Skin changes in the course of inflammatory bowel disease

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Abstract
Crohn’s disease and ulcerative colitis are classified as chronic inflammatory bowel diseases (IBD), which not only affect the intestinal tract but also involve other organs, including skin and mucous membranes. More than half of patients with IBD suffer from parenteral symptoms. Skin lesions may be related to the underlying disease and its complications or may have a reactive character. Most common dermatoses coexisting with inflammatory bowel diseases are: pyoderma gangrenosum, erythema nodosum, Sweet’s syndrome, polyarteritis nodosa, leukocytoclastic vasculitis, erythema multiforme, mucosal lesions and local complications (fistulae, fissures and abscesses). This paper presents a rich spectrum of dermatological conditions associated with IBD.

Key words: inflammatory bowel disease, skin lesions, cutaneous Crohn’s disease, pyoderma gangrenosum.

Introduction
Chronic inflammatory bowel disease (IBD) includes two enteritis: ulcerative colitis (colitis ulcerosa – CU) and Crohn’s disease (Leśniowski-Crohn’s disease – LCD). The etiology of both remains unknown. Genetic, environmental, infectious and immunological factors leading to chronic intestine inflammation with erosions, ulcers and necrosis are believed to contribute to the development of the two diseases. Parenteral IBD symptoms occur in more than half of patients. Inflammatory bowel disease mostly leads to the development of articular changes (peripheral arthritis, axial arthritis), mucosal and skin lesions as well as to eye symptoms (conjunctivitis, iritis and uveitis) [1].

In the course of chronic inflammatory bowel disease, skin lesions are found in approximately 5-50% of patients [2-4]. Statistically, more skin symptoms occur in patients with LCD (15-20%) than in patients with CU (10%) [5, 6]. They may develop in the course of the primary disease, as a complication in the form of fistulae, fissures and abscesses, or less commonly, as a cutaneous or mucosal variety of the disease. Skin lesions may also be reactive. The most common reactive dermatological diseases occurring in the course of IBD are erythema nodosum and pyoderma gangrenosum (PG) [7-10]. Less frequently the coexistence of IBD and Sweet’s syndrome [11], nodular arteritis, leukocytoclastic vasculitis or erythema multiforme has been reported. Casuistic publications report the coexistence of IBD with epidermolysis bullosa [12, 13]. In patients with IBD, skin lesions may also occur as a complication of the therapy.

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Fistulae and fissures
Fistulae and fissures are a common complication of IBD. It is estimated that these lesions develop over a lifetime in 20-40% of patients [14, 15]. According to some reports, the risk of developing fistulas reach even 85% [16]. These complications are often observed in patients with LCD, but do not belong to a typical clinical presentation of ulcerative colitis [14-16].

Fistulae and fissures are a symptom of an ongoing “transmural” inflammatory process. In patients with LCD, internal fistulae are formed between the intestine and the adjacent organs (e.g. entero-intestinal, vesicointestinal fistulae) and may be asymptomatic. The external fistula develops between the bowel wall and the surface of the adjacent skin, around the stoma or in the perianal location. Mostly cutaneous and perianal fistulae are diagnosed. They are accompanied by pain and characterized by the presence of seeping discharge irritating the surrounding skin, and the development of abscesses.

Treatment of fistulas in the course of LCD is complicated and depends on the location, severity of symptoms, num-
ber of branches of the fistula, the patient’s nutritional status, their operational history and the presence or absence of changes in the perianal area. Therapy involves surgical management, treatment with antibiotics, steroids, immunomodulatory, immunosuppressive drugs (sulfasalazine, azathioprine, cyclosporine A, methotrexate, tacrolimus, mycophenolate mofetil) and biologics (infliximab) [14-17].

Changes in the oral cavity

Changes in the oral cavity occur in 4-20% of patients with LCD [18]. Aphthous stomatitis characterized by the presence of shallow, circular ulcers covered by fibrin with an erythematous halo is frequently observed. Other lesions in the oral mucosa characteristic of IBD are: small nodules appearing on the gums, linear ulcers, perleche, gingival hyperplasia, granulomatous inflammation of the lips (Miescher cheilitis), cobblestoning and pyostomatitis vegetans (hyperplastic suppurative inflammation of the mouth) manifested by white-yellowish pustules which burst, leaving erosions and ulcers [5, 19].

Miescher cheilitis (granulomatous inflammation of the lip, cheilitis granulomatosa) (Figure 1) is a rare inflammatory disease, which was described in 1945 by Miescher. It is characterized by a painless, diffuse, sometimes asymmetric edema of the lip. The etiology is unclear, however, many authors emphasize the coexistence of Miescher cheilitis with LCD. Ratzinger et al. have demonstrated the coexistence of this illness with LCD in 30% of patients. Therapy is based on clofazimine and corticosteroids. Infliximab appears to be a promising alternative [20-22].

