American Journal of Medicine and Medical Sciences 2022, 12(9): 912-915
DOI: 10.5923/j.ajmms.20221209.13

Intraintestinal Lesions in Nonspecific Ulcerative Colitis (Literature Review)

S. B. Azimova[1], A. A. Khamraev[2], N. S. Nurmukhamedova[3]

[1]Associate Professor of the Chair of Normal and Pathological Physiology, Tashkent Medical Academy, Uzbekistan
[2]Doctor of Medical Sciences, Professor, Head of the General Practitioner Chair №2, Tashkent Medical Academy, Uzbekistan
[3]Assistant of the General Practitioner №2, Tashkent Medical Academy, Uzbekistan

Abstract Inflammatory intestinal diseases including non-specific ulcerative colitis remain one of serious problems of modern clinic of internal diseases. Versatility of clinical picture, complexity of diagnostics, lack of general practitioners vigilance concerning these diseases result in great number of diagnostic mistakes and, consequently, in loss of precious time for adequate treatment assignment. NSC can develop a number of extraintestinal lesions, among which changes in the liver and biliary tract are of particular importance. It is important to remember that extraintestinal lesions often manifest earlier than intestinal symptoms. Extraintestinal lesions greatly complicate the course of the underlying disease and complicate differential diagnosis and therapy. This paper presents a review of studies on extraintestinal complications.

Keywords Non-specific ulcerative colitis, Inflammatory bowel disease, Extraintestinal manifestations, Liver

1. Introduction

Inflammatory bowel disease, which includes non-specific ulcerative colitis, remains one of the serious problems of modern internal medicine. Inflammatory bowel disease is a systemic disease with an extremely varied clinical picture of bowel involvement and a wide range of possible extraintestinal manifestations, which makes primary diagnosis extremely difficult. Non-specific ulcerative colitis (UC) is a diffuse chronic recurrent disease of the colon that predominantly affects the mucosa of the colon.

The disease is found in all countries of the world. Between 3 and 15 new cases per 100,000 people are diagnosed each year, and the incidence is as high as 50-80. Men and women have the same incidence. The first peak in the detection of NSC is between 20 and 40 years of age, and the second peak is between 60 and 70 years of age [3,11].

The disease is most common in the countries of Northern Europe, the USA and Canada. In Russia, the incidence of ulcerative colitis is 2-3 cases per 100,000 people, which is much lower than in other European countries and the USA. Due to improved diagnostic capabilities, there has been a significant recent increase in the incidence of NCD [2].

Currently, there is no clear information about the etiology and pathogenesis of the disease. Changes in immunological reactivity, dysbiotic shifts, allergic reactions, genetic factors, and neuropsychiatric disorders are assumed to play a role in the pathogenesis of the disease. The variety of causative factors in their interplay may explain the variability in the clinical course and morphological manifestations of UC associated with disorders of immunogenesis [1], epithelial and neuroendocrine cell death and regeneration, and the extent of colorectal inflammation [15]. The most commonly considered predisposition to develop an autoimmune inflammatory process in the colonic mucosa in response to surface exposure to micro-organisms and viruses, as well as to food contact is inherited. This view is based on the frequent association of NSCLC with other autoimmune processes [4]. The long-standing view of ulcerative colitis as an autoimmune disease has recently been reinforced by evidence that the commensal microflora and their products serve as autoantigens and that ulcerative colitis develops by loss of tolerance to substances of normal intestinal flora, which are usually harmless. The discovery of IgG-antibodies to epithelial cells and p-ANCA in the colonic mucosa only strengthened the supporters of this hypothesis [12]. Studies performed to determine the ratio of T-lymphocytes in the colonic mucosa indicate impaired immunoregulatory interactions between activated CD4- and CD8-lymphocytes. Synthesis of human monoclonal antibodies to the pANCA antigen has helped to identify cross-reactive antigens, among them: cytoplasmic antigen of mast cells located in the colonic mucosa, ocular antigens of the ciliary body and retinal ganglion cells, and, more significantly, proteins of commensal bacteria such as Bacteroidescassae and E. coli [16]. There is a genetic predisposition to NSC (familial cases of ulcerative colitis) and an association of NSC with HLA histocompatibility complex antigens [5]. Among close

Received: Aug. 17, 2022; Accepted: Aug. 31, 2022; Published: Sep. 15, 2022
Published online at http://journal.sapub.org/ajmms

relatives, the incidence of NSC is 15 times higher than in the general population. There is also a familial predisposition to NSC, with first-line relatives having a much higher incidence than the population average, and the use of oral contraceptives, as well as dietary and psychosocial problems, being clear risk factors [6].

