Dactylitis in enteropathic spondyloarthritis

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Abstract

Objective

Dactylitis has long been recognised as one of the significant features of spondyloarthropathies. In the literature, the prevalence of dactylitis in enteropathic spondyloarthritis (EASpA) ranges between 2% and 4%. The aim of this study was to identify the prevalence of dactylitis in EASpA patients and to investigate its association with clinical subset and with articular and bowel disease activity.

Methods

78 EASpA patients and 78 controls were enrolled for this study. All patients and controls underwent a rheumatological and a gastroenterological clinical examination. Demographic and clinical features were recorded. Diagnosis of dactylitis was made by physical examination and was evaluated using the Leeds Dactylitis Instrument (LDI).

Results

In our study the prevalence of dactylitis in EASpA was 15.38%, mainly in patients with Crohn's disease (CD) and peripheral arthritis. A significantly higher articular and bowel disease activity was found in patients with dactylitis compared to those without it. The family history of psoriasis represented a predictor of occurrence of dactylitis. Finally, a significant correlation between disease activity and LDI score was found in EASpA.

Conclusion

The results of our study showed a high prevalence of dactylitis in EASpA. It was more frequent in patients with CD and peripheral involvement with a higher articular disease activity, confirming that dactylitis may be a severity marker and a prognostic factor for EASpA. The significant correlation between disease activity and LDI score could address LDI as a potential tool of assessment of dactylitis.

Key words

enteropathic arthritis, dactylitis, inflammatory bowel disease, spondyloarthropathies

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Introduction

Musculoskeletal manifestations are the most common extra-intestinal findings of inflammatory bowel disease (IBD) with frequency ranging from 16% to 39% depending on the diagnostic criteria used and on patient selection (1-8). In about 10% of IBD patients, the onset of musculoskeletal manifestations can occur at the same time with first phases of the disease and occasionally before (9).

IBD arthritis, recognised also as enteropathic spondyloarthritis (EASpA) are divided into two different clinical subsets: axial (including sacroiliitis with or without spondylitis) and peripheral joint involvement.

The spectrum of axial involvement ranges from inflammatory lower back pain with or without radiological evidence of sacroiliitis (sometimes asymptomatic) to spondylitis characterised by the classic clinical and radiologic features of the idiopathic ankylosing spondylitis (AS). It is found to be present in a range between 2% and 16% of IBD patients, with a higher prevalence in Crohn's disease (CD) patients than in ulcerative colitis (UC) ones. The prevalence of sacroiliitis is between 10% and 25% for spondylitis and from 30% to 36% for sacroiliitis (10-12).

Peripheral involvement is a common complication in both CD and UC, with high prevalence (range: 0.4–34.6%) in patients with IBD. It is reported to be more frequent in CD than UC (20% and 10%, respectively) (13) and it meanly affects the joints of the lower limbs (14).

Another clinical feature of peripheral involvement is dactylitis, a characteristic and highly specific feature of SpA. Until today, available data on the prevalence of dactylitis in patients with EASpA are reported in studies by Salvarani *et al.* (4) and Palm *et al.* (15), who reported a prevalence of 2% and 4%, respectively.

The aim of this study was to evaluate the prevalence of dactylitis among patients affected by EASpA and to investigate its possible association with clinical subset and with articular and bowel disease activity.

Materials and methods

Study design

The present study included 78 patients affected by EASpA (52 female and 26 male; mean age ± SD: 46.19±11.72yrs; range: 21–69yrs), consecutively admitted to the Spondyloarthropathy Research Unit of University "Federico II" of Naples, between December 2012 and December 2013.

The diagnosis of UC and/or CD was made by one of our Authors (FM and/or FC) and based on clinical, endoscopic and histological evaluation (16). The diagnosis of EASpA was made according to the ESSG criteria (17).

Control subjects, matched with cases for age and gender, were recruited from the hospital staff. Both patients and controls underwent a rheumatological clinical examination and demographic data (age, gender, ethnicity, current and previous smoking habit, duration of smoking habit) were recorded. For each patient we also recorded the disease characteristics (age of onset, disease duration, subset of disease and disease activity) and the laboratory tests (rheumatoid factor [RF], erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]).

EASpA patients were classified on the basis of the articular involvement into peripheral and axial subsets. Patients with peripheral subset were classified in three forms (type 1, type 2 and type 3) according to the classification proposed by our research group (8).

Articular disease activity was calculated by DAS28 for peripheral subset and BASDAI for axial subset. Bowel disease activity was calculated according to the Harvey-Bradshaw Index (HBI) (18), and the Simple Clinical Colitis Activity Index (SCCAI) (19) for CD and UC, respectively.

