Musculoskeletal Manifestations of Inflammatory Bowel Disease

Leonidas A. Bourikas, MD, and Konstantinos A. Papadakis, MD, PhD

Abstract: Extraintestinal manifestations develop in ≈25% of patients with inflammatory bowel disease (IBD). Musculoskeletal symptoms are the most common extraintestinal manifestations of IBD, often associated with colonic involvement, and present as either articular (arthritis) or periarticular inflammation including enthesitis, myositis, or soft tissue rheumatism (fibromyalgia). Musculoskeletal manifestations can precede or be synchronous with the development of bowel disease or develop following the diagnosis of IBD. Their clinical course often correlates with IBD activity but it can also be independent of the activity of bowel disease. Controlling intestinal inflammation remains the cornerstone therapeutic approach for the musculoskeletal manifestations of IBD.

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Key Words: musculoskeletal manifestations, intestinal inflammation, inflammatory bowel disease

The inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC), are inflammatory diseases affecting the gastrointestinal tract and are often associated with several extraintestinal manifestations. Approximately 25% of patients with IBD have combinations of several extracolonic manifestations. A relationship between the presence of extracolonic manifestations and the extent of colonic involvement has been demonstrated[1] since ≈75% of patients with extracolonic manifestations have extensive colitis. Musculoskeletal symptoms are described in 6%–46% of IBD patients and they are considered the most common extraintestinal manifestations in IBD.[2] Skeletal pain is a very common symptom in IBD patients and its origin cannot be easy identified in all cases. Articular, periarticular, and muscular involvement, osteoporosis and related fractures, and fibromyalgia are the main causes of skeletal pain in these patients. In this review we focus on the clinical evaluation and management of musculoskeletal manifestations in patients with CD and UC except for osteoporosis and related fractures, which have been reviewed previously in the journal.

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From the Department of Gastroenterology, University Hospital of Heraklion, University of Crete Medical School, Crete, Greece.

Reprints: Konstantinos A. Papadakis, MD, PhD, Associate Professor of Medicine, University of Crete, Faculty of Medicine, Division of Gastroenterology, University Hospital of Heraklion, PO Box 1352, Heraklion, Crete, Greece (e-mail: Kpapadakis@med.uoc.gr or Papadakis.konstantinos@gmail.com)

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ARTICULAR INVOLVEMENT IN IBD

Inflammatory arthritis is characterized by pain with local increase of temperature and swelling of the joint and the synovium with or without effusion (with inflammatory characteristics of the articular fluid) leading to decreased joint mobility. Morning stiffness and pain relief after mobilization can be helpful in the differential diagnosis of inflammatory arthritis from osteoarthritis, the most common form of denaturing arthritis worldwide. Axial skeleton (sacroiliac joints, the spine, hips, and shoulders) and/or the peripheral joints can be affected. Other periarticular features including enthesopathy, tendonitis, and other features such as clubbing, dactylitis (sausage fingers or toes due to inflammation) (Fig. 1), periostitis, and granulomatous lesions of joint and bone may also occur. Peripheral or axial articular involvement can precede, be synchronous with the development of bowel disease (usually of less than 6 months duration), or develop following the diagnosis of IBD, often as late as 10 years following the diagnosis of IBD. IBD-related arthropathy is classified into the wider group of inflammatory arthritides, which are historically called seronegative spondyloarthropathies, including idiopathic ankylosing spondylitis (AS), reactive arthritis (ReA), psoriatic arthritis (PsA), and undifferentiated SpA. The diagnosis is usually delayed by 5–6 years, especially in patients who present with an early or incomplete clinical picture.[3,4] Based on the type of articular involvement in IBD and the number of joints that are affected, the following clinical classification has been proposed (Table 1).

PERIPHERAL ARTHROPATHIES

The peripheral arthropathies associated with IBD occur in 5%–20% of patients.[5] The presence of peripheral arthropathy is a fairly accurate clinical indication of active colonic IBD. It is most frequently present in patients who have extensive UC or CD affecting the colon rather than the small intestine. In UC, in particular, there is a relationship between disease flares and their severity and the development of arthritis, although the onset of joint disease may occur with bowel disease presentation or precede it by several years.

