

RHEUMATIC PATHOLOGIES IN SUBJECTS WITH INFLAMMATORY BOWEL DISEASE

Giovanni Tomasello¹, Alessandro Geraci², Antonio Sanfilippo², Provvidenza Damiani³, Stefania Termine⁴, Roberta Margherita Maritano⁵, Alfonso M. Maiorana¹, Michele D'Arienzo²

Abstract

Inflammatory bowel diseases (IBD) are commonly associated with rheumatic diseases of the joints. Sixty-five patients were selected during a 5-year study period. All patients were analyzed with clinical, laboratory and *radiographic exams*. 38 patients had ulcerative colitis (mean age 42.1 years, range: 19-75) and 27 patients had Crohn's disease (CD) (mean age 37.2 years, range: 17-64 years). Arthritis occurred in 11 patients (17%): 7 with UC (18.4%) and 4 with CD (14.8%). The mean age of patients with arthritis was 35 and mean disease duration of pain and limitation symptom was 28 months. In 9 patients, arthritis appeared after the onset of bowel symptoms with mean duration of 20 months in UC and 24 months in CD; in two patients, arthritis preceded the onset of bowel symptoms some months before. The objective of this article is to establish to establish the incidence and clinical characteristics of arthritis in a group of patients suffering from CD and UC.

Keywords: IBD, arthritis, ulcerative colitis, Crohn's disease

Address of the authors:

- 1) Department of General and Emergency Surgery and Organ transplant, University of Palermo, Italy.
- 2) Orthopaedic and Traumatology Unit, University of Palermo, Italy.
- 3) Department of Internal Medicine, Cardiovascular Disease and Nephro-Urology, University of Palermo, Italy.
- 4) Unit of Dermatology and Sexually Transmitted diseases, University of Palermo, Italy.
- 5) Faculty of Pharmacology, University of Torino, Italy

Send correspondence:

Dr. Alessandro Geraci
Email: geracialessandro@libero.it

Received: June 10th, 2010

Revised: June 30th, 2010

Accepted: July 07th, 2010

Language of the Article: English

No conflicts of interest were declared.

© CAPSULA EBURNEA, 2010
ISSN: 1970-5492

DOI: 10.3269/1970-5492.2010.5.24

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of unknown cause involving gastrointestinal tract. UC and CD are a group of idiopathic chronic inflammatory disorders, involving the small and the large intestine. The CD involves all part of digestive tract (from mouth to anus) discontinuously (1). The UC involves more often the distal part of rectal tract; the inflammation always begins in the rectum, extends proximally a certain distance and the abruptly stops (2). Pathophysiology of IBD is under active investigation. Patients with IBD have a genetic predisposition (or perhaps susceptibility) for the disease (3). The triggering event for the activation of the immune response has to be identified (4). Possible factors related to this event include a pathogenic organism (not yet identified), an immune response to an intraluminal antigen (e.g. protein from cow milk) or an autoimmune process whereby an appropriate immune response to an intraluminal antigen and an appropriate response to a similar antigen is present on intestinal epithelial cells (e.g. alteration in barrier functions) (5). IBD is complicated by many local and systemic disorders (6). Among the extraintestinal complications the most common diseases are rheumatic diseases of the joints. Some people with inflammatory bowel disease have a type of arthritis that is similar to rheumatoid arthritis in some way, even if there are some important differences. The arthritis associated with IBD tends to involve only large

joints and also involves both sides equally. For example, it might affect the knee on one side and the ankle on the other. In rheumatoid arthritis more joints are involved especially those in the hand and wrist and those on both sides of the body. An antibody commonly found in the blood of people with rheumatoid arthritis usually is not found in the blood of people with IBD arthritis. Unlike rheumatoid arthritis, associated with IBD can affect the lower spine, especially the sacroiliac joints and it is associated with certain gene (called HLA-B27) (7). Arthritis associated with IBD can occur with three different symptoms: sacroileitis, spondylitis, peripheral arthritis. Some of spinal arthritis symptoms are pain, stiffness in the joints of spinal column especially in the morning, but can improve with physical activity. Moreover, spinal arthritis can lead to fusion of the bones of the vertebral column. This permanent complication can cause a decrease in range of motion in the back and a limitation of rib motion that impairs the ability to take deep breaths. In peripheral arthritis the main symptoms are pain, swelling and stiffness in one or more joints of the arms and legs (wrists, knees and ankles) that may migrate between joints. When the pain of the peripheral arthritis is untreated, it can last from several days to weeks. Fortunately, this kind of arthritis does not generally cause any permanent damage.