Morphologically, there is inflammation in different parts of the colon. The mucosa is hyperemic, edematous, ulcerated; round ulcers of various sizes. Microscopic changes are characterized by infiltration of mucosal plate with plasma cells, eosinophils, lymphocytes, mast cells and neutrophils.

Clinical features. The clinical picture is characterized by three main syndromes associated with intestinal damage: stool abnormalities, hemorrhagic and pain syndromes [10]. The onset may be acute or gradual.

The main symptom is repeated (in severe cases up to 20 times a day) watery stools with blood, pus and mucus in combination with tenesmus and difficult defecation. Often the urge to defecate produces only bloody mucus. Diarrhoea is most pronounced in the right side of the large intestine where water and electrolytes are absorbed. If the inflammatory process spreads proximally into most of the large intestine, the disease is accompanied by significant haemorrhage. Constipation may occur at the onset of proctosigmoiditis, mainly due to spasm of the sigmoid colon. During remission, diarrhoea may cease altogether. The following signs are present: abdominal pain - usually aching, less often cramping. The localisation of the pain depends on the extent of the pathological process. Most often it is in the sigmoid, colon and rectum, less often in the perineal or right ileum. An increase in pain before defecation and a decrease in pain after emptying the bowels are typical. In many patients the intensity of the pain increases 30-90 minutes after a meal. As the disease progresses, the relationship between food intake and abdominal pain is lost (i.e. the gastrocolytic reflex, which is followed by increased intestinal peristalsis after food intake, dies down).

- Tenesmus - false urges with a discharge of blood and pus ('rectal spit-up') of almost no stool masses; this is a sign of a highly active inflammatory process in the rectum.
- Constipation (usually combined with tenesmus) is due to spastic contraction of the intestinal segment above the lesion and is characteristic of limited distal forms of NSCLC.
- General symptoms later on are anorexia, nausea and vomiting, weakness, weight loss, fever and anaemia.
- The fulminant form is almost always characterised by total involvement of the colon, complications (toxic dilatation of the colon, perforation) and in most cases requires urgent surgical intervention. The disease begins acutely, with a pronounced clinical picture unfolding over 1-2 days with a frequency of bloody stool more than 10 times a day, a decrease in haemoglobin levels below 60 g/l, and elevated sedimentation rate of more than 30 mm/h.

2. Extraintestinal Manifestations of IBD

Extraintestinal symptoms of NSCLC are found in 20% of patients. These include erythema nodosa, gangrenous pyoderma, inflammatory eye disease, arthritis, ankylosing spondylitis, respiratory dysfunction, myositis, vasculitis, glomerulonephritis and other pathological processes outside the colonic wall [13,17]:

- Erythema nodosum and gangrenous pyoderma due to the presence of circulating immune complexes, bacterial antigens and cryoproteins.
- Aphthous stomatitis occurs in 10% of patients with NSCLC, with aphthae disappearing as the underlying disease subsides.
- Eye lesions include episcleritis, uveitis, conjunctivitis, keratitis, retrobulbar neuritis and chorioiditis. It occurs in 5-8% of cases.
- Inflammatory joint involvement (sacroiliitis, arthritis, ankylosing spondylitis) may be associated with colitis or occur before the main symptom.
- Bone manifestations such as osteoporosis, osteomalacia, ischaemic necrosis and aseptic necrosis are complications of corticosteroid therapy.

NSC can develop a number of extraintestinal lesions, among which changes in the liver and biliary tract are of particular importance. Extraintestinal lesions greatly complicate the course of the underlying disease and complicate differential diagnosis and therapy.

