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Occult radiological sacroiliac abnormalities in patients with inflammatory bowel disease who do not present signs or symptoms of axial spondylitis

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ABSTRACT

Objective. *To investigate radiological sacroiliac abnormalities in IBD patients without musculoskeletal symptoms and to determine the clinical and familiar differences between IBD patients with and without radiologic sacroiliac joint (SIJ) abnormalities. Subsequently, the patients with x-ray alterations were followed for 3 years in order to assess the onset of chronic inflammatory back pain (IBP).*

Methods. *81 patients (55 Crohn - CD- and 26 ulcerative rettocolitis - UC) with remittent and low active IBD, from a tertiary referral centre of gastroenterology Unit, were studied using SIJ x-rays. Differences in IBD clinical variables (activity and duration of CD and UC, extra-intestinal involvement, treatment with surgery and not, ESR and CRP levels), familiarity (for psoriasis, IBD, spondyloarthritis, coeliac syndrome), between patients with SIJ x-ray findings and without were investigated. Patients with radiological sacroiliac joint abnormalities were followed up clinically for 3 years and the onset of symptoms of chronic (higher than 3 consecutive months) IBP was investigated.*

Results. *22/81 patients (27.1%) showed radiological SIJ abnormalities at baseline: isolated sclerosis in 17/22 (77.3%) and localised erosions in 12/22 (54.5%). Radiological SIJ involvement did not correlate with IBD clinical and familial variables. All patients were HLA B27 negative. At 3 years, 4/22 patients (18.1%) presented chronic IBP symptoms with bone oedema at MRI.*

Conclusions. *In IBD, occult radiological SIJ alterations might precede the onset of axial symptoms but, in the absence of clinical signs, it is not possible to identify some IBD features or familiar predisposition that might be more frequent when SIJ abnormalities are involved. Clinical follow-up might be useful in these patients for a diagnosis of axial spondyloarthritis onset.*

Introduction

The involvement of sacroiliac joints (SIJ) is the major expression ofspondylitis associated to inflammatory bowel disease (IBD) and it is well known that the early detection of SIJ inflammation is essential to identify and treat the disease on time (1).

Otherwise, the SIJ abnormalities might be frequently under-diagnosed (2) and the onset of inflammatory processes might precede – even many years before – the emergence of symptoms (3).

Even if the magnetic resonance (MRI) is now widely accepted as the gold standard of SIJ involvement of SpA (4, 5) and also other new promising imaging techniques were studied (6), x-ray is still the cheapest and most accessible imaging technique to evaluate the pelvis. X-ray uses a limited quantity of ionising radiation and – even if less sensitive than MRI – is a specific diagnostic tool for low grade sacroiliitis in early SpA (7).

Previously, few studies demonstrated the presence of "occult" SpA disease in IBD patients without musculoskeletal symptoms (3, 8, 9) but did not evaluate the possible evolution in axial spondyloarthritis (aSpA) (10), or investigate any association with genetic and clinical risk factors, to detect a possible predictable pattern for future axial disease.

We aimed to investigate radiological SIJ abnormalities in IBD patients without musculoskeletal symptoms and to determine the clinical and familiar differences between IBD patients with and without radiologic sacroiliac (SIJ) abnormalities. Then, we aimed to clinically follow-up the patients with sacroiliac x-ray alterations and evaluate the onset of chronic inflammatory back pain (IBP).

Methods

Eighty-one Italian and Caucasian patients (55 Crohn [CD] and 26 ulcerative rettocolitis [RCU], 43 female and 38 male, 41.3±12.4 years old, min 18 years and max 68 years, BMI 22 (3.1), min 17 max 25, Caucasian race) with inactive (67) and low active (12) (either clinically or at endoscopy) disease without any signs and symptoms of inflammatory musculoskeletal involvement, were consecutively collected from gastroenterology clinics in a tertiary centre and successively studied with x-rays of SIJ (postero-anterior and dedicated oblique views).

At baseline, all patients did not have

symptoms and signs of entheses, joints or axial involvement. The signs were tested by an experienced rheumatologist with a full clinical examination (MASES, 68/66 joint count, and SIJ palpation and BASMI).

Exclusion criteria were: age <18 years, scoliosis, obesity (BMI>30), osteitis condensans in female, past pelvis trauma (including difficult childbirth for females), past spine surgery and injections, agonistic sport and loading work condition.

The local ethics committee approved the study (protocol no. 0005766 ref. no. 134/10) and informed consent, according to the Declaration of Helsinki, was signed by patients.

Abnormalities of SIJ were analysed independently and blindly by two expert rheumatologists (BF, GL), according to the New York definition: irregular joint space without well-defined erosions (score 1), small localised erosions and sclerosis (score 2), widening, narrowing or partial ankylosing (score 3), complete anlylosing (score 4). Interobserver variability of the two readers was evaluated in all patients. Only in doubtful cases of interpretation, magnetic resonance (MRI) was performed to confirm x-ray evaluation and examined by the rheumatogists. CT analysis was not performed for ethical reasons: excessive quantity of high ionising radiations, which was not justified by the clinical conditions.