FIGURE 1. A case of dactylitis in a female patient with CD (courtesy of Dr. H. Kritikos). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Arthritis is typically seronegative (rheumatoid factor-negative), nondeforming, and nonerosive, although erosive disease affecting the hip, elbows, metacarpophalangeal joints, metatarsophalangeal joints, and an erosive polyarthritis resembling rheumatoid arthritis (RA) have been described.[6–8] In contrast to RA, the radiological appearance of the metacarpophalangeal and metatarsophalangeal joints reveals a predominantly asymmetric and pauciarticular arthritis with evidence of reactive bone formation but little bony fusion.

Type 1 (pauciarticular)—classic—arthropathy affects fewer than 5 joints, usually involves acute self-limiting attacks of less than 10 weeks duration, is strongly associated with extraintestinal manifestations of IBD such as erythema nodosum and uveitis, and there is a strong correlation with exacerbations of bowel symptoms.

Type 2 (polyarticular) arthropathy affects 5 or more joints, symptoms usually persist for months to years, and are commonly associated with uveitis but not with other extraintestinal manifestations of IBD. The course of this type of arthritis appears to be independent of the activity of IBD.

In a large retrospective series from Oxford of 976 patients who had UC and 483 patients who had CD, type 1 arthropathy occurred in 3.6% of patients who had UC and in 6% of patients who had CD, whereas type 2 arthropathy occurred in 2.5% of patients who had UC and in 4% of patients who had CD.[6] Figure 2 depicts a suggested algorithm for the management of arthritis in IBD patients and when referral to a rheumatologist is appropriate.

IBD-related Spondyloarthropathy ("Type 3")

The term IBD-related spondyloarthropathy (SpA) encompasses a variety of symptoms that are the result of predominantly axial involvement seen in active sacroiliitis or spondylitis. SpA commonly coincides with peripheral involvement including synovitis, dactylitis, or signs of enthesopathy such as Achilles tendinitis, plantar fasciitis, and chest wall pain.

The IBD-related SpA can simulate idiopathic AS, where the presence of peripheral arthritis may also coexist. The diagnosis of SpA is often missed or delayed, especially in a primary care setting.[4,9] An anteroposterior radiograph of the pelvis is adequate in most patients by the time they are seen by a rheumatologist to establish the diagnosis[10] (Fig. 3). In many patients with AS it may take years from the onset of inflammatory back pain to the development of radiographic sacroiliitis, despite the long-standing presence of clinical manifestations such as back pain and stiffness.

Axial involvement is generally more common in CD (5%–22% of patients) than in UC (2%–6% of patients). AS in IBD can occur at any age, whereas in idiopathic AS age of onset after 40 is rare. In idiopathic AS, men are more commonly affected (2.5:1), whereas in AS related to IBD the sex ratio is 1:1. The course of IBD and the onset of axial involvement are usually independent, and axial symptoms frequently precede bowel disease by several years. Thus the diagnosis of an undifferentiated SpA can precede the diagnosis of IBD. These patients might have subclinica1 intestinal inflammation, usually affecting the ileum. Overall, AS occurs in 3%–12% of patients with IBD, but radiological evidence of sacroiliitis is much more frequent (in ≈14%–20% of patients). Asymptomatic—subclinical—sacroiliitis refers to an increasing group of IBD patients with radiological signs of sacroilitis on magnetic resonance imaging (MRI) but without clinical symptoms of SpA. In a Spanish prospective study including 62 IBD patients without axial symptoms who were evaluated by MRI, 24% showed signs of subclinical sacroilitis, while 57% of them had a diagnosis of CD.[11]

MRI is the most recent imaging milestone in the diagnosis of the preradiographic phase of AS whether or not it is related to IBD,[12–14] confirming that active inflammation of the sacroiliac joints and/or the spine is present long before the appearance of unequivocal sacroiliitis on plain radiography.[9,12] MRI using the short-tau inversion recovery (STIR) technique is an excellent tool to demonstrate sacroiliitis and enthesitis without the risk of exposure to ionizing radiation. The STIR technique can show clear evidence of inflammation and bone marrow edema, indicating active ongoing inflammation without the added cost of gadolinium enhancement.[15–18] MRI may often detect bone edema and even bony erosions that are still not detectable by conventional radiographs[12] (Figs. 4, 5). Many patients with idiopathic AS have evidence of chronic microscopic bowel inflammation affecting mainly the terminal ileum simulating IBD, while none of the patients with normal histology

