

High frequency of inflammatory back pain and other features of spondyloarthritis in patients with rheumatoid arthritis

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Abstract The aim of this study was to investigate the frequency of patients with rheumatoid arthritis (RA) who have inflammatory back pain (IBP) and meet the existing classification criteria for ankylosing spondylitis (AS) and spondyloarthritis (SpA). We included 167 patients fulfilling the ACR 1987 revised criteria for RA. After obtaining a medical history and performing a physical examination, standard pelvic X-rays for examination of the sacroiliac joints (SIJ) were ordered in all patients. A computed tomography (CT) or magnetic resonance imaging (MRI) of SIJ was performed in patients with suspected radiographic sacroiliitis and MRI of SIJ in those who have IBP but no radiographic sacroiliitis. IBP was defined according to both Calin and experts' criteria. The modified New York (mNY) criteria were used to classify AS, both ESSG and Amor criteria for SpA and ASAS classification criteria for axial SpA. There were 135 female and 32 male patients with a mean age of 54.8 years. The mean disease duration was 9.8 years. RF was positive in 128 patients (79.2 %) and anti-CCP in 120 patients (81.1 %). Twenty-eight patients with RA (16.8 %) had IBP (Calin criteria), and four (2.4 %) had radiographic sacroiliitis of bilateral grade 3. Three patients (1.8 %) fulfilled the mNY criteria for AS, 31 (18.6 %) ESSG and 26 (15.6 %) Amor criteria for SpA. Nine patients (five with MRI sacroiliitis) (5.3 %) were

classified as having axial SpA according to new ASAS classification criteria. This study suggests that the prevalence of SpA features in patients with RA may be much higher than expected.

Keywords Rheumatoid arthritis · Ankylosing spondylitis · Spondyloarthritis · Prevalence · Coexistence

Introduction

Spondyloarthritis (SpA) and rheumatoid arthritis (RA) are two most common forms of inflammatory arthritis [1, 2]. We previously found that the overall prevalence of SpA, including ankylosing spondylitis (AS), was 1.05 % in Turkey [3]. In this population-based epidemiological study, the prevalence for AS was found to be 0.49 % [3], and it was equal that of RA in the same population [4].

Rheumatoid arthritis typically presents as a symmetrical polyarthritis, affecting more women than men, and is linked with the presence of autoantibodies in the serum such as cyclic citrullinated peptide antibody (anti-CCP) and rheumatoid factor (RF) [5]. Axial skeletal involvement is rarely seen except cervical spine in RA [6]. In contrast, AS and related spondyloarthritis are characterized by axial disease involving the sacroiliac joints (SIJ) and the spine, causing inflammatory back pain (IBP). Peripheral arthritis is less common and mainly non-symmetrical oligoarticular and typically found in the lower limbs. Enthesitis and uveitis are other frequent findings. SpA is strongly associated with HLA-B27 [7–9]. The term “axial SpA” includes AS and undifferentiated SpA without radiographic sacroiliitis but with clinically predominant axial involvement [10]. According to the ASAS classification criteria for axial SpA [11], a patient with IBP and

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some further SpA features can be classified as having axial SpA if magnetic resonance imaging (MRI) sacroiliitis or HLA-B27 is present even in the absence of radiographic sacroiliitis. Therefore, the new definition “axial SpA” may help to establish an early diagnosis of axial SpA.

Coexistence of RA and AS has rarely been reported [12–21], but there is no data about the prevalence of IBP among RA patients. Furthermore, the frequency of patients with RA also fulfilling the existing classification criteria for AS and SpA has not been investigated previously.

The objective of our study was to determine the prevalence of IBP and sacroiliitis in patients with RA. We also aimed to estimate the frequency of RA patients who also fulfilled the European Spondyloarthropathy Study Group (ESSG) criteria [22] and/or Amor criteria [23] for the classification of SpA, and the modified New York (mNY) criteria [24] for the classification of AS. Moreover, RA patients with IBP were assessed for whether they fulfilled the ASAS criteria for the classification of axial SpA [11].

