patients with recent inflammatory back pain (IBP) and compared the clinical features, disease activity and laboratory and imaging findings for patients with and without psoriasis.

PATIENTS AND METHODS

Ethics approval

This 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 accordance with the Declaration of Helsinki and the guidance for good clinical practice. All participants gave written informed consent to participate in the study.

The DESIR cohort

The Devenir des Spondylarthropathies Indifférenciées Récentes (DESIR) is a French prospective, multicentre, longitudinal cohort established to explore the nature and consequences of early IBP suggestive of spondyloarthritis. Of the 708 patients included in the DESIR cohort (inclusion period October 2007 to April 2010), 654 (92.4%) fulfilled at least one of the following criteria for AS and spondyloarthritis at baseline: modified New York criteria,

European Spondylarthropathy Study Group criteria, Amor criteria and assessment in AS classification criteria for axial spondyloarthritis.[20 21] The present work is a cross-sectional analysis of baseline data for all patients included in the DESIR cohort and for whom data on the presence or absence of psoriasis were available (n=692; 98%). The last patient was recruited on 29 April 2010, and the database used in our study was locked on 30 June 2010.

Recruitment, inclusion and exclusion criteria

Twenty-five centres were selected based on the experience of investigators in conducting clinical studies, and had to fulfil predefined quality standards. Recruitment was performed in close connection with local community rheumatologists. Each centre acted as an observational centre and did not interfere with the patients' treatments.[22]

To be included in the cohort, patients had to be over 18 and less than 50 years old and have IBP according to the Calin[23] or Berlin criteria[24] and symptoms suggestive of spondyloarthritis for more than 3 months but less than 3 years. The Calin criteria require the presence of four of the following five items: age at onset less than 40 years, duration of back pain over 3 months, insidious onset, morning stiffness of more than 30 min duration and improvement with exercise. The Berlin criteria require the presence of two of the following items: morning stiffness of over 30 min duration, improvement in back pain with exercise but not with rest, nocturnal awakening (second half of the night only) and alternating buttock pain. Patients were excluded if they had received tumour necrosis factor alpha blockers or had conditions that might have interfered with their giving informed consent and/or impaired optimal compliance (eg, alcoholism, psychiatric disorders).[21]

Demographic and clinical variables collected in DESIR

The whole protocol and the case record form are accessible on the DESIR website.[25] Baseline characteristics recorded included age, body mass index (BMI), date at onset of IBP and peripheral arthritis, nature of IBP, history and the presence or absence of spondyloarthritis features, relevant personal and family history, and medication, including the use of non-steroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs. The presence or absence of psoriasis at baseline was recorded as a dichotomous variable (yes/no) with the date of onset but without an evaluation of severity.

Physical examination was performed to determine the Ritchie articular index score (53 joints), the synovitis score (swollen joint count in 28 joints), spinal mobility and chest expansion. Patients completed the Bath ankylosing spondylitis disease activity index (BASDAI), the Bath ankylosing spondylitis functional index (BASFI) and the health assessment questionnaire for ankylosing spondylitis to assess functional status. In addition, patients completed the ankylosing spondylitis quality of life scale and the medical outcomes survey short form 36 (SF-36) to assess health-related quality of life.

Biological data and imaging

Patients underwent blood testing for C-reactive protein (CRP) level, erythrocyte sedimentation rate, human leucocyte antigen (HLA)-B27 antigen positivity, lipid profile and fasting glycaemia. All patients (n=692) had radiography and MRI results. More than half of the patients (n=390/692; 56%) also underwent power Doppler ultrasonography (PDUS) of the Achilles tendons, performed in 14 of the 25 recruiting centres.

Patients underwent x-ray imaging of the cervical spine, lumbar spine and sacroiliac joints, which was graded by regional radiologists or rheumatologists. Sacroiliac joint radiographs were graded according to the following grading scale: 0, normal; 1, doubtful; 2, obvious; or 3, fusion. Radiographic bilateral sacroiliitis was defined by an obvious grading scale. The modified Stoke ankylosing spondylitis spine score was calculated by radiography of the cervical and lumbar spine. Hip involvement was defined as a Bath ankylosing spondylitis radiological index score of 2 or greater.

