Treatment with Infliximab in a Patient with Ankylosing Spondylitis and Crohn’s Disease

Simona Rednic¹, Claudiu Marinescu¹, Romeo Chira², Liliana Rogojan³, Nicolae Rednic⁴

¹) Department of Rheumatology. 2) Department of Endoscopy – 1st Medical Clinic
3) Department of Pathology. 4) 4th Medical Clinic, University of Medicine and Pharmacy, Cluj-Napoca

Abstract

The association of Crohn’s disease and ankylosing spondylitis is described in up to 30% of cases. Treatment of both conditions is not an easy task. We present the case of a 53 year old woman, diagnosed with colonic Crohn’s disease and ankylosing spondilitis, treated initially with increasing doses of sulphasalazine and moderate dose of corticosteroids, with the persistence of severe gastrointestinal and articular symptoms. She underwent therapy with tumor necrosis factor alpha (TNFα) inhibitor Infliximab, with a spectacular improvement of symptoms, signs and quality of life.

Key words

Crohn’s disease- ankylosing spondylitis- Infliximab

Case presentation

A 53 year old woman was referred to our service for severe inflammatory low back pain, morning stiffness lasting 2-3 hours, dispnoea at small efforts, arthralgias of the left hip, knees and hands, plantar pain. She also had a history of crampy abdominal pain, especially in the right lower part and middle of the abdomen, persistent diarrhea (over 3 months), with frequent liquid stools (4-5/day), containing mucus, intermittent rectal bleeding, tenesmus, important weight loss (10 kg in 3 months). The patient had no family history of ankylosing spondylitis (AS), psoriasis or chronic inflammatory bowel disease. Physical examination revealed total limitation of motion in the lumbar spine (Schober test measuring 10 cm), the absence of chest expansion, loss of the lumbar lordosis, limitation of the neck movements, tenderness and limitation at the mobilization of the left hip, Achille’s tendonitis, tenderness at palpation in the right lower part and middle of the abdomen, two anal fissures. Laboratory tests showed a very elevated erythrocyte sedimentation rate (ESR) (98/h), elevated value of C-reactive protein (CRP) (2.5 mg/dl), anemia (Hb = 8.5 g/dl, hematocrit 27%, microcytosis, iron deficiency). Serum electrolytes, glucose, urea, and creatinine were normal. Radiographs of sacroiliac joints and lumbar spine detected a grade IV bilateral sacroileitis, left coxitis and syndesmophytes and squaring of the vertebral bodies, realizing the “bamboo spine”). Dual X-ray absorptiometry revealed osteopenia (T score = -1.2). Colonoscopy showed cecum and ascending colon with dehaustration, visible but anachronic vascular ramification and small aphthous ulcerations toward the right angle, the transverse colon with reduced dimensions, cobblestone pattern, serpigineous ulcerations and large areas without vascularization, the descending colon also with large zones without visible vascularization, large stenosis, ulcerations (Fig.1) and an 8 mm pediculated polyp (Fig.2). The sigmoid colon and rectum were normal. Biopsy revealed inflammatory polyp and colonic wall with ulcerations, mild glandular atrophy, intense inflammatory infiltrate consisting of lymphocytes and polymorphonuclear neutrophyles, cryptitis and cryptic abscesses, reduced fibrosis (Fig.3). Standard ultrasonography of the colon showed segmental wall thickening of the transverse and descending colon up to 8-10 mm, affecting only mucosa and submucosa (Fig.4). Hydrosonography revealed an important stenosis at this level and the pericolic adipose connective tissue presented a nodular agglomeration at the site of the lesions described above (Fig.5).

A diagnosis of AS stage IV and Crohn’s disease (CD) of the colon, with secondary anemia was made and we initiated therapy with sulphasalazine 2 g/day, in association with prednisone 0.75mg/kg/day in a decreasing dose and the correction of iron deficiency. Further evaluation showed an improvement of symptoms, with the absence of peripheral joint involvement, but with the persistence of low back pain and prolonged morning stiffness. She continued to have liquid stools (2-3/day), intermittent cramps and did not gain weight. Laboratory parameters revealed persistent inflam-
matory syndrome (ESR = 60/h, CRP = 1.8 mg/dl), anemia (Hb = 10 g/dl, Ht = 33.6%, microcytosis). We therefore modified the therapy with sulphasalazine at 3 g/day and increased again the prednisone dose, but with no significant improvement. Therapy with the TNFα inhibitor infliximab was started (5 mg/kg intravenously at 0, 2, 6 weeks and then
and the evolution of the patient was surprising. Evaluation after six months revealed that the low back pain, morning stiffness, liquid stools had completely resolved. The inflammatory every 8 weeks syndrome was attenuated (ESR = 23/h, CRP negative), and anemia and iron deficiency disappeared. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) had a reduction from 64.3 to 4.77 and Crohn’s Disease Activity Index (CDAI) was reduced from 256 to 126. Post therapeutic colonoscopy showed cecum and ascending colon with no ulcerations and partial dehaustration, transverse colon with two ulcerations and persistence of the large stenosis (Fig 6). Biopsy revealed the reduction of the inflammatory infiltrate, some areas of cryptitis and the absence of cryptic abscesses (Fig 7). Control ultrasonography revealed only a mild wall thickening of the transverse colon (5-6 mm). We reduced sulphasalazine to 1 g/day and discontinued prednisone. The patient continues the biologic therapy.

Discussion

Joint involvement is well recognized in CD. It includes peripheral and axial syndromes and it is considered to be part of the wider group of seronegative spondyloarthropathies, including idiopathic AS, reactive arthritis and psoriatic arthritis (1). Studies report symmetrical small joint arthropaty present in 20% of cases, axial spondyloartropathy in 15%, sacroilitis in 5% and AS in up to 30% of cases (2).

Treatment of these two associated conditions represents a challenge for both doctor and patient. Ankylosing spondylitis is often poorly responsive to disease modifying drugs (including sulphasalazine, methotrexate, leflunomide, azathioprine) and the possibility of a drug triggered intestinal activation or relapse significantly limits the use of several drugs (3, 4). Recently published studies realized with sulphasalazine report that there is no evidence for a clinically relevant benefit on spinal symptoms or function, but it may have a role in peripheral joint disease present in AS (5).

Studies with methotrexate and leflunomide in AS have shown no significant differences in effect compared with placebo (3, 6). Large, methodologically rigorous studies have also demonstrated that sulphasalazine is only modestly effective for inducing remission of mild to moderate CD. It appears that its greatest benefit is likely realized when CD is located in the colon (4, 6). Treatment with mesalazine given in rectal suppositories has shown good results in controlling symptoms of CD, but there are no convincing reports concerning its benefit in treating AS (7). Azathioprine and methotrexate proved to be effective in inducing and maintaining remission in patients with inflammatory bowel disease. They are frequently used for steroid–dependent or resistant patients and it may take up to 6 months or more of therapy to see results (8, 9). Cyclosporin, tacrolimus and mycophenolate mofetil are other options in the treatment of these two conditions, but need more conclusive data on their efficacy and safety (3, 4). The TNFα blocker infliximab used in the treatment of spondyloarthropaty associated with CD has improved both gastrointestinal and overall articular symptoms (general musculoskeletal and spinal pain, peripheral arthritis). Infliximab induces and maintains remission of CD, closure of fistulae, healing of lesions and improvement in the quality of life. The results suggest that this medication should be preferred for the treatment of active and severe AS associated with active or quiescent CD (10-13).

References