Diagnosis of dactylitis, defined as an acute diffuse swelling of a digit with painful inflammatory changes, or chronic, where the digit remains swollen despite the disappearance of acute inflammatory changes, was made by physical examination by two clinicians (RP and RS); and was confirmed and measured using the Leeds Dactylitis Instrument (LDI). The LDI measures the ratio of the circumference of the affected digit to the circumference of the digit on the opposite hand or foot: using a minimum difference of 10%

to define a dactylitic digit. The ratio of circumference is multiplied by a tenderness score. The clinician squeezes the affected fingers with moderate pressure and documents the patient's response: 0=no tenderness, 1=tender, 2=tender and winces, and 3=tender and withdraws (20).

Informed consent was obtained from all subjects and the study protocol was approved by the local Ethics Committee.

Statistical analysis

Statistical analysis was performed with the SPSS 16 system (SPSS Inc., Chicago, IL, USA). Continuous data were expressed as means ± SD, and categorical variables were expressed as %. To compare continuous variables an independent sample *t*-test was performed. To analyse categorical data, the chi-square test was performed. When the minimum expected value was <5, the Fisher's exact test was used**.** To adjust for all of the other demographic and clinical variables and to evaluate the relative risk (RR) a multivariate logistic regression analysis was adopted, with the presence of dactylitis as the dependent variable and major clinical and demographic characteristics as independent variables. Correlation was assessed using the Pearson's linear correlation coefficients (r). All the results are presented as 2-tailed values with statistical significance if *p*-values <0.05.

Results

The demographic characteristics of the patients with EASpA are reported in Table I.

Of the 78 patients with EASpA, 44 and 34 were diagnosed as being affected by CD and UC, respectively. Twenty-seven out of 78 EASpA patients showed axial and 51 peripheral involvement. Twenty of these had polyarticular and 31 oligoarticular subset (Table I). Type 3 subset of peripheral form was not found in our population study. Disease duration and disease activity are reported in Table I for all patients and for each subset of EASpA.

Among 78 patients EASpA, 12 showed acute dactylitis, with a prevalence of 15.38%. Three of the 12 EASpA patients with dactylitis (25%) were male and 75% were female. The mean age (±SD) was 47.92 (±10.37) yrs and the mean disease duration of the articular involvement was 7.75 (±3.69) yrs (Table II). Eight of the 12 patients with dactylitis had a single digit involved, and 4 (33.33%) had multiple digits affected. In detail, fingers were more frequent involved than toes (82.35% *vs*. 17.65%, respectively), and the second digit was the most frequent localisation (47.06%). The mean number of digits affected per patient was 1.42. The Leeds dactylitis index for each patient is shown in Table III.

Dactylitis was evidenced more fre-

Table I. Characteristics of the study population.

Characteristics	EASpA patients	Controls	*p*-value*
n.	78	78	
F/M	52/26	52/26	1.000
mean age ± SD	46.18 ± 11.72	43.07 ± 9.53	0.834
disease duration of IDB, mean ± SD	7.23 ± 5.91	NA	NA
disease duration of arthritis, mean ± SD	6.75 ± 4.26	NA	NA
BASDAI, mean ± SD	4.23 ± 1.56	1.06 ± 0.21	*p*<0.001
DAS28, mean ± SD	5.15 ± 1.04	1.72 ± 0.32	*p*=0.015
LEEDs dactylitis index, mean ± SD	3.34 ± 1.92	1.21 ± 0.84	*p*=0.001
SSCAI, mean ± SD	8.21 ± 3.80	1.32 ± 1.24	*p*=0.002
HBI, mean ± SD	9.95 ± 3.14	1.54 ± 0.57	*p*=0.001
ESR, mean ± SD (n.v.: 10 - 20)	21.27 ± 19.07	15.12 ± 8.65	*p*=0.029
CRP, mean ± SD (n.v.: <5.00)	4.87 ± 10.95	3.75 ± 1.56	*p*=0.047
Dactylitis, n. patients (%)	12 (15.38)	1 (1.28)	*p*<0.001
Subset of arthritis			
Axial, n. patients	27	NA	
Peripheral, n. patients	51	NA	NA
Subset of inflammatory bowel disease			
Ulcerative colitis, n. patients	34	NA	
Crohn disease, n. patients	44	NA	NA

*NA: not applicable; EASpA: enteropathic spondyloarthritis; IBD: inflammatory bowel disease; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; DAS28: Disease Activity Score 28; HBI: Harvey-Bradshaw Index; SCCAI: Simple Clinical Colitis Activity Index; CRP:C-reactive protein; ESR: erythrocyte sedimentation rate.

Table II. Clinical and disease characteristics of EASpA patients.

