Original Article

Capsula Eburnea

BONE AND JOINT MANIFESTATIONS IN PATIENTS AFFECTED BY INFLAMMATORY BOWEL DISEASE.

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SUMMARY

Onset of the symptoms in patients with ulcerative colitis and Crohn's disease is sometimes characterized by osteoarticular manifestations. The usual presentation of peripheral arthritis is asymmetric, polyarticular and migrant, often involving large joints of the upper and lower limbs, unlike rheumatoid arthritis. This study analyses the statistical incidence of arthritic manifestations in elderly patients with inflammatory bowel disease.

INTRODUCTION

Ankylosing spondylitis [1] (AS) has a strong genetic association, with 90% of patients affected expressing the Histocompatibility Leukocyte Antigen (HLA) B27 genotype. However, this positivity is not always present in AS: in fact, HLA-B27 negativity in a typical case of AS significantly increases the likelihood of the patient also being affected by inflammatory bowel disease (IBD). This disease is characterized by an early involvement of the pelvis and vertebral column (sacroiliitis), as well as enthesitis with an accumulation of subchondral granulation tissue and synovitis with inflammatory granulation tissue formation at the junction between the cartilage ring and spinal bone margin. Bone erosion is repaired by new tissue growth, forming osteophytes that later fuse and grow toward the adjacent vertebral bodies; these pathological changes cause clinical manifestations such as back pain, lower back stiffness with functional limitation, including impaired anterior and lateral flexion and extension in the morning, but improved with movement, as well as reduction in chest expansion. Peripheral arthritis in patients with AS usually presents with synovial hypertrophy, lymphoid infiltration, and synovial pannus formation, without the presence of changes typical of rheumatoid arthritis; in fact, central cartilage erosions are common in AS, but very rare in RA. Shoulder and hip involvement is observed in 25-35% of cases, with peripheral arthritis developing subsequently in about 30% of patients. Both ulcerative colitis (UC) and Crohn's disease (CD) have no known etiology, but it is commonly thought that in predisposed individuals, exogenous

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(bacterial microflora and infectious agents) and endogenous (mucosal barrier function) factors cause alterations in the mucosal immune response [2]; IBD is therefore considered to be caused by an inappropriate immune response to microbial flora. Normally, antigen-reactive T cell deletion and anergy at the oral level result in suppression of immune response against food antigens and commensal flora. In both CU and CD, T cd4+ cells in the basal membrane and peripheral blood secrete proinflammatory cytokines; T cd4+ cells can be divided into Th1 and Th2: the former secrete interferon-γ and tumor necrosis factor-α, that induce a transmural granulomatous inflammation typical of CD, whilst the latter secrete interleukin-4, interleukin-5, interleukin-13, causing an inflammation of the mucous membrane typically observed in UC. In UC, the lesions are commonly located in the rectum and extend to the entire colon without alternate areas of undamaged mucosa. In UC with mild inflammation, the mucosa appears hyperemic, while in more severe cases, the mucosa is bloody and ulcerated, with pseudopolyps resulting from epithelial regeneration in long-term illness; microscopically, UC is characterized by crypt distortion, goblet cell depletion and inflammatory cell infiltration (mainly by neutrophils). Crohn's disease can involve any part of the intestinal mucosa, with the lesions typically having a segmental distribution with unaffected areas of mucosa along the intestine. CD rarely affects the rectum, with a possible presence fistulas, abscesses and/or anal stenosis, while involvement of the pancreas and liver is likely; multiple ulcers may join together to form irregular shapes with islands of normal mucosa in between. The presence of fistulas, fibrosis and stenosis in the intestine is characteristic of this form of IBD. The microscopic characteristics of CD include ulcerative lesions encircled by macrophages, leading to the formation of noncaseating granulomas which are pathognomonic of this disease. The main symptoms of UC are diarrhea, rectal bleeding, tenesmus, the presence of mucus in stools and abdominal pain; the severity of symptoms is related to the extent of the disease. Other symptoms in moderate-severe disease include anorexia, nausea, vomiting, fever and weight loss. In CD, the clinical presentation depends on the location of the disease; the most commonly affected area is the terminal ileum, with recurrent pain in the right lower quadrant and leukocytosis with fever that may be confused with appendicitis. In proximity to the affected region, a mass may be palpable, which can also obstruct the ureter causing dysuria or anuria. After several flare-ups of the disease, the formation of inflexible stenotic tissue can cause chronic obstruction. Ileocecal fistulizing processes in the affected area can create a connection to the bladder, causing leakage of intestinal gas and fecal material with the urine; these processes can also create fistulas connecting to the vagina. In patients with ileo-jejunal CD malabsorption and steatorrhea are common, with the former causing vitamin D deficiency (that may result to fractures, especially with prolonged use of corticosteroids) [3], as well as vitamin PP and vitamin B12 deficiency (megaloblastic anemia). When the disease affects the colon and rectum, the patient may have fever, rectal bleeding and

CLINICAL CHARACTERISTICS	ULCERATIVE COLITIS	CROHN'S DISEASE
Number of patients	44	19
Mean age	69	71
Schober's Test	≤ 4	≤ 3
Arthritis	18	13
Spondylitis	2	2
Weight loss	21	14
Bloody diarrhea	33	9

Table 1: - Clinical manifestations in patients with IBD: The table shows the number of patients affected by major clinical manifestations, divided into ulcerative colitis and Crohn's disease.

