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Seropositive rheumatoid arthritis associated with Crohn's disease

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ABSTRACT

In the present study we report a patient with long-standing seropositive rheumatoid arthritis, who developed Crohn's disease. We discuss the possible pathophysiologic mechanisms and their associations between these two entities.

Introduction

Rheumatoid arthritis (RA) is a chronic multi-systemic disease affecting primarily the synovium, leading to joint damage and bone destruction. Extra-articular manifestations of RA include rheumatoid nodules, pleurisy, Raynaud's phenomenon and skin vasculitis (1).

Gastrointestinal involvement in RA is usually associated with systemic vasculitis or is related to drug intolerance (2). In this report we present the case of an RA patient who developed Crohn's disease (CD) and discuss the possible pathophysiologic mechanisms for the coexistence of the two diseases.

Case report

The patient was a 46-year-old female who had longstanding seropositive RA since 1989 according to the 1987 American College of Rheumatology criteria (3). She presented to our out-patient rheumatology clinic because of abdominal pain and discomfort. Clinical examination revealed thickening of the second and third metacarpophalangeal (MCPs) joints bilaterally and the third proximal interphalangeal (PIP) joint bilaterally. In addition, two subcutaneous rheumatoid nodules were presented over the extensor surface of the left forearm. Abdominal examination revealed no abnormalities and rectal examination was negative. Digital examination for the presence of occult blood was negative. No previous treatment with gold salts or D-penicillamine was recorded. The current treatment was methotrexate (MTX) 10 mg/week, cyclosporine A (CsA) 100 mg/day and prednisone (2.5 mg/day).

Laboratory evaluation revealed hemoglobin 8.6 gr/dl; the white blood cells and differential count were within normal limits and platelets were normal. The erythrocyte sedimentation rate was 50 mm/h, C-reactive protein 19.5 mg/L (normal values < 6 mg/L), and IgM rheumatoid factor 1/640 (Latex test). Serum iron was 30 μgr/dl (normal values >45) and serum feritin levels 2.6 ng/ml (normal values > 10). Finally, total iron binding capacity was within

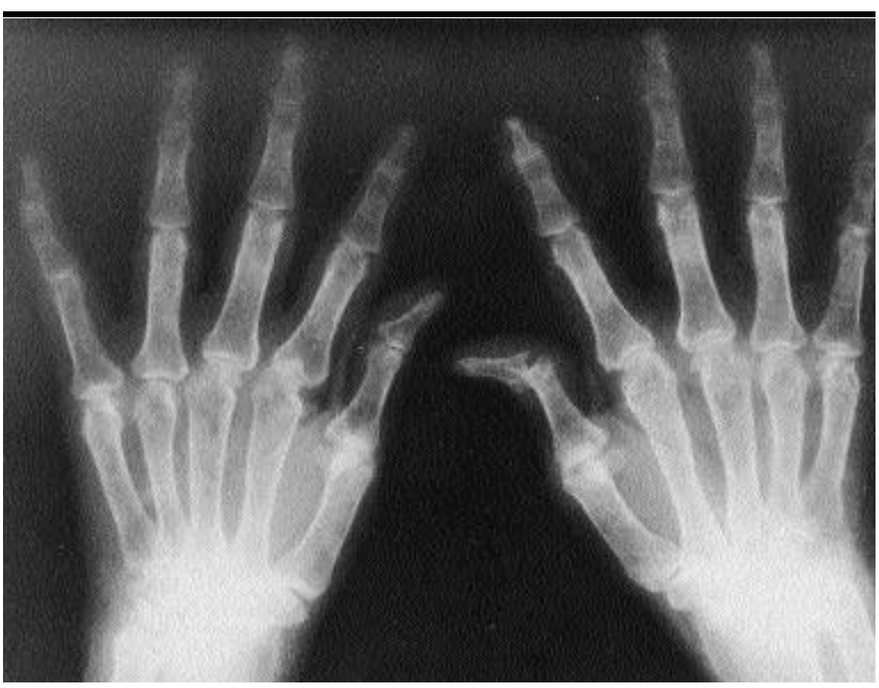

Fig 1. Hand and wrist roentgenograms showing erosive change affecting the wrists bilaterally. In addition,joint space narrowing and erosive changes are also evident on the metacarpophalangeal and proximal interfalangeal joints bilaterally.