The clinical and laboratory data of all patients, related to IBD, were analysed: disease activity (CDAI and Truelove score, confirmed by endoscopic evaluation by gastroenterologists [MM, BS]), duration of symptoms, bowel previous surgery, extra-articular involvement – erythema nodosum, uveitis – contemporaneous treatments (including steroids, salazopyrin, mesalazyn, azatiopryn, anti-TNF-alpha), ESR, CRP. Familiarity (for psoriasis, IBD, SpA, coeliac syndrome) and HLA B27 positivity (PCR analysis) were also investigated.

In the past, 77/81 (95%) received: high dosage of steroids (55/81), mesalazyn (53/81), salazopyrin (10/81), azatiopryn (16/81) and anti-TNF-alpha (9/81); 22/81 (27.1%) patients underwent bowel surgery for IBD. At the moment of study inclusion, only 3/81 were under treatment with anti-TNF-alpha.

Patients with radiologic SIJ abnormalities were successively clinically followed up for three years, and investigated for the onset of chronic (>3 consecutive months) inflammatory back pain (IBP) symptoms, defined using the Berlin criteria (10). Patients with chronic IBP were successively assessed with T2 fat suppression (STIR) and T1 contrast sequences at MRI, to define either bone oedema or osteitis in the very early phases of disease. In fact, even if STIR is commonly is considered sufficient to detect bone oedema, the use of gadolinium seemed more useful to better enhance the hyperintensity of signal and to show the increase in bone perfusion (osteitis) (3).

Statistical analysis

Means, standard deviations (SD), confidence interval and percentage were used to present the data, and the level of statistical significance (*p*) was considered to be lower than 0.05.

Normal distribution of each examined parameter was verified by Kolmogorov-Smirnoff test.

Interobserver variability of two observers of x-ray was evaluated with Kappa Cohen test.

Differences in age, duration of symptoms, ESR and CRP (continuous parameters) between patients with SJ x-ray abnormalities and without were analysed with the non-parametric Mann-Whitney test.

Differences in IBD activity (remittent/low active disease), previous bowel surgery (presence/absence), erythema nodosum and uveitis (presence/absence) and familiarity (for psoriasis, IBD, coeliac syndrome, SpA) (presence/absence) between patients with SIJ New York abnormalities and without were investigated using the Chi-square test.

Results

The clinical and laboratory data of patients are shown in Table I. None of the patients was HLA B27 positive.

22/81 (27.1%) patients showed SIJ abnormalities on x-ray: 17/22 (77.2%) isolated sclerosis and 5/22 (22.7%) localised erosions with sclerosis. In 10/22 the SIJ involvement was symmetric (45.4%): 6/10 isolated sclerosis, 4/10 localised erosions and sclerosis. None of the patients presented partial or complete ankylosis.

The inter-observer radiological evaluation was 0.9 (90%) of the K test. In 8 doubtful cases, MRI confirmed the presence of initial abnormalities with minimal sclerosis (but not erosions) of SIJ in 5 cases and was completely negative in 3 patients.

There were no significance differences of age, IBD clinical features (activity, duration, surgery, extra-intestinal involvement – erythema nodosum, uveitis), familiarity (for psoriasis/IBD/coeliac syndrome/SpA) or ESR/CRP levels among patients showing the presence or absence of radiological SIJ involvement.

At the time of radiological examination, the patients with SIJ radiological alterations were treated with steroids (2/22), mesalazyn (13/22) and salazopyrin (1/22). Previously, some of them had taken steroids (12/22) and anti-TNF-alpha (3/22) with suspension almost one year before evaluation.

Drugs for IBD were not washed out for ethical reasons, nor were other therapies added for the absence of gastrointestinal flares.

Three years after the first clinical evaluation, 4/22 patients (18.1%) presented the Berlin Criteria of IBP (3/4 two criteria and 1/4 only one). All of these patients showed SIJ bone oedema and osteitis at MRI (2/4 also showed erosions at MRI) and met the indication for anti-TNF-alpha treatment. None of these 4 patients had previously assumed biologic therapies.

Discussion

Our results showed that asymptomatic radiological SIJ abnormalities are present in 27% of patients. This datum is in agreement with the results of McEnnif *et al*. who demonstrated a high prevalence of sacroiliitis on x-ray (18%) and CT (32%) (2). Unlike McEnnif, we did not find patients with partial or complete ankylosis.

The presence of an "occult" disease before the onset of clinical manifestation in SpA was investigated previously

Table I. Demographic, clinical and laboratory findings in IBD patients with and without radiological SIJ involvement.