Materials and methods

During the period 2004–2008, at ambulatory of Policlinico of Palermo, 65 patients

with IBD were retrospectively studied. Diagnosis of IBD (UC and CD) was made according to accepted clinical, endoscopic, radiological and histological criteria, or was confirmed at surgery, in agreement with criteria described by Schachter and Kirsner (8). The results of a latex fixation test for rheumatoid factor (RF) was recorded in patients with joint symptoms. Arthritis was defined as joint pain associated with stiffness and swelling stimulate by motion during the examination. The patients with arthritis were classified into the categories used by Gravallesse and Kantrowitz for IBD: peripheral arthritis, spondylitis, sacroileitis.

Results

Of the 65 patients with IBD, 38 patients had UC (mean age 42.1 years, range: 19-75) and 27 patients had CD (mean age 37.2 years, range: 17-64 years). There were more female patients in UC (M:F = 14:24) than in CD (M:F = 12:15). In CD arthritis not occurred in patients without colitis. Predominant symptoms are abdominal pain and weight loss; sporadically diarrhea and hematochezia. It was observed only one skin disorder: a case of pyoderma gangrenosum (incidence of 1.53%). Arthritis occurred in 11 patients (17%): 7 with UC (18.4%) and 4 with CD (14.8%). The mean age of patients with arthritis was 35 and mean disease duration of pain and limitation symptom was 28 months. In 9 patients, arthritis appeared after the onset of bowel symptoms with mean duration of 20 months in UC and 24

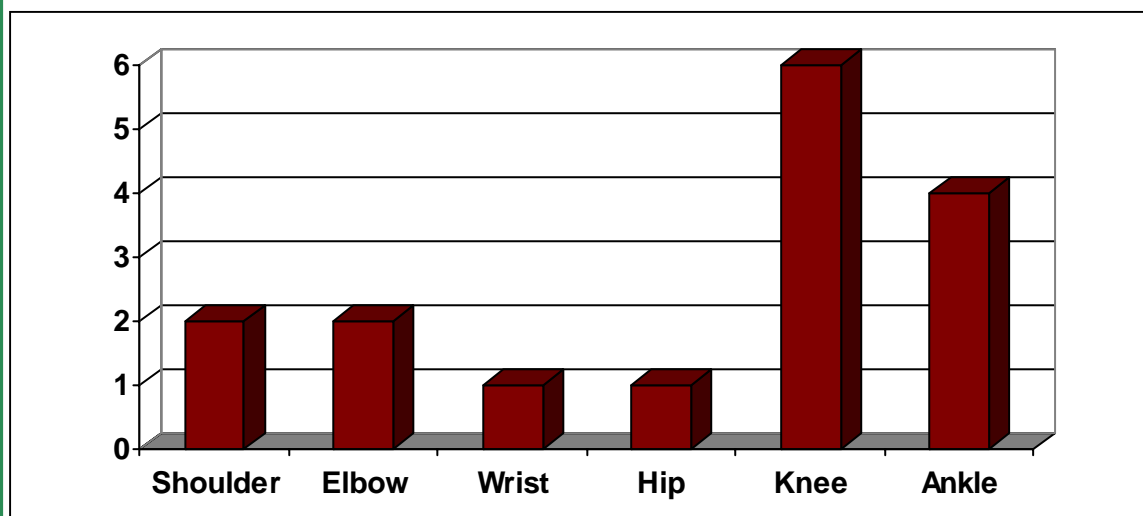


Figure 1: Joints involved in patients with arthritis.