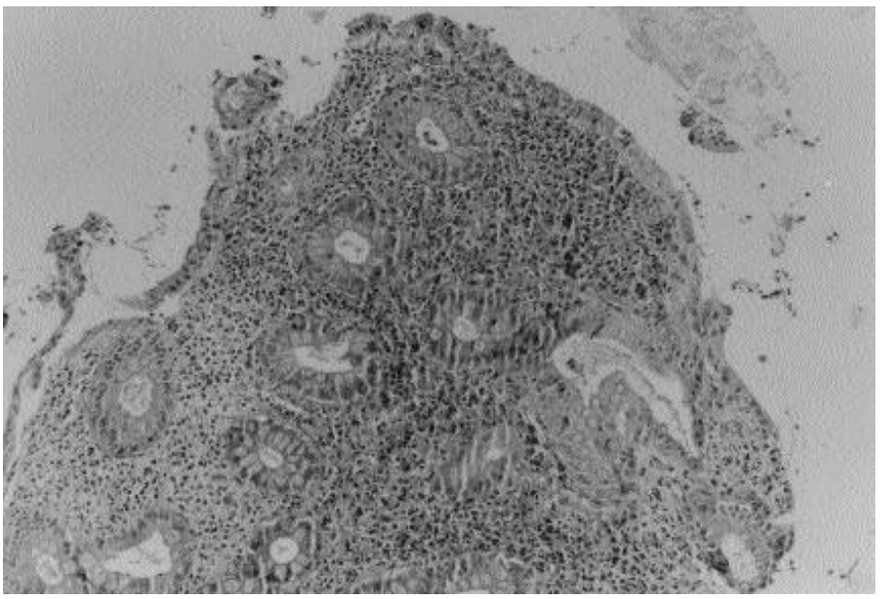

Fig 2. Rectal biopsy with surface erosion, deformity of crypts, and a patchy heavy infiltration of the mucosa by plasma cells, lymphoid cells,eosinophils and polymorphs. The latter infiltrates the epithelium without crypt abscesses formation. A slight degree of goblet cell depletion was also found. (H/E x100)

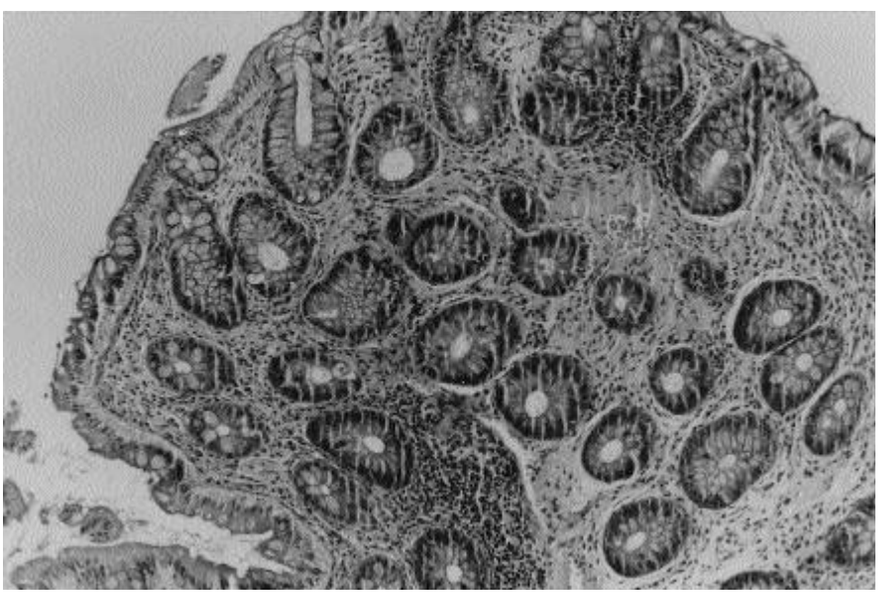

Fig 3. Biopsy specimen from the sigmoid colon showing slight crypt distortion and mucosal lymphoid aggregates. The goblet cells are well preserved. (H/E x200)

normal limits. The remainder of the laboratory tests revealed no abnormalities. A chest radiograph and tuberculin skin test were negative. Hand and wrist x-rays showed erosive changes affecting the MCPs, PIPs and wrists bilaterally (Fig. 1).

