Gut Inflammation in Patients with Spondyloarthropathy is Prevalent and is Linked to Crohn’s Disease

Spondyloarthropathies (SpA) are a related group of frequent disorders with common clinical and genetic characteristics. Ankylosing spondylitis (AS) is the prototype disease in this concept. Over recent years, evidence has accumulated that the gut mucosa is an important disease-related site of inflammation in the SpA complex, and that this type of gut inflammation is immunologically strongly related to Crohn’s disease (CD). Not only is CD prevalent among patients with arthropathy and chronic abdominal pain or other clinical symptoms reminiscent for inflammatory bowel disease (IBD), as outlined elsewhere in this journal issue. Silent or subclinical gut inflammation has been described in up to two-thirds of patients with SpA. Different molecular features link the gut inflammation in SpA patients with classical CD. These features include lymphocyte homing markers and macrophage markers. Also, immunological features like disease-specific antibodies (anti-Saccharomyces cerevisiae antibodies or ASCA) may link SpA to IBD.

E-cadherin mediates intercellular adhesion in epithelial cells (not only epithelial cell–cell adhesion; also affinity with the αEβ7 integrin on intra-epithelial T cells). An upregulation of E-cadherin and its associated catenins was demonstrated in clinically overt IBD. In SpA, similarly, an increased expression of the proteins of the E-cadherin/catenin complex in subclinical gut inflammation has been described. A particular subset of macrophages expresses the scavenger receptor CD163. Functional analysis of the CD163 macrophages suggests that they could contribute to the inflammation process of chronic gut and joint inflammation, amongst others because of their capacity to produce the proinflammatory cytokine TNFα. In SpA, increased representation of the CD163 subset has been observed in gut mucosa as well as in synovium. The ASCA are typical seruman antibodies in patients with CD. Recently, we described increased levels of ASCA (IgA isotype) in patients with AS.

What has become clear from the different studies describing immune alteration in the gut in patients with SpA, is the fact that there is a whole immune cascade from early preclinical molecular immune changes to clinically overt CD. The genetic or environmental factors that determine the progression within this cascade are largely unknown. Indeed, over time, some patients with SpA and gut inflammation may reverse to normality, while others progress to develop overt CD.

The recognition of the immune link between SpA and IBD, has given a special impetus towards the development of new therapies in SpA. Indeed, given the immunological link between the gut in SpA and IBD on the one hand and between gut and joint inflammation in SpA on the other hand, it was an attractive hypothesis to test that immunomodulators interfering with gut inflammation would also be of benefit for patients with SpA. Not only was salazopyrine first evaluated and found effective in patients with SpA. More recently, TNF antagonists like infliximab were successfully developed in AS and SpA. A special scientific challenge in this respect is the fact that more TNF blockers than in the case of IBD are effective in AS. Etanercept is an example of such a drug with discordant efficacy in both diseases. The biological basis of this discrepancy is currently still under research.

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References