As previously described,[20 21] T1-weighted fast spin echo and short τ inversion recovery 1–1.5 tesla MRI of the whole spine and the sacroiliac joint was performed to assess inflammatory and structural lesions. MRI were classified by regional radiologists or rheumatologists as having definite, doubtful or absent inflammatory and/or structural lesions at the spinal and sacroiliac joint levels. Only definite lesions were considered positive images in our analyses.

PDUS examination of the Achilles tendons was performed in some centres by rheumatologists experienced in musculoskeletal ultrasound. Each tendon was scanned in both longitudinal and transverse planes. PDUS was performed in B mode to detect morphological abnormalities (thickening, calcific deposits, bone erosion), then with power Doppler to detect abnormal vascularisation, as described.[26]

Statistical analysis

We calculated the prevalence of psoriasis and 95% CI. We then identified the factors associated with psoriasis by univariate analysis (χ^2 test or Fisher's test for categorical variables and analysis of variance for continuous variables). Factors with a p value of less than 10% on univariate analysis were entered into a stepwise logistic regression model of predictors of psoriasis; $p<0.05$ was considered statistically significant. Statistical analysis involved the use of SAS 9.1.

RESULTS

Demographic and clinical characteristics at baseline

Our cohort population consisted of 692 patients with recent IBP (mean age 33.3±8.5 years, 53.8% female, 58.3% HLA-B27 positive). The prevalence of psoriasis was 16.6% (n=115/692, 95% CI 13.9 to 19.3). Psoriasis occurred before IBP for 79% of patients but after or concomitant with IBP onset for 15% and 6% of patients, respectively. The prevalence of psoriasis in patients with a family history of psoriasis was 32.9% (n=45/137, 95% CI 25.0 to 40.7). Patients with and without psoriasis did not differ in age, sex or HLA-B27 positivity (table 1). However, patients with rather than without psoriasis more often reported a family history of psoriasis (40.5% vs 16.4%; $p<0.0001$), dactylitis (24.3% vs 10.7%; $p<0.001$) and enthesitis (59.1% vs 47.5%; $p=0.02$). At the clinical examination (table 2), patients with psoriasis had higher BMI (24.6±4.5 kg/m^2 vs 23.8±3.9 kg/m^2; $p=0.05$) and a higher synovitis score (0.4±1.4 vs 0.1±0.6; $p=0.004$). The two groups did not differ in spinal mobility, except for cervical spine rotation, which was decreased in patients with psoriasis ($p=0.05$). The prevalence of patients who had a history of inflammatory arthritis was 36.9%, and it did not differ between groups.

Association of psoriasis, disease activity, function and quality of life

Table 3 compares function, quality of life and disease activity for patients with and without psoriasis. The presence of

Table 1 Demographic characteristics of patients with and without psoriasis

	Whole population N=692	Psoriasis N=115	No psoriasis N=577	p Value
Age (years, mean±SD)	33.3±8.5	33.2±7.8	33.3±8.6	NS
Male (%)	46.2	49.6	45.6	NS
HLA-B27 positive	58.3	53.1	59.3	NS
First localisation of clinical symptoms				
Buttock	16.9	14.8	17.3	NS
Lumbar spine	39.2	43.5	38.3	NS
Thoracic spine	11.3	13.9	10.7	NS
Cervical spine	3.3	3.5	3.3	NS
History or current symptoms of				
Anterior chest wall pain	44.7	51.3	43.3	NS
Peripheral arthritis	36.9	41.2	35.7	NS
Enthesitis	49.4	59.1	47.5	0.02
Dactylitis	13.0	24.3	10.7	<0.0001
Acute anterior uveitis	8.7	8.7	8.7	NS
Inflammatory bowel disease	5.2	5.5	5.2	NS

Data are percentages of patients unless indicated.
HLA, human leucocyte antigen; NS, not significant.

