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The Joints Manifestation of Inflammatory Bowel Diseases

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Abstract: Joint manifestations of inflammatory bowel diseases (IBD) are observed in 30% of cases. Their largest share is in total forms of ulcerative colitis (UC) 85-90% and Crohn's disease (CD) involving the colon 30-35% or large and small intestines 60%. The pathogenesis of articular manifestations remains unclear. The importance of increased permeability of the intestinal wall, which is noted in patients with UC and CD, is discussed, as a result of which the components of the membrane wall of bacteria enter the bloodstream. These components act as peptide antigens that can lead to the development of arthritis. Contacting the molecules of histocompatibility complexes and further activating T-lymphocytes, peptides lead to joint inflammation. From the point of view of a rheumatologist, the articular manifestations of IBD are classified as seronegative spondyloarthropathies. During 2013-2020, we studied the frequency of treatment of patients with IBD with extraintestinal articular manifestations for examination to a rheumatologist. We analyzed the ratio of the number of patients with IBD having joints manifestations, which were confirmed and diagnosed by a rheumatologist or consulted in the areas of a gastroenterologist and a surgeon-proctologist. All patients who turned to a rheumatologist with joints manifestations over the years were referred by a gastroenterologist (38%), surgeon-proctologist (14%) and these extraintestinal manifestations of IBD were suspected and confirmed by a rheumatologist (48%). The need for a differentiated approach to the treatment of peripheral arthritis and any axial skeletal lesions is noted, the role of 5-aminosalicylic acid (5-ASA) drugs, steroidal and non-steroidal anti-inflammatory drugs (NSAIDs), immunosuppressant and biological drugs in the treatment of articular syndrome in IBD is evaluated. It is indicated that patients with IBD having of joints manifestations should be observed jointly by a rheumatologist, gastroenterologist and a proctologist. Regional or granulomatous ileitis is a chronic bowel disease (Crohn's disease) that covers all the layers of the intestinal wall (transmural lesions), and sometimes spreads to the mesentery, regional lymph nodes affecting both the small and large intestines, but most often localized in the terminal section of a thin guts (regional, terminal ileitis). These diseases can be accompanied by damage to the peripheral joints, spine, or joints and spine. The clinical manifestations of the joint syndrome in both processes are the same. The pathogenesis of the intestinal process and joint damage has not been fully established, but it is believed that many mechanisms participate in it, and in particular, toxic, immune, autoimmune. In the blood of patients, antibodies to the cells of the intestinal mucosa, lymphocytotoxic antibodies, circulating immune complexes, in which, possibly, antigenic components of intestinal microbes, etc., are also present. In Crohn's disease, articular manifestations usually occur in childhood and adolescence. The development of peripheral arthritis in these diseases is usually not associated with the carriage of the histocompatibility antigen B27. Ankylosing spondylitis is more common in men than in women (3: 1). This disease usually develops in people who have HLA B27. Articular changes with regional ileitis occur more often in patients with other extraintestinal manifestations of the processes - with ulcers of the oral mucosa, exacerbate erythema nodosum, gangrenous pyoderma.

Keywords: Joints, Manifestation, Inflammatory, Bowel, Diseases

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Introduction

Regional or granulomatous ileitis is a chronic bowel disease (Crohn's disease) that covers all the layers of the intestinal wall (transmural lesions), and sometimes spreads to the mesentery, regional lymph nodes affecting both the small and large intestines, but most often localized in the terminal section of a thin guts (regional, terminal ileitis).

These diseases can be accompanied by damage to the peripheral joints, spine, or joints and spine. The clinical manifestations of the joint syndrome in both processes are the same. It is important to note that the course of ankylosing spondylitis (AS) varies greatly from person to person. So too can the onset of symptoms. Although symptoms usually start to appear in late adolescence or early adulthood (ages 17 to 45), symptoms can occur in children or much later in life.

The most common early symptoms of AS are frequent pain and stiffness in the lower back and buttocks, which comes on gradually over the course of a few weeks or months. At first, discomfort may only be felt on one side, or alternate sides. (Danoy et al., 2010; Burton et al., 2007). The pain is usually dull and diffuse, rather than localized. This pain and stiffness is usually worse in the mornings and during the night, but may be improved by a warm shower or light exercise.

Note that AS can present differently at onset in some people. This tends to be the case in women more than men. Quoting Dr. Elaine Adams, "Women often present in a little more atypical fashion so it's even harder to make the diagnosis in women." For example, we have heard anecdotally from some women with AS that their symptoms started in the neck rather than in the lower back. (Mielants et al., 1995; Thjodleifsson et al., 2007).

Varying levels of fatigue may also result from the inflammation caused by AS. The body must expend energy to deal with the inflammation, thus causing fatigue. Also, mild to moderate anemia, which may also result from the inflammation, can contribute to an overall feeling of tiredness.

Chronic inflammatory arthritis, a hallmark of several inflammatory rheumatic diseases, and inflammatory bowel disease are both life-long conditions, with substantial morbidity and even mortality. These diseases are highly prevalent—for example, chronic arthritis has a frequency of approximately 2%–3% within a given population. Interestingly, the co-existence of gut and joint inflammation was found to be prominent in spondyloarthritis, a family of interrelated rheumatologic diseases. (Jacques & Elewaut, 2008).