TABLE 1. Musculoskeletal Manifestations of IBD

	Clinical Features	Sites Involved	Effect of Disease Activity	Treatment
Peripheral arthritis:				
Type I	Acute self-limiting attacks of less than 10 weeks duration, Strongly associated with EIM	< 5 joints involved (knee, hip, elbows) predominantly asymmetric, nondeforming and nonerosive	Strongly related	Treatment of bowel disease
Type II	Symptoms usually persist for months to years and are commonly associated with uveitis but not with other EIM	>5 joints involved (metacarpophalangeal metatarsophalangeal joints) predominantly symmetrical, nondeforming and nonerosive, rarely polyarthritis resembling RA	Not related	Sulphasalazine (2-3gr/day) Glucocorticoids Anti-TNFagents
Axial arthritis	Back pain, morning stiffness	Sacroileal joints and /or the spine, +/- synovitis, dactylitis or enthesopathy (achilles tendinitis, plantar fasciitis, and chest wall pain).	Not related	Glucocorticoids Anti-TNF agents
Osteoporotic fractures	Back pain, neurologic signs	Hip, vertebrae	Related to chronicity and corticosteroid treatment	Analgesics, Antiosteoporotic therapy
Localized myositides:				
a) Orbital myositis	Acute orbital pain, diplopia, swelling of the eyelid, conjunctival injection, exophthalmos	Diffuse enlargement of extra ocular muscles on cranial MRI	Not related	Glucocorticoids Anti-TNF agents
b) Gastrocnemius myalgia syndrome	Calf located myalgia	Heterogenous histopathological findings on muscle biopsy	Not related	Glucocorticoids
Polymyositis, dermatomyositis	Weakness, myalgias, elevated serum CPK	Characteristic muscle biopsy and EMG findings.	Possibly related with cancer or high grade dysplasia development	Glucocorticoids Azathioprine

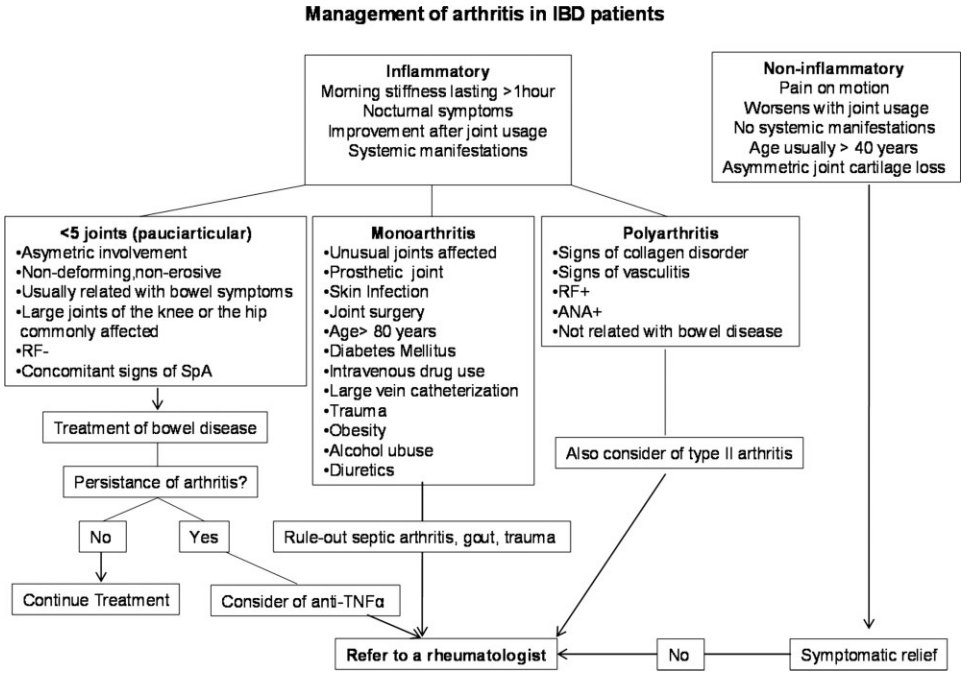

FIGURE 2. Management of arthritis in IBD patients.