Table 2 Clinical features of patients with and without psoriasis

	Whole population N=692	Psoriasis N=115	No psoriasis N=577	p Value
BMI (kg/m^2)	23.9±4.0	24.6±4.5	23.8±3.9	0.05
Synovitis score (0–28)	0.2±0.8	0.4±1.4	0.1±0.6	0.004
Joint tenderness (0–53)	4.4±8.6	5.5±9.2	4.1±8.5	NS
Modified Schober's test (cm)	3.8±1.6	3.7±1.4	3.8±1.6	NS
Chest expansion (cm)	6.0±4.7	5.5±20	6.1±5.1	NS
Occiput-to-wall distance (cm)	0.8±1.9	0.9±1.8	0.7±2.0	NS
Tragus-to-wall distance (cm)	11.1±2.5	11.2±2.1	11.1±2.6	NS
Finger-to-floor distance (cm)	13.2±13.0	14.7±14.8	12.9±12.6	NS
Lateral spinal flexion (cm)	31.4±16.4	32.5±16.3	31.1±16.4	NS
Intermalleolar distance (cm)	110.3±38.0	108.1±23.3	110.7±40.4	NS
Cervical spine rotation (degree)	73.5±15.4	70.9±16.1	74.0±15.2.	0.05

Data are mean±SD.
BMI, body mass index; NS, not significant.

psoriasis was associated with more active disease (BASDAI 4.8±1.8 vs 4.4±2.0; p=0.05) and poorer functioning (BASFI 3.6±2.2 vs 3.0±2.3; p=0.006; SF-36 (physical function) 61.9±24.4 vs 66.9±24.9; p=0.04). In addition, SF-36 social functioning scores were lower for patients with rather than without psoriasis (53.8±27.0 vs 59.6±27.2; p=0.04).

Laboratory values

The CRP level was significantly higher in patients with than without psoriasis (11.4±16.8 vs 8.6±14.2 mg/dl; p=0.02), as were levels of total cholesterol (5.2±1.2 vs 4.9±1.1 mmol/l; p=0.01) and triglycerides (1.3±0.9 vs 0.9±1.1 mmol/l; p=0.02) (table 4).

Psoriasis and imaging features

Among all patients, the prevalence of radiographic evidence of sacroiliitis and MRI evidence of active inflammatory lesions at the sacroiliac level was 15.3% and 19.2%, respectively, and did not differ by the prevalence of psoriasis (table 5). In addition, the two groups did not differ in the modified Stoke ankylosing spondylitis spine score score or MRI evidence of active inflammatory lesions at the spinal level. By contrast, PDUS of Achilles tendons revealed an association of psoriasis and bone erosions (15.4% vs 4.2%; p=0.0003) and abnormal vascularisation (6.5% vs 1.9%; p=0.04).

Factors associated with psoriasis

The dependent variables selected for regression analysis were BASDAI and BASFI scores, SF-36 physical and social functioning scores, BMI, cholesterol and triglyceride levels, the presence of dactylitis and enthesitis, synovitis score, cervical spine rotation and family history of psoriasis. Multivariate regression analysis for 597 patients revealed psoriasis associated with increased BASFI score (OR 1.1, 95% CI 1.0 to 1.2; p=0.03), increased cholesterol level (OR 1.2, 95% CI 1.0 to 1.5; p=0.02), dactylitis (OR 2.6, 95% CI 1.5 to 4.6; p=0.0006) and a family history of psoriasis (OR 3.8, 95% CI 2.3 to 6.1; p<0.0001).

DISCUSSION

We found a prevalence of 16.6% for psoriasis in our large cohort of patients (n=692) with recent IBP suggestive of AS, which is slightly lower than the 24% found in a similar but smaller 'early spondyloarthritis clinic' cohort of 68 patients with recent IBP.[27] In the German Spondyloarthritis Inception Cohort, the prevalence of psoriasis was 8.1% for patients (n=236) with a definite diagnosis of axial spondyloarthritis according to the New York or the European Spondylarthropathy Study Group criteria.[28] Although these frequencies differ slightly among the three cohorts, probably because of differences in recruitment, they highlight that psoriasis is more frequent in patients with