Methods

We included 167 patients with RA who fulfilled “the American Rheumatism Association 1987 revised criteria for the classification of RA” [25] in this study. The study was conducted in accordance with the recommendations of the Declaration of Helsinki. All patients gave informed consent.

A rheumatologist and two rheumatology fellows, using a standard questionnaire, obtained a detailed medical history and performed a complete physical examination in each patient. Standard pelvic X-rays for examination of the SIJ were ordered in all the patients. The radiographs were mixed with those of healthy controls and control AS patients. They were read blindly by an experienced rheumatologist (FO) and reported according to the established grading system [26]. In subjects whose pelvic X-rays showed suspicion of sacroiliitis, a computed tomography (CT) or MRI (STIR sequences) of SIJ was ordered to help in reaching a final consensus. In addition, MRI of SIJ was performed in RA patients who have IBP but have no radiographic sacroiliitis. CT and MRI investigations of SIJ were evaluated by an experienced radiologist (MM), unaware of the clinical and X-ray findings.

Inflammatory back pain was defined according to both Calin [27] and experts’ [28] criteria. The mNY criteria [24] were used to classify AS, and both the ESSG criteria [22] and Amor criteria [23] for SpA. A diagnosis of axial SpA was made if the ASAS classification criteria for axial SpA [11] were met.

HLA-B27 was investigated in patients who met any of the classification criteria for SpA (ESSG and Amor criteria) or AS (mNY criteria). Its typing was performed by serological methods.

Table 1 Demographic, clinical and laboratory features of patients with rheumatoid arthritis

Female <i>n</i> (%)	135 (80.8)
Mean age, years (SD)	54.8 (11.7)
Mean disease duration, years (SD)	9.8 (9.4)
Mean age at diagnosis, years (SD)	46.1 (13.0)
HAQ-DI (SD)	0.8 (0.7)
DAS-28 (SD)	3.8 (1.3)
ESR, mm/h (SD)	35.8 (23.1)
CRP, mg/L (SD)	14.7 (28.5)
Rheumatoid factor positivity (%)	79.2
Anti-CCP positivity (%)	81.1

Statistical analysis

Statistical analysis was done by using SPSS version 9.0 (Chicago, IL, USA). Data were given as mean \pm SD or proportion. Relationship between different parameters was evaluated by the “phi coefficient” or “Spearman’s rho.”

Results

Of the 167 RA patients included in the study, 135 were female (80.8 %) and 32 were male (19.2 %) with a mean age of 54.8 years. The mean disease duration was 9.8 years, and the mean age at diagnosis was 46.1 years. One hundred twenty-six patients with RA (79.2 %) had positive RF, and 120 (81.1 %) had positive anti-CCP. The mean serum titers of RF and anti-CCP were 141.8 IU/mL and 147.7 RU/mL, respectively. The demographic, clinical and laboratory features of patients are demonstrated in Table 1.

Twenty-eight patients with RA (16.8 %) had IBP (Calin criteria). Pelvic radiography could be performed in 164 patients with RA, and four of these patients (2.4 %) were reported to have bilateral grade 3 sacroiliitis. Among 23 patients with suspected sacroiliitis, CT of SIJ was performed in 10 patients and MRI of SIJ in 11. There was no sign of sacroiliitis on CTs, but MRI showed acute inflammation on SIJs in one patient. Classification steps for AS (mNY) and axial SpA (ASAS) are shown in Fig. 1.

The number of IBP patients with normal pelvic radiographs was 15 according to Calin criteria and 17 according to experts’ criteria. MRI of SIJ could be performed in 11 of them. Three patients in the first group and four in the latter showed sign of sacroiliitis on MRI.

HLA-B27 was investigated in 33 patients who met any of the classification criteria for SpA (ESSG and Amor criteria) or AS (mNY criteria). Clinical and laboratory features regarding SpA in RA patients are demonstrated in Table 2.