Sweet’s syndrome

World literature also describes the coexistence of Sweet’s syndrome (acute febrile neutrophilic dermatosis) and IBD (approximately 40 cases) [29]. It is a disease similar to PG in terms of both histology and the mechanism of the formation of skin lesions. However, the clinical pictures are significantly different. In the course of Sweet’s syndrome, pruritic, erythematous, edematous-infiltrative lesions which are frequently associated with fever and leukocytosis are observed. In the treatment, corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs) and immunosuppressive drugs are useful [9, 29, 30].

Reactive skin lesions in the course of inflammatory bowel disease

Pyoderma gangrenosum

Pyoderma gangrenosum (Figure 2) is a rare, ulcerative skin disease associated with many systemic diseases, including IBD. It is characterized by massive infiltration, consisting of neutrophils and secondary vascular damage. The available literature suggests that the disease is more frequently associated with ulcerative colitis than with LCD [4, 23]. Diagnosis is usually based on exclusion and the clinical presentation. It is important to remember that PG-like ulcers may occur in cutaneous LCD. Laboratory tests may be useful in searching potential basic diseases. Histology is not specific [24]. The most important aspect of the therapy is the treatment of the basic disease. In addition, the corticosteroids, cyclosporine A, mycophenolate mofetil, tacrolimus or TNF-α antagonists if associated with (rheumatoid arthritis) RA or LCD have been used [25-27]. Local management involves elevation of the extremities, careful dressing, avoiding surgical treatment, topical medication containing corticosteroids, cyclosporine and tacrolimus [27, 28].
Erythema nodosum

Erythema nodosum (Figure 3) occurs in about 4% of patients with IBD [31]. It is the most common form of subcutaneous tissue inflammation (panniculitis) characterized by deep, erythematous nodules, which usually symmetrically occupy the front surface of lower legs. Diagnosis is based on the clinical presentation and prognosis depends on the underlying disease [32]. Treatment is based on systemic corticosteroids, potassium iodide, colchicine, NSAIDs and adjuvant compression therapy. Relieving the affected legs is also recommended [33].

Vascular diseases

The cutaneous form of polyarteritis nodosa (CPAN) is very rare in the course of LCD. In 1970, Dyer et al. described 4 cases of CPAN concomitant with LCD [34]. Since then about 13 similar cases have been reported. In the course of the disease, painful nodules along the medium vessels or the presence of livedo reticularis, often followed by ulceration, may occur. These symptoms may be accompanied by fever and joint pain [34-36].

In the course of inflammatory bowel disease, another vascular disease caused by circulating immune complexes may develop. This is leukocytoclastic vasculitis. Skin lesions show high diversity. They mostly affect lower extremities with common coexistence of edema and pain. Therapy is based on systemic corticosteroids [37, 38].

Erythema multiforme

Erythema multiforme (EM) (Figure 4) and its heavier form, called Stevens-Johnson syndrome, occurring in the course of IBD is usually associated with the toxic effect of medications (mainly sulfonamides). However, there are reports that suggest that the inflammation itself can cause intestinal lesions characteristic of EM. The role of immunological phenomena in that process has been underlined [39, 40].

Acquired epidermolysis bullosa

What can also coexist with IBD is acquired bullous epidermolysis (epidermolysis bullosa acquisita – EBA). The pathogenesis of this correlation is unclear. Immune mechanisms have been found contributory in that case and the improvement of skin condition during the remission of bowel disease has been observed [12, 13, 41].

Cutaneous Crohn’s disease

This is a rare disease, more common in women. It usually affects adults (average start at the age of 35 years), but pediatric cases have also been reported. Skin lesions may be the first manifestation of the disease. Erythematous and infiltrative plaques are often located within the external genital organs. Skin changes that may be recognized as LCD, which affect extremities but do not spread continually, occur very rarely and are referred to as...
metastatic LCD [3, 18]. In the differential diagnosis, other granulomatous diseases such as tuberculosis, sarcoidosis, fungal infections and reactions to foreign bodies must be considered. Cutaneous LCD is characterized by a chronic course. The severity of lesions correlates with the severity of intestinal changes. The treatment includes a dose of metronidazole 3 × 250 mg per day, often in combination with topical corticosteroids [42, 43]. A systemic therapy of this disease with corticosteroids, sulfasalazine, azathioprine, cyclosporine A and inhibitors of TNF-α has also been reported. Surgical treatment is not recommended [44-46].

As IBD may be accompanied by a wide variety of skin eruptions, patients with inflammatory bowel disease frequently turn to specialists in dermatology for help. Therefore, knowledge of the clinical presentation of skin lesions is absolutely necessary for all dermatologists.

References