	Radiological SIJ positive patients (22/81; 27.2%)	Radiological SIJ negative patients (59/81; 72.8%)
Age (years)	45,1 ± 10,8	40 ± 12.5
CD/UC	16 (72.7%) / 6 (27.3%)	39 (66.1%) / 20 (33.9%)
Remittent/low active IBD	19 (86.4%) / 3 (13.6%)	49 (83%) / 10 (17%)
Duration of IBD symptoms (years)	10.8 ± 10,8	8 ± 5,9
Previous bowel surgery	4 (18.2%)	18 (30%)
Familiarity	Psoriasis: 3 (13,6%)	Psoriasis: 10 (16.9%)
	IBD: 1 (4.5 %)	IBD: 7 (11.9%)
	Spa: 3 (13.6%)	Spa: 1 (1,7%)
	Coeliac: 1 (4.5%)	Coeliac: 1 (1.7%)
Erythema nodosum	2 (9%)	3 (5%)
Uveitis	3 (5%)	2 (9%)
ESR (mm/h)	17.6 ± 8,4	20.6 ± 14.5
CRP (mg/dl)	0.44 ± 0,4	0.52 ± 0.43

in other issues: both sacroiliitis (3, 9) and entheseal involvement (8, 11-12) were found in asymptomatic patients. According to the data of Huerta-Sil *et al*. (7), our results showed that minimal abnormalities of SIJ on x-ray might precede the onset of a defined SpA in IBD patients. This datum might suggest a possible role of this old technique in early disease. On the other hand, mechanical conditions (excluded in this analysis) and other confounding factors can produce minimal abnormalities of SIJ on x-ray. In addition, previous treatment might modify the onset of clinical symptoms in IBD patients, such as anti-TNF-alpha, but all patients with initial SIJ abnormalities on x-ray had not received biologic treatments at baseline or during follow-up.

Unfortunately, our study did not detect any possible risk factor for SIJ involvement at baseline.

Firstly, no significant differences in duration of bowel symptoms have been found between patients with radiological sacroiliitis and without, in agreement with McEniff *et al*. (2) and Peeters *et al*. (13). On the other hand, both de Vlam (14) and Palm (15) *et al*. found that sacroiliitis was more prevalent in patients with a long history of IBD.

Further investigation on a larger number of patients should be conducted to better clarify this contradiction and to investigate the correlation between duration of IBD and severity of SIJ abnormalities.

Furthermore, our study indicates that SIJ involvement might not be related to gut activity, according to McEnnif *et al*. (3). These results might suggest that enteric disease and rheumatologic involvement are probably the consequence of different moments of pathogenesis pathways, in agreement with previous data on entheseal involvement in IBD (8), even if, previously, Mielants *et al*. hypothesised a possible link between gut histology and peripheral manifestation of spondyloarthritis (16). Therefore, we analysed only remittent and low active IBD and concluded that patients with high-active manifestations should be considered in future studies to confirm our data.

No significance association has been found between radiological SIJ involvement and bowel surgery, in agreement with other evidences regarding entheseal involvement in IBD (8), confirming the hypothesis of two possible mechanisms underlying SIJ and bowel inflammation.

Interestingly, none of our patients was HLAB27-positive: this datum showed the importance of imaging for SpA subclinical involvement in IBD.

In fact, HLA-B27 certainly has an important role in the pathogenesis of IBD manifestation and rheumatologic disease (17) but its prevalence in IBD is lower than in ankylosing spondylitis (9, 18) and is not frequently correlated to radiological sacroiliitis in IBD (9, 19-20). Furthermore, this aplotype shows a wide variation across populations and ethnic groups and could be absent in a small group of Italian Caucasian people such as ours.

Larger studies on other aplotytes should be conducted to better elucidate the correlation between genetic predisposition and SIJ involvement in IBD.

Finally, familiarity for psoriasis, coeliac syndrome, IBD and SpA has been investigated in all subjects but none of them correlates to radiological sclerosis or presence of erosion.

At present, there are no other studies available in the literature to confirm this datum.

Finally, after 3 years since the initial radiologic evaluation, 4 out of 22 patients developed a chronic IBP with MRI SIJ bone oedema, indicating that asymptomatic SIJ abnormalities on x-ray might precede in a low percentage later development of a SpA. This aspect might also suggest the importance of a clinical follow-up when axial involvement is suspected. However, larger studies are necessary to confirm the utility of SIJ x-ray scanning in early phases of IBD-related SpA. Furthermore, this observation of patients with SIJ abnormalities will continue for a longer period of time.

Key message

- SIJ x-ray abnormalities in IBD might be under-diagnosed and might precede the onset of axial SpA.
- It is not possible to identify IBD clinical or familiar factors of risk for subclinical x-ray sacroiliitis.

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