subsequently developed IBD. This observation leads to the chicken-and-egg causality dilemma: is this an IBD-related SpA or is it a form of AS with extraarticular bowel involvement? The recent genealogic study from Iceland suggests a common genetic background for IBD and AS patients. Both patient groups are reported to be significantly more related to each other than to randomly sampled control subjects in terms of an increased risk of either or both conditions developing in third-degree relatives. This suggests that IBD and AS may represent 2 different manifestations of the same or similar initial genetic defect.[19]

Increased clinical awareness is needed especially in young patients with a history of low back pain that can be attributed to a misdiagnosed IBD related SpA. Even after making the diagnosis the clinician has to consider not only the large spectrum of extraintestinal manifestations of IBD but also possible drug-induced skeletal comorbidities. For example, prolonged therapy with corticosteroids or

FIGURE 3. Plain radiograph of the sacroiliac joints obtained from the same patient demonstrates that both the sacral and iliac sides of both sacroiliac joints show erosion and sclerosis. The findings are characteristic of the symmetric seronegative spondylarthropathies, including ankylosing spondylitis and arthritis associated with IBD.

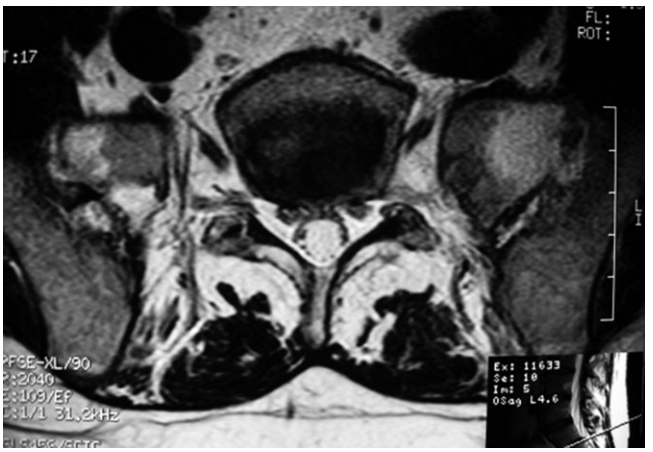

FIGURE 4. T2-weighted image showing increased intensity signals in both the sacral and iliac bones indicative of edema extending into the bone medulla.

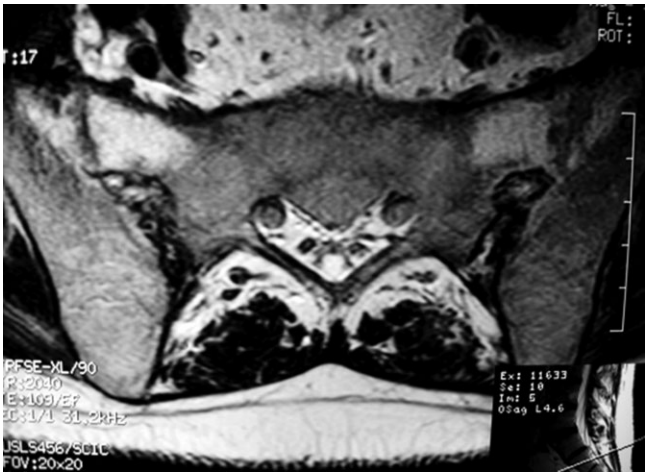

FIGURE 5. T2-weighted image showing sclerotic elements of joint surfaces bilaterally and indicate the chronicity of the joint involvement.

quinolone antibiotics, a common treatment during flares of IBD or perianal CD, can be related to the development of tendinitis and tendon ruptures simulating IBD enthesopathy. Figure 6 depicts a suggested algorithm for the clinical evaluation of low back pain in IBD patients.

ARTHRITIS IN CHILDREN WITH IBD

In a recent large cohort of 1649 pediatric IBD patients, arthritis was the most common extraintestinal manifestation (26% of all extraintestinal manifestations).[20] IBD-related arthritis in childhood is more commonly peripheral than axial and it is usually associated with the presence of active bowel disease and similar topography of bowel involvement, as has been described in adults, but it is less frequently related to flares of IBD than in adults.[21] Arthritis tends to be pauciarticular; ankles, knees, elbows, and hips are most commonly affected.[22] Symmetrical finger involvement with boutonniere deformities and sacroiliac erosions and more destructive clinical course can be recognized in children with CD.