Abdominal pain and discomfort were persistent for several days, thus a further gastroenterological investigation was decided on. Gastroscopy showed no abnormalities. Colonoscopy demonstrated diverticulosis at the sigmoid and descending colon. A micronodular appearance of the intestinal mucosa with superficial erosions at the ascending colon and cecum were also observed. At the terminal ileum discernible ulcerations with normal interstitial intestinal mucosa were observed. Multiple biopsies from the terminal ileum and ascending colon revealed abnormalities compatible with inflammatory bowel disease (IBD), particularly CD (Fig. 2,3).

Discussion

RA is a systemic inflammatory disease that predominantly affects the synovial membrane of the diarthrodial joints (1). Involvement of the sacroiliac joints, thoracic and lumbar spine are not specifically related to RA (4). Extra-articular disease affecting a variety of organs occurs in the majority of patients and it is a significant factor in the morbidity and mortality of patients with RA. Gastrointestinal manifestation are usually associated with systemic vasculitis, drug-related reactions, collagen colitis or amyloidosis. Drug-related colitis is associated mainly with the use of gold salts, D-penicillamine, non-steroidal anti-inflammatory drugs and other drugs (5). Gold salt-induced colitis is a rare, some times serious and even life-threatening adverse event. Colonoscopy reveals erythematosus colonic mucosa with frequent ulcerations that can be difficult to distinguish from an inflammatory bowel disease. Biopsy specimens reveal lymphocytes and plasmacell infiltrations of the lamina propria with crypt abscess formations or ulcerations. It seems that gold-related colitis is due to hypersensitivity reactions (5). Our patient did not receive gold salts and this possibility therefore seems unlikely.

Collagen colitis is a rare form of inflammation colitis which is associated with many autoimmune rheumatic diseases such as scleroderma, seronegative spondylarthropathies, RA and others. This disorder has a distinct histopathological picture with the presence of subepithelial collagen deposition, which is different from the histological picture described in our patient (6). Finally, gastrointestinal amyloidosis is a rare complication of RA which also has distinct histological features with the deposition of amyloid protein (7). The histopathological findings in our patient did not show the presence of amyloid protein.

On the other hand, CD is a recurrent chronic IBD characterized by patchy transmural inflammation that may involve any segment of the gastrointestinal tract from the mouth to the anus. One-third of CD cases involve the small bowel but it most commonly

affects the ascending colon and terminal ileum (ileocolitis - ileitis). CD may present with fever, weight loss, abdominal pain and tenderness, diarrhoea, steatorrhoea, and extra-intestinal manifestations (8).

Arthritis is the most common extra-intestinal manifestation of CD. The arthritis occurs with equal frequency in men and women and in children and adults. Arthritis in CD manifests as monoarthritis or asymmetrical polyarthritis, and the joints most often involved are the knees, ankles, elbows and hips, and rarely the small joints. CD can affect the sacroiliac joints in approximately 10-20% of patients (9). Rheumatoid factor usually is negative, but in some cases this autoantibody may be detectable in low titers (10). In general, the arthritis is non-deforming and non-destructive; however, some cases with erosive changes have been reported (11,12). The entire spectrum of CD may also remain silent, although ileocolonoscopic biopsy specimens taken from the terminal ileum reveal mild to severe inflammatory lesions indicating the presence of subclinical CD (13). The lack of granuloma from the biopsy specimen is probably related to the use of immunosuppressive drugs since MTX acts mainly on macrophages and CSA inhibits T-lymphocytes. It is known that granuloma formation requires the presence of macrophages and activated T-lymphocytes. Thus, both drugs may modulate macrophage and T-lymphocyte functions, which result in the absence of granuloma formation. In addition, the symptoms of CD were subclinical and mild due to the fact that our patient was treated with MTX and CSA, immunosuppressive drugs typically used in the treatment of CD which can influence disease expression and outcome (14, 15).

It seems that the two diseases RA and CD both have an autoimmune basis. On the other hand it is known that RA is associated with other autoimmune diseases such as Sjögren's syndrome and Hashimoto thyroiditis. Thus,it is possible that both diseases may coexist or that RA may develop an associated CD.

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