Number of typical clinical and genetic characteristics, including peripheral arthritis (particularly of lower limb joints) as well as inflammation of the axial skeleton (e.g., spine). Moreover, different forms of may also affect other organs, such as the skin (psoriasis) or the eye (anterior uveitis), demonstrating the systemic nature of these diseases. Various subtypes have been described based upon clinical features, but any two may share important characteristics. (Burton et. al., 2007).

The prototypical disorder of the family is Ankylosing spondylitis (AS), which is characterized by prominent inflammation of the axial skeleton (spine, sacroiliac joints), although other joints may also be affected. Other diseases include infection-triggered reactive arthritis, some forms of juvenile idiopathic arthritis, arthritis in association with inflammatory bowel diseases (IBD), and some forms of psoriatic arthritis.

Method

The pathogenesis of the intestinal process and joint damage has not been fully established, but it is believed that many mechanisms participate in it, and in particular, toxic, immune, autoimmune. In the blood of patients, antibodies to the cells of the intestinal mucosa, lymphocytotoxin antibodies, circulate immune complexes, in which, possibly, antigenic components of intestinal microbes, etc., are also present.

A recent study found a strong association between increased levels of an inflammatory marker in the gut and the subsequent development of Crohn's disease in those with existing ankylosing spondylitis. Patients participating in the study were asked to provide stool and blood samples, as well as to complete a questionnaire at the beginning of the study, (to establish their baseline scores) and once again five years later at the follow up visit. Of the patients with ankylosing spondylitis initially enrolled in the study, 80% completed the study by returning for the follow up examination. (Sulima & Sulyma, 2020).

Researchers found that an elevated level of gut inflammation at the start of the study – as evidenced by increased levels of a protein called calprotectin in the stool – was a strong predictor of the development of Crohn's disease within five years.

The striking relationship between IBD and AS has been recognized for many years: up to 10% of IBD patients develop AS, and, vice versa, IBD commonly develops in patients primarily diagnosed with AS. As both have an important underlying genetic heritability, it has been suggested that the two diseases could have an overlapping set of predisposing genes.

Strong evidence for this idea has been derived from the Icelandic genealogy database: it was shown that AS and IBD have a strong elevated cross-risk ratio in first- and second-degree relatives. However, the precise nature of the predisposing genes remained unknown for some time.

Results and Discussion

In Crohn's disease, articular manifestations usually occur in childhood and adolescence. The development of peripheral arthritis in these diseases is usually not associated with the carriage of the histocompatibility antigen B27. Ankylosing spondylitis is more common in men than in women (3: 1). (Braun & Sieper, 2007).

This disease usually develops in people who have HLA B27. One particularly interesting aspect of the paper is the elucidation of a strong association with genes implicated in the Th17 pathway, a lymphocyte subset that has gathered much attention lately because of its prominent role in a variety of immune-mediated inflammatory disorders, including psoriasis and CD.

While the association of AS with the receptor for IL-23, which is implicated in the expansion and survival of Th17 cells, has been previously reported, Danoy and co-workers provide two additional links to the Th17 pathway. Firstly, they report a clear association with STAT-3, which is, amongst other things, implicated in IL-23R signal transduction. In addition, an association with the p40 subunit shared between IL-12 and IL-23 was revealed. It is intriguing that so many genes predispose to AS. The functional significance of these associations is, however, presently unclear.

For example, some of the IL-23R single nucleotide polymorphisms associated with AS may confer either protection or susceptibility to the disease. Nevertheless, more than 30 years after the discovery of HLA-B27 as a strong heritability factor for AS, further evidence points to an important genetic susceptibility for adaptive immunity shared with CD.

Conclusion

Articular changes with regional ileitis occur more often in patients with other extraintestinal manifestations of the processes - with ulcers of the oral mucosa, exacerbate erythema nodosum, gangrenous pyoderma. However, one important limitation of the new study is the potential bias caused by subclinical bowel inflammation. Approximately two-thirds of patients suffering from AS, have microscopic signs of gut inflammation without any accompanying clinical gastrointestinal symptoms. In fact, mucosal alterations are one of the first signs of ongoing inflammation.

Histologically, the gut inflammation can be divided into acute (mimicking a short-term and self-limiting bacterial enterocolitis) and chronic types (with altered intestinal architecture, blunted and fused villi, and influx by mononuclear cells), common in enterogenic-triggered reactive arthritis and AS patients, respectively. Furthermore, 10%–15% of these patients eventually develop IBD, particularly CD. This progression to overt CD is a very peculiar feature of the chronic type of inflammation where up to 20% of those that have chronic gut inflammation develop CD.

Thus, it is clear that more studies are needed linking the presence of sub clinical gut inflammation in AS to the association of genes. Other items on the research agenda should include the functional significance of the identified gene polymorphisms in shaping the immune response and the potential interaction between the single nucleotide polymorphism of the various genes identified and their impact on clinical manifestation of disease. It is clear that exciting times lie ahead for this area of research.

Recommendations

This may be a recommendation for application in Divisions of Proctology and Rheumatology.

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Scientific Ethics Declaration

The authors declare that the scientific ethical and legal responsibility of this article published in EPHELS journal belongs to the authors.

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