There is a discrepancy in the subclassification of IBD-related arthropathies and optimization of treatment in clinical practice, especially after the introduction of biologics in the treatment of IBD. A more useful classification in clinical practice could be based on the therapeutic response of arthritis in relationship to the response of the bowel disease. According to this clinical classification, new prognostic factors and therapeutic guidelines may appear in the future.

RESPONSE OF IBD-RELATED ARTHRITIS TO TREATMENT

Response to Conventional Therapy

In enteropathic arthopathies, management of bowel inflammation is the main therapeutic target because this will indirectly induce remission of musculoskeletal manifestations. However, in a sizable number of patients, despite the amelioration or disappearance of gut inflammation, joint disease persists.[23] When both intestinal disease

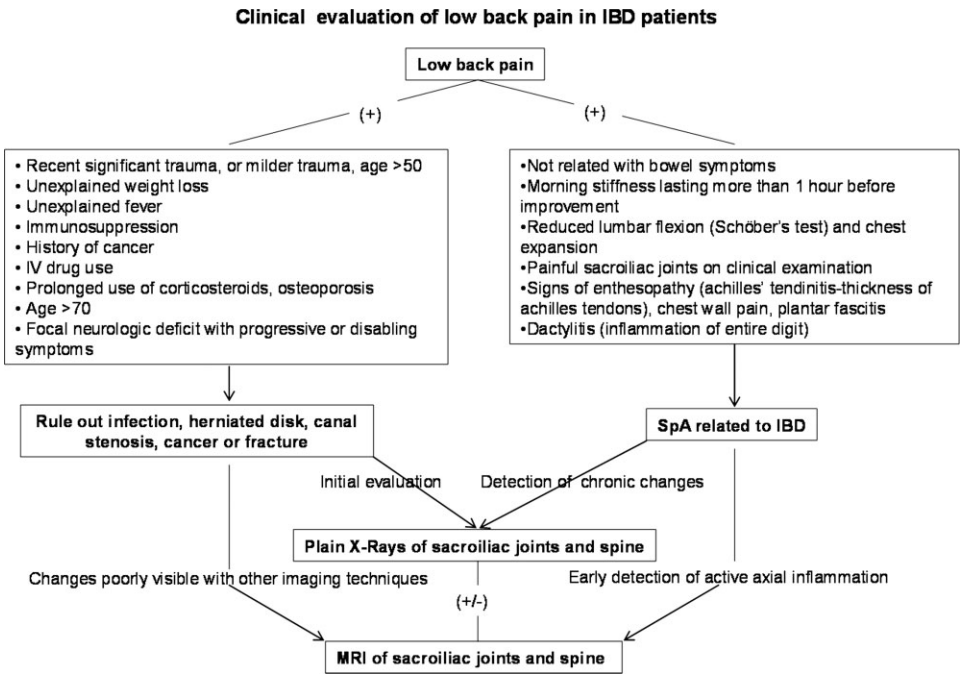

FIGURE 6. Clinical evaluation of low back pain in IBD patients.

and arthropathy are in an active phase, the preferred drugs are those potentially effective for both diseases. Sometimes, even though CD is in clinical remission and laboratory inflammatory markers are normal or scarcely altered, the musculoskeletal symptoms associated with SpA may persist. In these cases, control of the musculoskeletal symptoms, especially enthesitis and spinal pain that potentially mirror progression of the disease toward ankylosis,[24] becomes the primary therapeutic task together with the restoration of the quality of life of the patient.

Most patients who have an SpA will respond to nonsteroidal antiinflammatory drugs (NSAIDs), which are, however, contraindicated in IBD because of their association with the development of ulcerations in the small and large intestine and flares of IBD. Steroids and disease-modifying antirheumatic drugs (DMARDs) are often ineffective in controlling axial pain and enthesitis[25] and, with the exception of sulfasalazine and methotrexate, they cannot completely prevent relapse of bowel inflammation. Methotrexate has been used as an effective treatment in CD[26] but its effect on peripheral or axial articular involvement in AS is not well documented.[27] Sulfasalazine (2–3 g/day) has been shown to be effective in the treatment of both the underlying disease and flares of UC, but the situation is less clear-cut for CD.[28] Sulfasalazine has generally demonstrated efficacy at improving AS-associated peripheral arthritis, but not back pain. In a combined analysis of patients with seronegative SpAs (264 AS, 221 PsA, and 134 ReA), sulfasalazine produced better treatment response rates, compared to placebo, in patients with peripheral arthritis than in those with exclusively axial disease.[29] Thus, sulfasalazine should be considered as the first-line and low-cost treatment for patients with UC and peripheral arthritis, while the therapeutic approach becomes more complicated in CD patients with axial involvement.