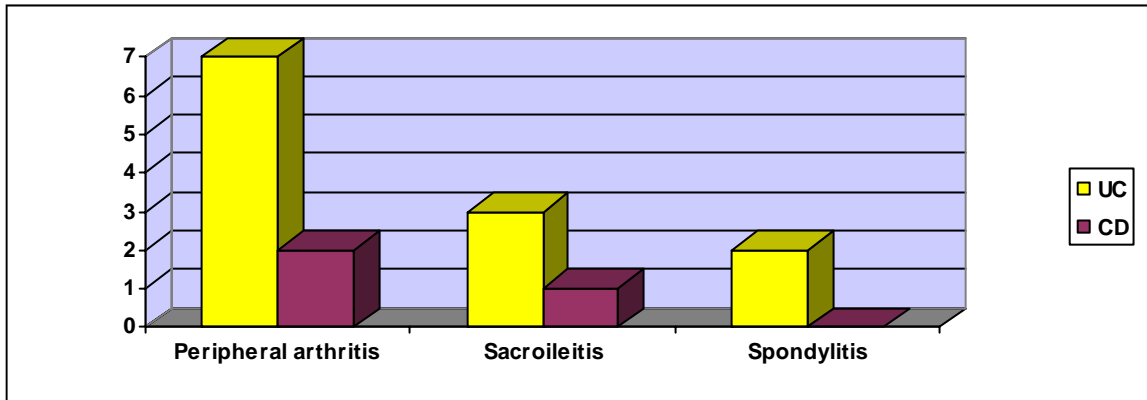


Figure 2: Joints manifestations in IBD patients

months in CD; in two patients, arthritis preceded the onset of bowel symptoms some months before. The arthritis in IBD was seronegative (negative RF) except one patient who showed low titer RF (22 IU/ml) and monoarticular involvement (knee). The patients with arthritis showed a higher erythrocyte sedimentation rate (51 mm/hr \pm 22) and C reactive protein (23mg/L \pm 13) compared to the patients without arthritis. Peripheral arthritis was found in 9 patients (13.8%); 7 patients with UC (18.4%) and 2 patients with CD (7.4%). Four patients had polyarticular involvement. The most frequently involved joint was the knee joint (6 patients), followed by the ankle (4 patients), elbow (2 patients), wrist (2 patients), proximal interphalangeal (2 patients), shoulder (2 patients), hip (1 patient) (Fig. 1). Spondylitis was diagnosed in 2 patients (3.07%). Sacroiliac joint abnormality was observed in 4 patients (6.15%), 3 with UC and 1 with. Both peripheral arthritis and spondylitis were found in three patients (only UC patients); both peripheral arthritis and sacroileitis in two patients (one with UC and one with CD) (Fig. 2).

Discussion

CD and UC are inflammatory chronic disease that involve primarily the gastrointestinal tract but that have long been recognized to cause extraintestinal complications too. The symptoms and the activity of the disease can come and go. Even though many effective medications are available to control the activity of this disease. A patient with inflammatory bowel disease can present many symptoms and many clinical manifestations, which often are the first signal of illness.

The IBD are not only a gastroenterology disease, but also surgical and orthopedic, because the extra-intestinal manifestations are painful and cause limitations in activities. The articular manifestations of CD have been characterized by many investigators since they were first described by Bargen in 1929 (9). Most series of patients with CD have estimated the frequency of joint involvement to 2-16% (10). In the present study the overall incidence of arthritis in CD was 14,8%. In old studies of literature, Wright and Watkinson found arthritis in 22% of patients with UC disease was 18,4%. Scarpa et al. however, showed a strong reverse relationship between the affected joint number and the extend of colitis (11) and suggested that the extent of the intestinal lesion in UC seems to be important in the expression of the articular complications. In 9 patients with peripheral arthritis associated with IBD, pancolitis was involved in 5 and rectosigmoid disease in 3. There was no difference in the incidence of arthritis according to the extent of bowel involvement in UC. In literature the incidence of RF positivity is not higher in patients with IBD and peripheral arthritis than in the general population (12, 13). In the present study only one patient showed low titer RF (22 IU/ml). In IBD, sacroileitis is the most important extra-intestinal manifestation. Studies have shown that spondylitis is clinically and radiologically indistinguishable from idiopathic ankylosing spondylitis and occurs in 3-6% of patients with IBD (14). Some of the first symptoms are insidious, like lower back pain and morning stiffness. These symptoms decrease with exercise and are aggravated by the bed rest. Dekker-Saeys et al. have shown that in IBD, the incidence of sacroileitis is

about 10% (15), while Mielants et al. found it to be about 5-12% (16).

Conclusion

IBD is a disorder that can have many complications, both within and outside of the intestinal tract. It's sure that the association between IBD and arthritis is reported in the literature and in our study, but the basis of this association is unknown. Both infection and immune mechanism have been postulated, Hodgdon et al. have demonstrated anticomplementary activity, suggesting immune complexes, in the serum of patients with active IBD and acute arthritis. A better understanding of the role of genetics and environmental factors in the cause of CD will improve the treatments and prevention of the disease. It is necessary the multidisciplinary approach (gastroenterologist, orthopedics, dermatologist, surgeon) of inflammatory bowel disease to improve quality of life of these patients.

