Clinical Silent Inflammatory Gut Lesions in Undifferentiated Spondyloarthropathies


Summary Gastrointestinal inflammation or infection can be associated with various forms of arthritis, such as, acute reactive arthritis triggered by enteritis due to gram-negative bacteria or ankylosing spondylitis and peripheral arthritis in relation to Crohn's disease and ulcerative colitis. Using colonoscopy, we have found a high prevalence of clinically silent inflammatory lesions in 38 patients (24 males and 14 females) affected by undifferentiated spondyloarthropathies (SpA). Microscopic inflammatory lesions were present in all the patients. Three patterns of nonspecific chronic inflammatory alterations were observed. No difference was noted between patients taking or not taking nonsteroidal anti-inflammatory drugs. Direct immunofluorescence demonstrated the presence of IgG, IgA, IgM, C3, C4 and fibrinogen in 75% of the specimens examined. The finding of chronic inflammatory gut lesions hypothesizes that a local activation of the immune system depending on the persistence of intestinal microbial antigens or toxins, due to impaired elimination or increased exposition, may have a part in the pathogenesis of SpA.

Key words Undifferentiated Spondyloarthropathies, Colonoscopy, Inflammatory Gut Lesions

INTRODUCTION

The association between inflammatory bowel diseases and joint inflammation is well known. Patients affected by ulcerative colitis or Crohn's disease have an increased risk for peripheral arthritis and axial spinal involvement (1-3). Acute enteric infections with gram-negative bacteria such as salmonella, shigella, yersinia and campylobacter may be complicated by sterile joint inflammation (4) and arthritis-dermatitis syndrome can follow jejuno-ileal bypass operation for morbid obesity (5). Recently, a high frequency of silent gut inflammation in association with chronic spondyloarthropathies (SpA) has been described (6,7).

SpA constitute a group of syndromes characterized by the presence of inflammatory pauciarticular and asymmetrical peripheral arthritis accompanied by enthesopathies, sacroiliitis and often spondylitis and by the absence of rheumatoid factor (8). These syndromes which share genetic predisposing factors, demonstrated by familial aggregation and HLA-B27 association, include ankylosing spondylitis, reactive arthritis including Reiter's syndrome, psoriatic arthritis and arthritis associated with chronic inflammatory bowel disease (6,7).

Patients with clinical and radiological features suggestive of SpA, but not fulfilling the diagnostic criteria for any of the currently established SpA have been defined as having undifferentiated SpA (9).

In the present study we have evaluated endoscopic and histologic features of colic mucosa in patients with undifferentiated SpA.

PATIENTS AND METHODS

Thirty-eight patients (24 males and 14 females, mean age 35.2 ± 1.4 years) complaining of inflammatory spinal pain and/or asymmetrical synovitis associated with enthesopathy and/or buttock pain alternating between right and left gluteal area and/or radiological sacroiliitis, were considered affected by SpA as defined by 1991 European Spondyloarthropathy Study Group criteria (10) and gave their informed consent to the study.

No patient had definite ankylosing spondylitis as defined by the New York criteria (11). Patients with psori-
asis or with history of abdominal pain, diarrhoea or recent alterations in bowel habits and rectal bleeding were not considered in the present study. Fecal cultures gave negative results for the growth of salmonella, shigella, yersinia enterocolica, campylobacter jejuni and clostridium difficile in all the patient's studied. No patient had a history or symptoms of urogenital infections and urethral cultures were negative for the growth of mycoplasmas or chlamydias. No patient was treated with steroids or immunosuppressive drugs. Twenty-six out of 38 patients have been treated with nonsteroidal anti-inflammatory drugs (NSAIDs), in the three months before the study. The control group consisted of 10 volunteer subjects (8 males and 2 females, mean age 51 ± 4 years) undergoing a routine colonoscopy following previous removals of benign colorectum adenomatous polyps.

X-rays of sacroiliac joints were obtained in all patients; axial skeleton X-rays only in patients complaining of back pain or presenting a reduced mobility of spinal segments. Radiological sacroilitis, grades 1 and 2, was present in 40% of the patients. Roentgenographic features of spondylitis were absent in all the patients studied.

Colonoscopy was performed by an experienced endoscopist using an Olympus Colonfibroscope (CF, I). The entire large bowel including caecum and ileocecal valve was visualized. In each patient and control 8 to 13 biopsies were taken of the colorectum, sigma, caecum and ileocecal valve with median number of 10 specimens per patient and control. Biopsies were taken at sites presenting abnormalities or blindly, if the mucosa macroscopically appeared normal.

The tissue was fixed in 10% formalin, dehydrated, and paraffin embedded and routinely stained with hematoxylineosin. Fresh tissue section from 16 patients was frozen at -40°C and stored for immunofluorescence examination. Direct immunofluorescence was tested using anti-IgG, IgA, IgM, C3, C4 and fibrinogen fluorescinate antibodies (Boehringer).

HLA A, B, C typing was performed in all the patients. X²-test was used for statistical analysis.

RESULTS

Thirteen patients (34.2%) and all the control subjects showed normal mucosa at the colonoscopic examination. In 25 patients (65.8%) the colonoscopy revealed an abnormal mucosa with patchy areas of oedema and erythema or perivascular erythema with small haemorrhages. Large bowel segments involved were rectum in 57%, sigma in 65%, descending colon in 50%, transverse colon in 42%, ascending colon, caecum and ileocecal valve in 34% of the patients.

Microscopically, the colon mucosal surface did not appear altered in controls. Microscopic studies revealed gut inflammation in all the patients studied. Three patterns of inflammatory changes were noted. Histologic ex-

Fig. 1: Type A: mucosal oedema and lympho-monocyte and plasma cells infiltrating the lamina propria.