Tumor necrosis factor alpha (TNF-α) is a crucial cytokine involved in the pathogenesis of many diseases of autoimmune or immune-mediated origin, including IBD, AS, and RA. Infliximab, a chimeric monoclonal antibody against TNF-α, was FDA-approved in 1998 for the treatment of moderate to severe CD and later an FDA approval was expanded for the treatment of RA and AS. There are 4 TNF-α antagonists currently available: adalimumab, a fully human monoclonal antibody, etanercept, a soluble TNF receptor construct, certolizumab pegol, a pegylated anti-TNF Fab fragment, and infliximab, and several others are in clinical development.

All 4 available agents have been studied in the management of moderate to severe CD, RA, and AS. Interestingly, many patients with rheumatic diseases and CD who are nonresponsive (either have lost response or are intolerant to 1 TNF antagonist) respond well when switched to a different TNF antagonist.[30–34] TNF-α blockade with etanercept is effective in the treatment of SpA, but not in the treatment of CD. One recent meta-analysis showed that, compared to infliximab, etanercept is rarely, although more frequently, associated with IBD activity in patients with AS, while more data are required for adalimumab.[35] Although infliximab and adalimumab have been thoroughly investigated in the treatment of IBD, few studies have examined the specific treatment of IBD-related arthritis.

There is only 1 study evaluating patients with both IBD and SpA. In this Italian study 24 subjects (16 with active CD, 8 with inactive CD) received infliximab 5 mg/kg at weeks 0, 2, and 6 followed by 3 mg/kg every 5–8 weeks if CD was in remission or 5 mg/kg every 5–8 weeks if CD symptoms persisted. The infliximab treatment group was compared to 12 control subjects with active CD who were treated with a variety of medications including corticosteroids, azathioprine, salicylates, and antibiotics.[36] All patients treated with infliximab had experienced a significant improvement in articular and periarticular manifestations compared to controls. Infliximab significantly and rapidly improved peripheral arthritis with treatment evaluation for up to 18 months. From the first infusions, infliximab produced a clear decrease of active enthesitis, which persisted at 6, 12, and 18 months of treatment. In many of the patients who did not achieve a complete remission of enthesitis, the number of inflammation sites was reduced or the clinical manifestations of enthesitis were improved. Finally, infliximab decreased both the general musculoskeletal and the spinal pain to a significant extent. The results of treatment were better in patients with type I pauciarticular peripheral disease.

Adalimumab has also been shown to be effective for the treatment of CD and AS,[37,38] but there is a lack of trials specifically examining the efficacy of adalimumab for patients with concomitant IBD and arthritis.

Response to Surgery

Surgical removal of the diseased part of the colon or total proctocolectomy for UC usually induces remission of peripheral arthritis but has no influence on axial involvement. The extent, location, duration of IBD, and the development of complications such as strictures or fistulae and amelioration of the bowel complications by surgery do not affect the progress of spondylitis or sacroiliitis. In CD, although colonic disease increases the likelihood of peripheral arthritis, surgical removal of the diseased part does not appear to affect the course of the arthritis.

LABORATORY DIAGNOSTIC TESTS

There is no reliable laboratory test that can be used as a diagnostic or activity index of IBD-related arthritis. A normal sedimentation rate does not exclude active disease.[39] The presence of HLA-B27 positivity is thought to be higher

in patients with idiopathic AS (prevalence >90%) compared to IBD-related SpA (prevalence of HLA-B27 in ≈20%–40%).[40] Nevertheless, it is not a safe index for a differential diagnosis. Moreover, in a recent study the prevalence of HLA-B27 positivity in peripheral IBD-related arthritis was as much as 66%, suggesting that diagnosis and characterization of IBD-related arthritis is mainly a clinical diagnosis.[41] In the same study the presence of antineutrophil cytoplasmic antibodies (pANCA) was found to be positively correlated with erythema nodosum and uveitis, but it was not associated with musculoskeletal manifestations of IBD.