References

1. Genser mann M, Wehkamp J, Feller mann K, Stange EF. Crohn's disease- defect in innate defence. *World J Gastroenterol.* 2008; 14: 5499-503.
2. Meyberry JF. Some aspects of the epidemiology of ulcerative colitis. *Gut* 1985; 26:968-974.
3. Barrett JC, Lee JC, Lees CW, et al. Genome-wide association study of ulcerative colitis identifies. Three new susceptibility loci including the HNF4A region. *Nat. Genet* 2009; 41:1330-1334.
4. Lettre G, Rioux JD. Autoimmune disease: insights from genome-wide association studies. *Hum Mol Genet.* 2008;17: R116-R121.
5. Ojetti V, Gigante G, Ainora ME, et al. Microflora imbalance and gastrointestinal diseases. *Dig Liver Dis* 2009, 3:35-39.
6. Greenstein AJ, Janowitz HD, Sacher DB. The extra-intestinal complications of Crohn's disease and ulcerative colitis: a study of 700 patients. *Medicine* 1976; 55:401-412.
7. Caillat-Zucman S. Molecular mechanism of HLA association with autoimmune diseases. *Tissue antigens.* 2009; 73:1-8.
8. Schachter H, Kirsner JB. Definitions of inflammatory bowel disease of unknown etiology. *Gastroenterology.* 1975; 68:591-600.
9. Bargen JA. Complications and sequelae of chronic ulcerative colitis. *Ann Intern Med* 1929; 3:335-352.
10. Loftus EV Jr. Management of extra-intestinal manifestations and other complications of inflammatory bowel disease. *Curr Gastroenterol Rep.* 2004; 6:506-513.
11. Scarpa R, D'Arienzo A, Del Puente A, Panarese A, Girolamo G, Valle G, Oriente A, Lubrano E, Oriente P. Reverse correlation between extent of colon involvement and number of affected joints in patients with ulcerative colitis and arthritis. *Am J Gastroenterol* 1990; 85:331-332.
12. Velayos FS, Sandborn WJ. Positioning biologic therapy for Crohn's disease and ulcerative colitis. *Curr Gastroenterol Rep.* 2007; 9:521-527.
13. Yamada R, Ymamamoto K. Recent findings on genes associates with inflammatory disease. *Mutat Res.* 2005; 573:136-135.
14. Sieper J. Developments in the scientific and clinical understanding of the spondyloarthritides. *Arthritis Res Ther.* 2009; 11:208.
15. Dekker-Saey s BJ. Meuwissen SG, Vanden Berg-Loonen EM, et al. Ankylosing spondylitis and inflammatory bowel disease: prevalence of peripheral arthritis, sacroileitis and ankylosing spondylitis in patients suffering from inflammatory bowel disease. *Ann Rheum Dis* 1978; 37:33-35.
16. Mielants H, Veys EM. The gut in the spondyloarthropathies. *J Rheumatol* 1990; 17:7-10.

PATOLOGIE REUMATICHE IN SOGGETTI CON MALATTIA INFIAMMATORIA CRONICA DELL'INTESTINO

Le malattie infiammatorie intestinali (IBD) sono comunemente associate con alcune malattie reumatiche delle articolazioni. Sessantacinque pazienti sono stati reclutati durante in un periodo di tempo e studio di 5 anni. Tutti i pazienti sono stati analizzati con esami clinici, dati di laboratorio, esame radiologico. 38 pazienti erano affetti da rettocolite ulcerosa (UC) (età media 42,1 anni, range: 19-75) e 27 dal morbo di Crohn (età media 37,2 anni, range: 17-64 anni). L'artrite si è verificata in 11 pazienti (17%): 7 con UC (18,4%) e 4 con CD (14,8%). L'età media dei pazienti con artrite è stata di 35 anni e la durata media della malattia con dolore e limitazione dei sintomi è stata di 28 mesi. In 9 pazienti, l'artrite è apparsa dopo la comparsa dei sintomi intestinali con durata media di 20 mesi in UC e 24 mesi in CD, in due pazienti i sintomi artritici hanno preceduto la comparsa dei sintomi intestinali di alcuni mesi. L'obiettivo di questo articolo è quello di stabilire l'incidenza e le caratteristiche cliniche di artrite in un gruppo di pazienti affetti da CD e UC.

Keywords: IBD, artrite reumatica, rettocolite ulcerosa, morbo di Crohn.

CAPSULA EBURNEA, 5(24):142-146, 2010