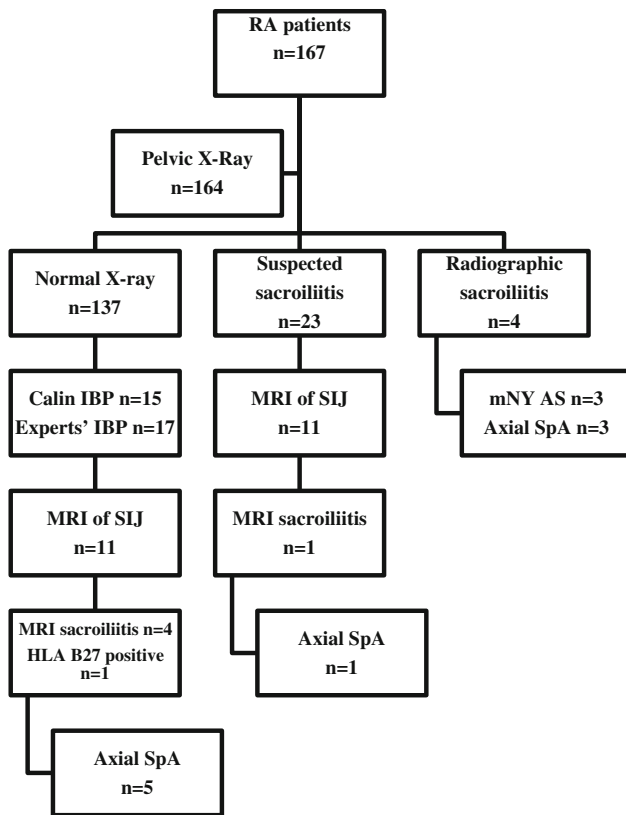


Fig. 1 Flow chart showing the classification steps for ankylosing spondylitis (mNY) and axial spondyloarthritis (ASAS)

Table 2 Frequency of spondyloarthritis features in rheumatoid arthritis patients

SpA feature (n = 167)	Number of patients (%)
Inflammatory back pain	
Calin criteria	28 (16.8)
Experts' criteria	19 (11.3)
Enthesitis	70 (41.9)
Enthesitis (radiographic)	54 (32.3)
Gluteal pain	59 (35.5)
Dactylitis	14 (8.4)
Asymmetrical oligoarthritis	11 (6.6)
Uveitis	3 (1.8)
Psoriasis	3 (1.8)
Previous genitourinary or gastrointestinal infection history	3 (1.8)
Family history	3 (1.8)
Inflammatory bowel disease	1 (0.6)
HLA-B27 positivity (n = 33)	3 (9.1)

Three of four RA patients with radiographic sacroiliitis (1.8 %) met the mNY criteria for the classifying of AS. One of them also had a history of psoriasis. All these

patients had characteristic clinical, radiological and laboratory findings of RA.

A total of thirty-one patients with RA (18.6 %) fulfilled the ESSG criteria (five with MRI sacroiliitis) and 26 (15.6 %) Amor criteria (five with MRI sacroiliitis) for the classification of SpA.

Among 19 patients with RA who have IBP according to “experts’ criteria,” MRI of SIJ was performed in 13 patients and HLA-B27 in 14 patients. Nine patients (three with radiographic sacroiliitis, five MRI sacroiliitis and one HLA-B27 positivity) out of 167 RA patients (5.3 %) were classified as having axial SpA according to new ASAS classification criteria [11] (MRI of SIJ or HLA-B27 test in three patients with IBP and only HLA-B27 test in two others were required to assess whether these patients fulfill the ASAS criteria for axial SpA but these investigations could not be done).

All RA patients coexisting with AS were found to be RF and anti-CCP positive. Among patients fulfilling the classification criteria for SpA/axial SpA, the frequency of RF and anti-CCP positivity was in the ranges of between 68–80 % and 74–80 %, respectively. However, we found no statistically significant association between the occurrence of any of the SpA features (IBP, radiographic or MRI sacroiliitis and the classification of AS/axial SpA or SpA) and the positivity of RF or anti-CCP. The features of SpA were also not related to the disease duration of RA or the DAS-28 and HAQ scores. There was only a tendency between the presence of radiographic sacroiliitis and hand/wrist erosions on radiographs ($p = 0.07$, $r = 0.139$).