Table 3 Disease activity, function and quality of life in patients with and without psoriasis

	Whole population N=692	Psoriasis N=115	No psoriasis N=577	p Value
BASDAI (0–10)	4.5±2.0	4.8±1.8	4.4±2.0	0.05
BASFI (0–10)	3.1±2.3	3.6±2.2	3.0±2.3	0.006
HAQ-AS score (0–3)	0.8±0.7	0.9±0.7	0.8±0.7	NS
SF-36 domains (0–100)				
Physical functioning	66.1±24.8	61.9±24.4	66.9±24.9	0.04
Physical role	44.7±39.6	45.6±37.0	44.5±40.1	NS
Emotional	53.4±41.8	54.8±43.1	53.1±41.6	NS
Vitality	37.1±19.7	36.3±20.2	37.2±19.6	NS
Emotional wellbeing	55.9±19.7	55.1±19.8	56.1±19.7	NS
Social functioning	58.6±27.2	53.8±27.0	59.6±27.2	0.04
Bodily pain	47.3±24.2	45.2±22.0	47.7±24.6	NS
General health	46.4±18.5	46.1±17.8	46.4±18.7	NS
ASQoL (0–18)	9.3±4.9	9.9±4.8	9.2±5.0	NS

Data are mean±SD.
ASQoL, ankylosing spondylitis quality of life scale; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; HAQ-AS, health assessment questionnaire for ankylosing spondylitis; NS, not significant; SF-36, medical outcomes survey short-form 36.

Table 4 Laboratory data for patients with and without psoriasis

	Whole population N=692	Psoriasis N=115	No psoriasis N=577	p Value
CRP level (mg/dl)	9.1±14.6	11.4±16.8	8.6±14.2	0.02
ESR (mm/h)	14±15.9	16.0±18.7	13.6±15.2	NS
Total cholesterol level (mmol/l)	5.0±1.2	5.2±1.2	4.9±1.1	0.01
HDL cholesterol level (mmol/l)	1.5±0.4	1.4±0.4	1.5±0.5	NS
Triglycerides level (mmol/l)	1.0±1.7	1.3±0.9	0.9±1.1	0.02
Glucose (mmol/l)	4.7±0.6	4.8±0.6	4.7±0.7	NS

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HDL, high-density lipoprotein; NS, not significant.

Table 5 Imaging features in patients with and without psoriasis

	Whole population N=692	Psoriasis N=115	No psoriasis N=577	p Value
Standard x-rays				
Hip involvement	5.2	4.5	5.4	NS
Bilateral sacroiliitis	15.3	14.4	15.5	NS
mSASSS (mean±SD)	1.1±2.9	1.2±2.9	1.0±2.9	NS
MRI				
Bilateral active inflammatory lesions (sacroiliac joints)	19.2	15.7	19.9	NS
Active inflammatory lesions (spine)	21.2	23.8	20.6	NS
Ultrasonography of Achilles tendon	N=390	N=78	N=312	
Abnormal thickness	10.5	14.5	9.5	NS
Bone erosion	6.4	15.4	4.2	0.0003
Vascularisation	2.8	6.5	1.9	0.04

Data are percentages unless indicated.
mSASSS, modified stoke ankylosing spondylitis spine score.

early inflammatory axial disease than in the general population, between 1.5% and 3% in Europe and North America.[1 2] Although psoriasis most often precedes the onset of peripheral arthritis or definite PsA according to the CASPAR criteria,[16 29 30] for 79% of our patients it also antedated IBP. This finding reinforces the concept of psoriatic spondyloarthritis independent of the HLA-B27 status but with a strong familial aggregation. Indeed, HLA-B27 in this cohort was recently found to be associated with a lower frequency of psoriasis in patients who fulfilled at least one of the spondyloarthritis criteria.[21] In addition, we found, as did others, that a family history of psoriasis was an independent risk factor associated with psoriasis (OR 3.8), which suggests that class I major histocompatibility complex genes other than the HLA-B allele B27 and/or non-major histocompatibility complex genes play a role in the genetic susceptibility of this condition.[31 32]