Antibodies recognizing cyclic citrullinated peptides (anti-CCP) are directed to proteins that contain the unusual amino acid citrulline, which is derived from the posttranslational calcium-dependent conversion of peptidylarginine to peptidylcitrulline, which is catalyzed by peptidylarginine deiminase (PAD) enzymes, a procedure called citrullination. The presence of citrullinated proteins was initially considered to be specific to the synovium in patients with RA.[42] However, recent reports showed that citrullinated proteins are also present in non-RA inflammatory synovitis.[43,44] Anti-CCP can be found in a small but significant proportion of patients with a clinical picture of PsA and are associated with erosive arthritis and multiple joint involvement.[45] Although colonic biopsy specimens from patients with IBD show various amounts of citrullinated proteins with no significant differences between macroscopically affected and nonaffected areas, the prevalence of anti-CCP antibodies in sera of IBD patients is low, suggesting that development of arthritic manifestations in IBD is not correlated with the presence of anti-CCP in serum.[46,47]

PREVALENCE OF OTHER ARTHRITIDES IN IBD PATIENTS

Restorative proctocolectomy with creation of an ileal pouch has been associated with the development of an acute symmetrical polyarthropathy, although this might be more like intestinal bypass arthritis rather than that associated with UC. A higher incidence of RA and psoriasis has been reported in patients with IBD. Bernstein et al[48] reported a similar prevalence ratio of psoriasis and pyoderma gagrenosum in IBD patients.

The incidence of other types of arthritis like osteoarthritis (OA) and gout is not known in IBD patients. Patients with IBD-related arthritides can be mistreated, as in OA or crystal-induced arthritides. The diagnosis of OA and gout can be missed especially in cases of "possible IBD related arthritis" not responding to therapy with anti-TNF-α agents. In our department a 34-year-old obese woman with ileocolonic CD and uveitis of 12 years duration presented with acute calf pain because of ruptured Baker cyst of the left knee associated with OA (unpubl. data). A 44-year-old man with a 10-year history of UC (pancolitis) on clinical remission also presented with bilateral effusions of both knees because of OA (unpubl. data). In both cases the articular fluid and radiological imaging of knees with MRI suggested a noninflammatory arthritis. The microscopic examination of articular fluid formation is an essential procedure for the classification of arthritis, while, especially in cases of monoarthritis, a septic joint should always be kept in mind. It is worth mentioning that treatment with azathioprine is contraindicated in patients with gout on allopurinol therapy.

MYOPATHIES IN IBD PATIENTS

Muscle involvement is a rare extraintestinal manifestation in IBD. Myopathy can be related either to therapy of IBD (steroids, 5-ASA, and azathioprine) or to disease-related myositis or to a coexistent autoimmune disorder affecting the muscle. Antigenic release due to bowel inflammation with subsequent antibody production and immune complex formation has been postulated as a possible pathogenetic mechanism of muscular involvement in IBD.[63] CD appears to be more commonly associated with an inflammatory myopathy than UC. Colonic disease is more often associated with the myopathy than is small bowel involvement alone. IBD preceded the development of myositis in most patients.[23,64]

POLYMYOSITIS AND DERMATOMYOSITIS

A few cases of polymyositis or dermatomyositis in association with CD have been reported[63,65,66] and 1 case of rhabdomyolysis associated with CD-related myositis has been reported.[67] All reported cases were characterized by weakness, myalgias, and elevated serum CPK with characteristic muscle biopsy and EMG findings. Infectious myositis due to *Streptococcus anginosus* with an adequate response to antibiotic therapy has also been described in 1 patient with Crohn's enteritis of 12 years duration.[68] Generalized seropositive myasthenia gravis has been reported in 1 IBD patient.

The development of dermatomyositis or polymyositis in the course of IBD, although rarely reported, should raise a red flag for cancer or high-grade dysplasia development in patients with long-lasting IBD. Moreover, the serum CPK should always be measured when symptoms of myalgias and weakness occur in a patient with IBD.