Discussion

This study suggests high frequency of IBP (16.8 %) and other SpA features such as radiographic sacroiliitis (2.4 %) and enthesitis (41.9 %) in patients with RA. Among RA patients, 1.8 % fulfilled the mNY classification criteria for AS, 18.6 % the ESSG criteria and 15.6 % the Amor’s criteria for SpA and 5.3 % the ASAS criteria for axial SpA. These figures are considerably higher than those expected in the general Turkish population [3].

The prevalence of chronic low back pain in patients with RA has been reported to be between 33.0 and 53.5 % in several studies [25, 29–31]. However, these studies did not investigate whether the patients suffering from inflammatory back pain. In fact, the available literature for the prevalence of IBP in general population is also very limited. Its prevalence was estimated to be 0.8 % in United States adults aged 25–49 years [32]. We found that 22.4 % of our RA patients had chronic back pain lasting ≥ 1 month. The prevalence of IBP was 16.8 % according to

Calin criteria and 11.4 % according to experts' criteria among all RA patients.

Radiographic sacroiliitis in RA patients have been found in frequencies varying between 0 and 70 % [33–35]. The high variability between these results may be due to genetic and environmental differences, as well as methodological factors. However, the finding of very high frequency of radiographic sacroiliitis reaching to 70 % in the absence of IBP suggests that degenerative sacroiliac disease may be misdiagnosed as sacroiliitis in relatively older patients with RA in these studies. The radiographic evaluation of sacroiliitis involves some difficulties mainly due to anatomical features of the SIJ. Therefore, we needed to perform SIJ CT or MRI for the differential diagnosis in the patients with radiographic findings of suspected sacroiliitis.

The coexistence of RA and AS in the same patient has rarely been reported [36]. The estimated frequency of this association is about 1:50,000–1:200,000 in the general population. However, in a hospital-based study, five cases of coexisting classical RA (2.7 %) have been found in a group of 184 patients with either AS or Reiter's syndrome [18]. The presence of a rheumatoid nodule, a positive rheumatoid factor or symmetrical peripheral arthritis in a long standing axial spondylitis were reported to be determinants of the presence of the coexistence [20].

The diagnosis of coexistence of RA and AS/SpA, especially in patients with mild axial symptoms, can be difficult due to the possibility of symmetrical peripheral joint involvement in AS/SpA. Moreover, synovial inflammation of large joints such as knees and ankles is a common feature shared by RA and AS/SpA. The presence of HLA-B27 or the positive RF may help to diagnose the coexistence, but their values are limited [36]. Dahlqvist et al. [37] reported the increased frequency of radiographic sacroiliitis (≥ 2 and ≥ 3 according to the mNY criteria) in HLA-B27 positive patients than those in HLA-B27 negative with classical seropositive RA. However, other larger studies, including population-based studies, did not confirm this relationship between sacroiliitis and HLA-B27 positivity in RA patients [38]. In our study, HLA-B27 was found to be positive in only three patients among 33 investigated patients who met any of the classification criteria for SpA (ESSG and Amor criteria) or AS (mNY criteria). On the other hand, all RA patients coexisting with AS and most RA patients coexisting with SpA or axial SpA were found to be RF and anti-CCP positive. These findings are consistent with previous reports which showed the association of the coexistence of RA and AS/radiographic sacroiliitis with RF positivity [39, 40]. To our knowledge, this is the first study reporting anti-CCP positivity, which is more specific than RF positivity for RA, in such patients. Radiographic sacroiliitis was also reported more frequently among RA patients with more severe [33, 39] and

longstanding disease [39, 41–43]. In our study, there was no relationship of radiographic sacroiliitis with RA disease duration, but it had a tendency to occur in patients with erosive arthritis.

In conclusion, this study suggests that the prevalence of SpA features in patients with RA may be much higher than expected. Although all the criteria used in this study were designed for the classification, not diagnosis, the frequent associations of high titers of RF and anti-CCP and of typical RA erosions with the coexistence of RA and AS/axial SpA suggest that this is a real coexistence at least in such patients.

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