Characteristics	EASpA patients		*p*-value*
	With dactylitis	Without dactylitis	
n.	12	66	
F/M	9/3	43/23	0.163
mean age ± SD	47.92 ± 1.37	45.86 ± 12.99	0.580
disease duration of IDB, mean age ± SD	6.94 ± 4.98	7.68 ± 5.66	0.364
disease duration of arthritis, mean age ± SD	7.25 ± 4.39	6.65 ± 4.28	0.720
BASDAI, mean ± SD	2.98 ± 1.50	4.08 ± 1.51	*p*=0.047
DAS28, mean ± SD	4.78 ± 1.27	3.45 ± 1.10	*p*<0.001
LEEDs index, mean ± SD	3.34 ± 1.92	NA	NA
SSCAI, mean ± SD	11.25 ± 0.21	8.02 ± 3.84	*p*=0.249
HBI, mean ± SD	12.52 ± 3.03	9.23 ± 2.84	*p*=0.003
ESR, mean ± SD (n.v.: 10 - 20)	25.27 ± 17.24	20.48 ± 19.46	*p*=0.450
CRP, mean ± SD (n.v.: <5.00)	5.02 ± 1.28	5.25 ± 2.85	*p*=0.914
Subset of arthritis			
Axial, n. patients	1	26	
Peripheral, n. patients	11	40	*p*=0.038
Subset of inflammatory bowel disease			
Ulcerative colitis, n. patients	2	32	
Crohn disease, n. patients	10	34	*p*=0.041

*NA: not applicable; EASpA: enteropathic spondyloarthritis; IBD: inflammatory bowel disease; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; DAS28: Disease Activity Score 28; HBI: Harvey-Bradshaw Index; SCCAI: Simple Clinical Colitis Activity Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

Table III. Clinical and disease characteristics of EASpA patients with dactylitis.

Case	subset	Number of Digit	Digit		Leeds dactylitis	DAS 28	BASDAI	Pearson's linear correlation coefficients (r)
			right	Left				
I	Peripheral	1	II(F)		2.38	3.9	2.1	
II	Peripheral	2	III(F)	II(T)	5.87	5.3	2.4	
III	Peripheral	1	IV(F)		2.25	3.8	2.2	
IV	Peripheral	1		II(F)	1.10	2.9	2.3	
V	Peripheral	2	II(T)	V(F)	4.31	4.6	2.2	
VI	Peripheral	1		III(F)	2.28	3.9	2.1	r=0.617, p=0.033‡
VII	Peripheral	1	II(F)		3.30	5.1	2.7	
VIII	Peripheral	1		II (F)	2.35	4.6	2.7	
IX	Peripheral	3	II (T)/IV (F)	III (F)	7.80	5.6	2.1	
X	Peripheral	1	III(F)		3.39	4.1	2.6	
XI	Peripheral	1	III(F)		1.21	3.1	6.4	r=-0.194, p=0.681‡
XII	Axial	2		II (F)/ V(F)	3.35	2.8	5.9	

‡Pearson's linear correlation coefficients between Leeds Dactylitis Index and DAS 28 (or BASDAI); EASpA: enteropathic spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; F: fingers; T: toes.

quently in EASpA patients with peripheral subset compared to patients with axial involvement (21.57% *vs*. 3.70%; *p*=0.038) (Table III), and the peripheral subset represented a predictor of occurrence of dactylitis with a RR of 1.34 (95% CI 0.98–1.84). In EASpA peripheral subset, the dactylitis was significantly more frequent in patients with polyarticular involvement compared to those with oligoarticular involvement (40.00% *vs*. 6.45%; *p*=0.014) and the RR of developing dactylitis in EASpA patients with polyarticular involvement was 2.15 (95% CI 1.31–3.53). Moreover, in EASpA patients with peripheral involvement a significantly higher disease activity was found in patients with dactylitis (DAS28=5.15±1.05) compared to those without dactylitis (DAS28=3.45±1.10) (*p*=0.0001). In patients with dactylitis, a direct correlation was found between Leeds dactylitis index and DAS28 (r=0.617, *p*=0.033) (Table III).

Moreover, EASpA patients with dactylitis showed a significantly higher prevalence of extra-articular manifestations (EAMs) (58.33%) compared to those without dactylitis (27.28%) (*p*=0.034) and the RR of developing dactylitis in EASpA patients with EAMs was 2.14 (95% CI 1.15–3.97). Finally, a high prevalence of dactylitis was found in EASpA patients with family history of psoriasis in relatives of first and/or second degree (53.33%) compared to those without it (6.35%) (*p*<0.0005); family history of psoriasis was a predictor of occurrence of dactylitis with a RR of 6.29 (95% CI 2.18–14.08).