ORBITAL MYOSITIS

Orbital myositis (inflammatory orbital pseudotumor) related to IBD is a nonspecific inflammatory process of unknown origin, affecting 1 or more of the extraocular muscles. The superior recto and oblique muscles, as well as the medial recto muscles, are most commonly affected. Clinically, it is characterized by acute pain exacerbated by eye movements while diplopia, swelling of the eyelid, conjunctival injection, and exophthalmos may also be present.

Diagnosis is based on history, clinical manifestations, and therapeutic response to steroids. Cranial MRI or computed tomography (CT) show diffuse enlargement of extraocular muscles, which exhibit slightly blurred margins.[69] This situation may be recurrent and simulates thyroid orbitopathy (ophthalmopathy). However, thyroid myopathy is usually painless at onset, symmetrical, slowly progressive, and associated with systemic manifestations of Graves' disease. The clinical improvement of 7 patients with recurrent episodes of orbital myositis after treatment with infliximab suggests that TNF-α mediated inflammation may be involved in the pathogenesis of orbital pseudotumor.[70]

There are a few case reports of orbital myositis as an extraintestinal manifestation of IBD.[71–73] In our department a diagnosis of orbital myositis that responded well to corticosteroids in a 35-year-old woman preceded 1 year before development of intestinal manifestations of colonic CD affecting mainly the right part of the colon (unpubl. data). Differential diagnosis should include IBD in these cases, especially when all thyroid tests are negative.[74]

GASTROCNEMIUS MYALGIA SYNDROME

Although there are few cases reported in the literature, "gastrocnemius myalgia syndrome" has been reported as a rare extraintestinal manifestation in the setting of IBD (especially in CD) characterized by calf myalgia with heterogeneous histopathological findings on muscle biopsy, including nonspecific myositis, granulomatous myositis, or vasculitis, without evidence of systemic myositis or vasculitis.[75,76] A rapid response to treatment with corticosteroids (prednisolone 0.5 mg/kg) has been reported in almost all cases. In 1 case c-ANCA were positive in the absence of other evidence of systemic vasculitis.[77] "Focal necrotizing neutrophilic myositis" has been proposed as a specific myositis entity related to IBD characterized by features that are unknown in disorders constituting the polymyositis and dermatomyositis syndromes.[78] Vasculitic lesions are reported.

Despite the rare appearance, calf-located myalgia in the setting of IBD may be underestimated. A higher index of clinical suspicion is indicated in patients with localized myositides for concomitant IBD symptoms. On the other hand, skeletal pain in the course of IBD cannot always be attributed to "arthralgias." This will permit a better characterization of myositides related to IBD and may possibly lead to novel epidemiologic and etiopathogenic correlations.

FIBROMYALGIA

Fibromyalgia (FM) is a syndrome of chronic widespread pain (CWP) defined by the American College of Rheumatology (ACR) 1990 classification criteria.[79] While the prevalence of FM in patients with chronic diseases appear to be significantly high, there are 2 previous studies for IBD patients with different outcomes. In a previous controlled study that included 112 IBD patients, the prevalence of FM was reported to be higher among patients with IBD, and in particular CD, where a lower pain threshold was reported.[80] In a previous Scandinavian prospective study[81] that included 521 IBD patients, the prevalence of FM and CWP were similar to those of the general population. No correlation with the extent of intestinal inflammation and the occurrence of FM and CWP was found and there were no differences in the prevalence of FM and CWP between UC and CD. These contradictory outcomes may reflect different genetic and environmental factors contributing to soft-tissue rheumatism between different ethnic groups of IBD patients.

CONCLUSIONS AND FUTURE PERSPECTIVES

Muscoloskeletal manifestations in IBD are common and can prove challenging for the physician caring for the patient with IBD. The most common involvement is peripheral arthritis and SpA. Treatment aiming at controlling intestinal inflammation is the cornerstone therapeutic approach for the arthritic manifestations of IBD. Consultation with a rheumatologist with experience in dealing with arthritic manifestations in IBD to accurately classify the disease and institute appropriate treatment is of paramount importance. Advances in biological treatment for IBD has also improved the outcome of patients with difficult to treat extraintestinal arthritic manifestations. Further research in the pathogenesis of musculoskeletal complications of IBD at the genetic and immunological level will be of utmost importance in our understanding of the relation between these complications and intestinal inflammation and assist the physician in efforts to prevent their expression.

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