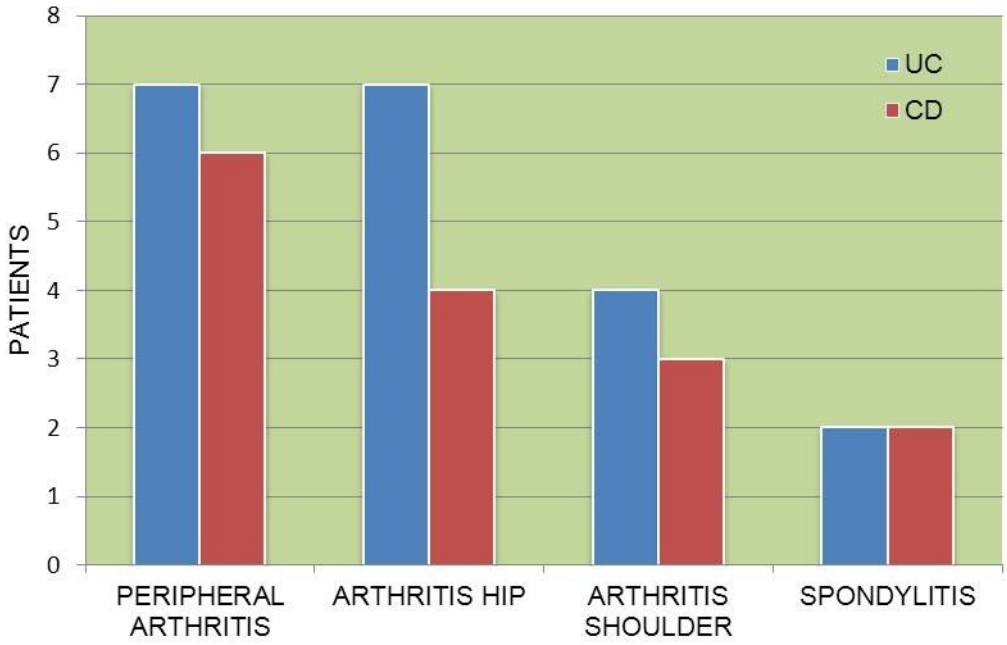

Fig. 1: - Main osteoarticular symptoms: this figure shows the number of patients with symptomatic osteoarticular disease, divided into ulcerative colitis and Crohn's disease.

cramping pain on defecation. Colonic fistulas connecting to the duodenum or stomach may cause fecal vomiting.

MATERIAL AND METHODS

From January 2009 to July 2011, we conducted a retrospective study on bone and joint manifestations in elderly patients diagnosed with inflammatory bowel disease (IBD) at the orthopedic clinic of the Polyclinic Palermo [4]. Patients seen at our clinic and included in this study were 63; a full medical history and a definite diagnosis of IBD were required for each patient. Patients were attending the clinic because of various bone and joint complaints, such as localized dull pain deep in the lumbar region or in the gluteus, associated with morning stiffness. The patients underwent further testing including Schober's Test to assess lumbar flexion (a distance of less than 4 cm between the reference lines to the pelvis and chest was considered a positive result (v.n. > 5 cm) [5], followed by biochemical tests for measuring erythrocyte sedimentation rate, C-reactive protein and alkaline phosphatase levels, as well as *testing for Histocompatibility Leukocyte Antigen HLA-B27 which was negative in 90% of patients*. The clinical study of patients was completed by performing magnetic resonance imaging [6], which allowed for an early and accurate diagnosis of joint inflammation and intramedullary edema.

RESULTS

Out of the 63 cases reviewed, 19 patients had Crohn's disease (CD) mean age 71 years, range 66-75) and 44 patients had ulcerative colitis (UC) mean age 69 years, range 65-74). The patients with arthritis showed a higher erythrocyte sedimentation rate (54mm/hr ± 18), C-reactive protein levels (27 mg/L ± 9) and a positive Schober's Test [table 1]. Peripheral arthritis was found in six patients with CD (30%) and seven patients with UC (15%); arthritis affecting the hips was found in four patients with CD (21%) and seven patients with UC (16 %); arthritis affecting the shoulder was observed in three patients

with CD (16%) and four patients with UC (9%); Spondylitis was found in two patients with CD (10%) and in two patients with UC (5%) [fig.1].

DISCUSSION

This study proves that during the clinical evaluation of orthopedic patients, a complete assessment of the patient's physical condition must always be considered in order to not just diagnose the symptom, but the disease; inflammatory bowel disease (IBD) has many symptoms and manifestations, some of them extraintestinal, which often represent the earliest signs of disease [7]. Sacroiliitis is the main symptom during the onset of IBD, but in the elderly patient, arthritic involvement of the hip, shoulder and lumbar spine prevail. These patients also have global symptoms including anemia, weight loss, reduced muscle mass and general fatigue. It is very important to underline the fact that bone or joint symptoms, overlapped with ankylosing spondylitis, are correlated with a possible IBD diagnosis, whose likelihood increases in patients with serological negativity for HLA-B27. Therefore, this study, like many others in the literature, clinically demonstrates the relationship between IBD and bone/joint manifestations. However, the etiopathogenetic mechanisms are still unknown.

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