Patients developing inflammatory bowel disease before spondyloarthritis manifest significantly higher rates of enthesitis: findings from a single-center real-life cohort

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Background.

Inflammatory bowel diseases (IBD) and spondyloarthritis (SpA) share numerous pathogenetic mechanisms and therapeutic options (i.e. biologics targeting TNFα and IL-23 inhibitors), especially in the case of psoriatic arthritis (PsA). Musculoskeletal symptoms may precede or follow intestinal manifestations leading to two phenotypes with potential differences or similarities. From a clinical standpoint, subclinical enthesitis has been observed by ultrasonography in patients with IBD.

Aims.

To analyze a cohort of patients diagnosed with both SpA/PsA and IBD and to compare the clinical features of patients presenting first with rheumatological manifestations (SpA>IBD) versus those developing IBD first (IBD>SpA).

Methods.

This is a retrospective study of patients with IBD and SpA/PsA being followed by a multidisciplinary team of gastroenterologists and rheumatologists at the Humanitas ImmunoCenter between March 2022 and March 2023. From all patients, demographic data and clinical characteristics including comorbidities, complications and therapeutic history were compared between SpA>IBD and IBD>SpA.

References.

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Results.

The analysis included 48 patients (**Table 1**) with SpA/PsA and IBD. The IBD>SpA group showed **significantly higher rates of enthesitis both at baseline (p=0.015) and during the course of disease (p=0.043)** compared to SpA>IBD group. Other clinical differences did not reach statistical significance but patients with SpA>IBD tended to have more frequently peripheral arthritis (p=0.091) and elevated C-reactive-protein (value >1 mg/dl; p=0.061), used more NSAIDs (p=0.064), were more frequently obese (p=0.056) and referred gastro-esophageal reflux disease (p=0.085).

Variable	IBD onset (IBD>SpA) [n=36]	Arthritis onset (SpA>IBD) [n=12]	P value
Age (years) (median; IQR)	49 (45-52)	51 (43-59)	0.707
Female gender [n (%)]	23 (64%)	5 (41%)	0.176
Surgery for IBD [n (%)]	16 (44%)	4 (33%)	0.499
Chron Disease [n (%)]	19 (53%)	9 (75%)	0.176
Ulcerative Colitis [n (%)]	17 (47%)	3 (25%)	0.176
Peripheral arthritis [n (%)]	**24 (67%)**	**11 (92%)**	**0.091**
Axial Involvement [n (%)]	25 (69%)	7 (58%)	0.480
Psoriasis [n (%)]	16 (44%)	4 (33%)	0.499
Dactylitis [n (%)]	2 (6%)	0 (0%)	0.404
Enthesitis [n (%)]	**18 (50%)**	**2 (17%)**	**0.043**
Nail Disease [n (%)]	7 (19%)	0 (0%)	0.098
Obesity [n (%)]	**2 (6%)**	**3 (25%)**	**0.056**
Fibromyalgia [n (%)]	5 (14%)	2 (17%)	0.813
Hypercholesterolemia [n (%)]	4 (11%)	2 (17%)	0.614
Hypertension [n (%)]	7 (19%)	3 (25%)	0.682
Malignancy [n (%)]	7 (19%)	1 (8%)	0.371
Anxiety or Depression [n (%)]	5 (14%)	2 (17%)	0.813
MACEs [n (%)]	1 (3%)	2 (17%)	0.853
GERD [n (%)]	**1 (3%)**	**2 (17%)**	**0.085**
Fecal Calprotectin > 100 mg/Kg [n (%)]	13 (40%)	6 (56%)	0.380
CRP persistently > 1 mg/dL [n (%)]	**3 (13%)**	**7 (37%)**	**0.061**
Glucocorticoids [n (%)]	7 (20%)	1 (8%)	0.353
NSAID chronic use [n (%)]	**10 (29%)**	**7 (58%)**	**0.064**

Table 1 –Clinical and Demographical Characteristics of the cohort.

Variable	PsA [n=22]	SpA [n=29]	P value
Median Age (years) (median; IQR)	50±9.6 (IQ 95% 45.8-54.5)	48.8±2.4 (IQ 95% 43.9-53.6)	0.655
Males [n(%)]	12 (55%)	10 (35%)	0.152
Lenght of Disease (years) (median; IQR)	14.1 7.2 (IQ 95% 10.7-17.5)	11.5 10.7 (IQ 95% 7.4-15.6)	0.351
Articular onset [n(%)]	4 (18%)	9 (32%)	0.264
IBD onset [n(%)]	18 (83%)	19 (68%)	0.264
RCU [n(%)]	8 (36%)	13(44%)	0.543
Chron Disease [n(%)]	14 (64%)	16 (55%)	0.543
Intestinal surgery [n(%)]	11 (50%)	12 (41%)	0.540
Pheripheral Arthritis [n(%)]	**13 (59%)**	**24 (83%)**	**0.061**
Enthesitis [n(%)]	12 (55%)	10 (34%)	0.152
Dactilytis [n(%)]	1 (5%)	1 (3%)	0.842
Axial involvement [n(%)]	**16 (55%)**	**18 (83%)**	**0.046**
Smoking habits [n(%)]	15 (68%)	13 (44%)	0.097
Familiar History [n(%)]	**9 (41%)**	**5 (17%)**	**0.061**
Biological Therapy Multifailure [n(%)]	**13 (65%)**	**7 (29%)**	**0.017**

Table 2 – Clinical and Demographical Differences among PsA and SpA patients.

Nearly half of the patients (22/48, 46%) fulfilled also PsA classification criteria due to a familial or personal history of psoriasis, a nail disease or previous episodes of dactylitis.

PsA-like subgroup had peculiar features compared to other SpA patients (**Table 2**), including more common peripheral involvement (p=0.061), history of multiple therapeutic failures (p=0.017), family history of SpA (p=0.061), and current smoking habit (p=0.097). In terms of treatments possibly associated with the transition, the 11 of IBD>SpA cases that had received vedolizumab had a significantly higher frequency of elevated CRP (p=0.029) while none of the patients with SpA>IBD had been treated with IL-17A inhibitors.

Conclusions. In our real-world cohort of patients with IBD and SpA, **enthesitis may be the earliest clinical manifestation of SpA in patients already diagnosed with IBD** while the appearance of IBD in patients with SpA does not seem to be secondary to IL17A-targeting treatments.