Stratifying population according to inflammatory bowel disease, the dactylitis was more frequent in patients with CD (22.73%) than in those with UC (5.88%) (*p*=0.041); the RR of develop dactylitis in CD patients was 1.62 (95% CI 1.15–2.28). Moreover, in patients with CD, a significantly higher bowel disease activity was found in patients with dactylitis compared to patients without dactylitis (*p*=0.003) (Table II).

Discussion

Dactylitis represents a characteristic and highly specific manifestation of SpA (21-24) and its prevalence ranges from 4% to 23.6% (25- 27).

However, two studies have shown in EASpA, a low frequency, ranging from 2% to 4% (4, 15). On the other hand, data from our study show that dactylitis can occur with high frequency (15.38%) also in EASpA patients, mainly in patients with CD and peripheral arthritis.

However, a significantly higher articular and bowel disease activity was found in our patients with dactylitis compared to those without it. These could have lead to dactilytis as a consequence both of high-grade local and systemic inflammation.

In a recent cross-sectional retrospective study by Payet *et al*., the authors showed that dactylitis was found in 21.5% of SpA patients and it was more frequent in undifferentiated forms and less frequent in axial subset (28). Moreover, toes were more frequently involved than fingers and the most frequent localisation was represented by the second digit. In addition, dactylitis was evidenced more frequently in SpA patients with peripheral involvement; instead it was associated with degree of severity of SpA (28).

On the other hand, in our EASpA group showing dactylitis, fingers were more frequently involved than toes and the second digit was the most frequent localisation. Furthermore, dactylitis was more frequent in EASpA patients with peripheral subset than in with patients with axial involvement. Moreover, in EASpA peripheral subset, the dactylitis was significantly more frequent in patients with polyarticular involvement than in those with oligoarticular involvement. The peripheral subset represented also a predictor of occurrence of dactylitis.

Additionally, in our study, a high prevalence of dactylitis was found also in EASpA patients with psoriasis' family history compared to those without it. Moreover, EASpA patients with dactylitis showed a significantly higher prevalence of EAMs (58.33%) than those without dactylitis (27.28%) (*p*=0.034) and the RR of develop dactylitis in EASpA patients with EAMs was 2.14 (95% CI 1.15–3.97). The EAMs and family history of psoriasis represented predictors of occurrence of dactylitis.

Notably, dactylitis represents also one of the hallmark features of PsA (29, 30), due to its high frequency, and is one of the features of ClASsification for Psoriatic Arthritis (CASPAR) criteria (31-33). As reported in other studies on PsA (34, 35), also in our study, dactylitis, is slightly more frequent in polyarticular than in non-polyarticular subset.

In previous studies focused on IBD cohorts clinical diagnosis of dactylitis has not been evaluated by using instruments (36-40). We chose LDI with the aim of assessing dactylitis and studying its prevalence in patients with EASpA; in fact, LDI can provide a quantification of both the size of the swollen digit and the tenderness, and can differentiate between tender and non-tender dactylitis (20, 41).

We found also a significant direct correlation between LDI score and articular disease activity (DAS28) in patients with peripheral involvement, confirming that dactylitis could be considered a potential marker of EASpA activity. The significant correlation between disease activity and LDI score, found in our patients, could suggest to use LDI as a potential tool of assessment of dactylitis in EASpA and future studies are necessary to confirm this.

This study has some limitations. Firstly, a cross-sectional study enrolling consecutive EASpA patients only should be more appropriate for the evaluation of prevalence of dactylitis in these patients. Moreover, the use of DAS28 for the evaluation of disease activity is formally validated for rheumatoid arthritis (RA) (42, 43), but it is not for peripheral involvement in SpA. In fact, the 28-joint count excludes the feet, as well as the ankles and the DIP joints of the fingers in the evaluation of articular involvement; the use of 28-joint count, instead of *e.g.* the 66/68 joint count, may have underestimated clinical inflammatory joint involvement in our patients with toe dactylitis. Nevertheless, DAS28 has been used in randomised clinical trials for assessment of disease activity in PsA (44, 45, 46).

In conclusion, the results of our study showed a high prevalence of dactylitis (15.38%) in EASpA patients. It was more frequent in patients with peripheral involvement (in detail, polyarticular subset), as found also in other studies (27, 28) and in patients with a higher disease activity, confirming that dactylitis may be a severity marker and a prognostic factor for EASpA.

Data from our study can suggest that in EASpA patients dactylitis clinically and LDI-evaluated can suggest a high peripheral and bowel activity. In the next future, LDI could be investigated as a tool of assessment of dactylitis and disease activity also in EASpA.

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