Inflammatory Bowel Diseases and Spondyloarthropathies

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ABSTRACT. Spondyloarthritis (SpA) is a group of diseases with similar clinical, radiologic, and serologic features, including SpA associated with inflammatory bowel disease (IBD-associated SpA). SpA is the most frequent extraintestinal manifestation in patients with IBD. Separate recommendations/guidelines are available for the treatment of axial and peripheral SpA and for both Crohn disease and ulcerative colitis. When IBD and SpA coexist, the therapeutic strategy should be modulated taking into account the variable manifestations and complications of IBD in terms of intestinal and extraintestinal features, and the clinical manifestations of SpA. (J Rheumatol Suppl. 2015 Nov;93:21–3; doi:10.3899/jrheum.150628)

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Ulcerative colitis (UC) and Crohn disease (CD) are the 2 main forms of inflammatory bowel disease (IBD) and are lifelong, frequently debilitating, inflammatory conditions. Both UC and CD colitis (UC) are characteristically chronic, significantly impair quality of life, require prolonged medical and surgical interventions, and represent a major burden to society overall. What makes IBD particularly challenging is its still unknown cause, its unpredictable presentations and symptoms, the less than optimal treatments, and a continuous rise in its incidence and prevalence in many areas of the world. The disease course of UC and CD is characterized by periods of inflammatory activity alternating with periods of remission.

Clinically, UC is so strongly associated with rectal bleeding that its absence almost excludes the diagnosis. Bleeding may be associated with abdominal pain, diarrhea, and signs of systemic involvement such as fever or anemia when the disease involves a large part of the colon, but it may also be the only sign when a distal colitis or a proctitis are present[1].

The clinical presentation of CD is frequently far more ambiguous, reflecting the different locations and behaviors recognized for the disease. The typical symptoms of active severe CD include fever, malaise, anorexia, weight loss, abdominal pain, and frequent diarrhea with rectal bleeding. On external examination the patient is often thin, febrile, and may be fluid depleted. Since more than 80% of patients with CD have ileocolonic or colonic involvement, part of the symptoms and signs may be similar to those of UC[2]. Nearly 90% of all Crohn's patients will eventually develop a stricturing or penetrating complication, and surgery is often necessary for Crohn's-related complications, and an estimated 75% of the overall patient population will require surgery at some point in the course of their disease.

Because of the high degree of complexity and heterogeneity of CD and UC, a subclassification of IBD into more homogeneous subgroups has been proposed several times. The most widely disseminated and shared example is the Montreal classification[3]. This classification is based on age at diagnosis, location, and behavior, with perianal disease acting as a modifier for CD[2]. UC is mainly classified according to extent and activity[1].

It will be of great importance in clinical practice to identify early patients with a more aggressive course of disease, which can be of greater benefit with a more aggressive therapeutic approach. In both CD and UC a younger age at onset is associated with more aggressive disease; in UC, extensive disease is associated with more severe course. In CD, locations at the upper gastrointestinal site and proximal small bowel, distal ileum, perianal lesions have been associated with a more aggressive disease course. Active smoking increases disease severity in CD[2].

Besides having intestinal symptoms, patients with IBD may present other clinical entities during the course of disease, the so-called extraintestinal manifestations of IBD. These extraintestinal manifestations may involve several organs, and joints are among the most frequently involved. Sometimes, the occurrence of extraintestinal manifestations may even precede diagnosis of IBD by several years.

Several studies have estimated the occurrence of spondyloarthropathies (SpA) in patients with IBD ranging between 17% and 39%[4,5], confirming that SpA is the most frequent extraintestinal manifestation in patients with IBD.

SpA is a group of several diseases with similar clinical, radiologic, and serologic features in addition to familial and

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genetic relationships. The group includes ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), SpA associated with IBD (IBD-associated SpA), and forms that do not meet criteria for the definite categories of SpA, which are designated as undifferentiated SpA (uSpA). In about 20% of patients the onset of rheumatic symptoms, especially axial symptoms, may precede and raise suspicion of IBD decades before its appearance[5,6], but usually, the musculoskeletal symptoms are diagnosed after the occurrence of IBD. In fact, according to the European Study Group (ESSG) criteria[7], IBD is a diagnostic criterion of SpA.

The musculoskeletal manifestations of SpA occurring in patients with IBD can be split into 2 different clinical subsets: axial (including sacroiliitis with or without spondylitis) and peripheral. Axial involvement is found to be present in 2%–16% of patients with IBD, with a higher prevalence in patients with CD than in UC. Moreover, the prevalence of sacroiliitis (asymptomatic and symptomatic) is between 12% and 20%.

Other, more recent studies have shown that the prevalence of axial involvement is higher than previously reported[7]. In fact, in these studies, based on the ESSG criteria for SpA, the authors detected a frequency ranging between 10% and 25% for spondylitis and between 30% and 36% for sacroiliitis[4,9]. HLA-B27 is found in 25–75% of patients with IBD and AS but only in 7–15% of patients with isolated sacroiliitis[10,11]. The peripheral manifestations of SpA are common in both CD and UC, and their prevalence has been reported in 0.4%–34.6% of patients with IBD[6], with higher frequency in CD patients (20%) versus UC patients (10%)[12]; and the joints of the lower limbs are predominantly affected. Women show more frequent peripheral joint involvement, whereas men tend to have axial involvement[13]. Considering the classification of the Oxford group[13], which divided peripheral involvement into type I (pauciarticular) and type II (polyarticular), more recent studies showed that type I is observed in 4–17% of patients with IBD while type II, independent of intestinal disease activity, is observed in 2.5% of patients with IBD[11,12]. In 2001, Smale, *et al* proposed another form of peripheral arthritis, i.e., the type III or, overlap subset, which includes patients with both axial and peripheral joint involvement[14].

Interestingly, potential risk factors for arthritis in IBD patients are active bowel disease, family history of IBD, appendectomy, cigarette smoking, and the presence of other extraintestinal manifestations, such as erythema nodosum or pyoderma gangrenosum.

Management of Patients with IBD-associated SpA

In clinical practice it can be useful to define some "red flags" that will help clinicians make a correct diagnosis of IBD-associated SpA. From the point of view of the rheumatologist, family history of IBD, clinical symptoms (chronic diarrhea and/or rectal bleeding, abdominal pain, weight loss, and/or persistent fever), presence or history of previous perianal disease, and anemia should prompt a gastroenterological consult to study the patient as appropriate.

In contrast, for the gastroenterologist, suspicion of SpA should be prompted by the presence of chronic back pain (more than 3 months), peripheral joint pain/swelling, signs of enthesitis, and the presence or history of dactylitis or other types of tenosynovitis. In these cases, referral to a rheumatologist is required to determine which laboratory and imaging tests should be performed.

Separate recommendations/guidelines are available for the treatment of isolated forms of CD[15,16], UC[16,17], and of both axial[18] and peripheral SpA[19]. However, when IBD and SpA coexist, the therapeutic strategy should be modulated, taking into account the variable manifestations of IBD in terms of intestinal and extraintestinal features, and the clinical manifestations of SpA with particular attention to peripheral enthesitis, dactylitis, and anterior uveitis.

Very recently, different treatment algorithms have been proposed for the following associated disease forms: axial SpA and active luminal CD and UC; axial SpA and quiescent IBD; peripheral SpA (oligoarthritis and/or enthesitis and/or dactylitis); active luminal CD and UC, polyarthritis (> 4 joints); and active luminal UC and CD and peripheral SpA and IBD in remission[20].

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