Several studies have recently provided evidence that people with psoriasis[33 34] and those with AS or spondyloarthritis are at an increased risk of cardiovascular and cerebrovascular diseases.[35 36] Although the causal factors underlying this latter association have not been fully elucidated, the association probably results at least partly from chronic systemic inflammation and the atherogenic profile frequently encountered in people with these conditions. Likewise, patients with PsA may be even more prone to cardiovascular comorbidity than those with psoriasis without arthritis.[37] To determine whether psoriasis might influence the inflammation and the lipid profile in patients with IBP, we assessed levels of CRP, total cholesterol and

triglycrides and found all these factors but not glycaemia higher in patients with than without psoriasis; the levels of cholesterol remained significantly associated with psoriasis on multivariate analysis. Whether these lipid modifications reflect a true increased cardiovascular risk is unknown. However, these findings suggest that the presence of psoriasis should be taken into account when evaluating the cardiovascular profile of patients with IBP, especially with the long-term prescription of non-steroidal anti-inflammatory drugs, given their cardiovascular side effects.[38]

Another noteworthy finding from our study is that psoriatic patients had high BASDAI and BASFI scores, reflecting more active and severe disease, and decreased quality of life, as assessed by two domains of the SF-36. A few studies have evaluated the clinical differences between AS and axial PsA.[39–41] The studies found axial PsA frequently associated with peripheral involvement, as we observed in our patients with recent IBP. They also found overall that axial PsA is less severe in terms of clinical manifestations and mobility impairment than is AS. These findings contrast with our results, probably because of the greater disease duration and severity of AS in patients in the previous studies.[39 40] Indeed, the DESIR cohort is characterised by spondyloarthritis patients with short disease duration, with a mean duration of IBP of 1.5 years.

In addition to finding an association of psoriasis and clinical disease activity, functional status and lipid profile, we found psoriasis associated with peripheral features: dactylitis, synovitis and enthesitis, and in particular bone erosions and abnormal vascularisation on PDUS of the Achilles tendons. Even if our study does not demonstrate any causal relation, these data suggest that psoriatic inflammation might contribute directly or indirectly to increased severity of disease and provide additional support for the theory that enthesitis is a pivotal clinical feature of psoriasis in patients with recent IBP.[42] Of note, our findings extend those from several reports showing that subclinical enthesopathy can be found with MRI or PDUS in patients with psoriasis and without peripheral arthropathy.[43 44]

According to Helliwell and colleagues,[45 46] the axial involvement observed in patients with PsA could differ from that observed in AS patients. The features that could often be seen by x-rays in association with psoriasis are asymmetrical sacroiliitis, non-marginal and asymmetrical syndesmophytes, paravertebral ossification and frequent involvement of the cervical spine. In our study, although we found a decrease in cervical spine rotation in patients with psoriasis, we did not find any association of psoriasis and imaging features of the spine or sacroiliac joints, but again this may be related to the short disease duration of patients enrolled in our cohort. Unfortunately, we were unable to compute the prevalence of PsA in our cohort of patients using the majority of classification criteria for PsA, including the CASPAR, due to the lack of both peripheral x-rays and the search for the rheumatoid factor.

Our study has strengths and limitations. The DESIR cohort allowed us to study the impact of psoriasis per se in a large (n=692) and unique population of patients with recent, well-phenotyped IBP. However, diagnostic bias may have led to an underestimation of the prevalence of psoriasis. Indeed, the presence or absence of psoriasis was recorded by the rheumatologists who recruited patients. Psoriasis may be present but also may be hidden, for instance, under the breasts, around the umbilicus or in the hairline or may be misdiagnosed by rheumatologists.[47] Also, the severity of psoriasis was not systematically evaluated in the DESIR cohort, and quantifying the cumulative effects of its severity would have been interesting. Finally, the exclusion of patients with mild axial disease may also have introduced a selection bias.

In summary, we found that in patients with recent IBP, psoriasis is associated with active, severe axial disease and frequently concomitant enthesopathy, dactylitis and bone erosions at the calcaneus.

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Competing interests None.

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Ethics approval This 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.

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Notes