Extraintestinal manifestations in ECD occur in 5-25% of cases. The highest proportion is found in total NSC (87.5%) and CD with involvement of the large (29%) or small and large intestine (58.1%) [9]. The general systemic complications of IBD can be divided into three groups according to pathogenetic principle:

- arising from systemic hypersensitization - lesions of the joints, eyes, skin, oral mucosa;
- caused by bacteremia and antigenemia in the portal system - lesions of the liver and biliary tract;
- developing secondary to long-term disorders in the colon - anaemia, electrolyte disorders.

Liver lesions were detected in 32.2% of patients, mainly in advanced, moderate and severe cases and in highly active NSC [7]. Thus, literature data showed that parenchymatous liver lesions were found in 40 (22.2%) NSC patients, and changes of biliary tract in 18 (10.0%) patients with NSC. Nonalcoholic steatohepatitis (NASH), autoimmune hepatitis (AH) and primary biliary cirrhosis (PBC) in 40 (69,0%) patients with NSC, and changes of extra and intrahepatic bile ducts and gallbladder in 18 (31,0%). Among parenchymatous liver lesions, NASH dominated (53.5%). AH was diagnosed in 8.6% of patients, PBC in 5.2% of patients with NSC. All patients with NSC with NASH took essential phospholipids in a daily dose of 1800 mg (2 capsules 3 times daily) for 3 months besides basic therapy. After treatment only 2 (6.5%) patients had minor complaints. Before treatment all investigated patients showed significant

increases of AST and ALT in 2.3 and 2.2 times accordingly, in combination with elevated GGT in 3.7 times in comparison with a norm, which can testify to a moderately marked cytolysis syndrome [8].

The typical skin lesion in NSCLC is erythema nodosum, localized on the anterior surface of the lower legs, rarely on the face and trunk, with fever and pain syndrome [14]. The rash usually persists for several days and, as it disappears, it is replaced by ecchymoses and then by areas of discoloured skin. Chronic erythema nodosum is characterized by a persistent recurrent course, often with ulceration of the nodules. It occurs predominantly in the elderly. There is no specific treatment for erythema nodosum; therapy should be directed at the underlying disease.

Arthropathies are also considered to be the most common autoimmune extraintestinal manifestations in IBD. The incidence of arthropathies is as high as 20-40% in CD with colorectal involvement, while it is much less common at 6% in NSCLC. Bacterial agents are thought to penetrate easily into the vascular bed through the damaged intestinal membrane, causing a type III hypersensitivity reaction in the synovial membranes of the joints. The range of joint involvement is wide: ankle, knee and interphalangeal joints are usually affected. The intensity of the pain and the degree of limitation of movement in the joints are usually mild. In remission, the joint changes disappear completely, and no deformities or joint dysfunctions develop. Some patients have transient spondyloarthritis and sacroiliitis. The latter is more frequent and severe in the case of more extensive and severe lesions of the large intestine and is detected in approximately 10% of patients with NSCLC on radiographs. Symptoms of sacroileitis can precede the clinical manifestations of NSC for many years.

SCC is a systemic disease with an extremely varied clinical picture of intestinal involvement and a wide range of possible extraintestinal manifestations, making initial diagnosis extremely difficult. Often intestinal symptoms may be absent or subclinical. Correct interpretation of extraintestinal symptoms contributes to the diagnosis and timely treatment of this atypical variant, which in turn leads to a more sustained remission, avoids complications and prevents the development of treatment resistance.

3. Conclusions

Thus, inflammatory bowel diseases, which include non-specific ulcerative colitis, remain one of the serious problems of modern internal medicine. Versatility of clinical picture, complexity of diagnostics, lack of suspicion of general practitioners concerning these diseases lead to great number of diagnostic mistakes and, consequently, to loss of precious time for prescription of adequate treatment.

REFERENCES

[1] Ioffe A.Y., Zadorozhnaya T.D. Immunohistochemical features of markers of proliferation and apoptosis in patients with ulcerative colitis. Laboratory Diagnostics. 2015; 1(31): 50-53.

[2] Belousova Ye.A., Abdulganieva D.I., Alekseeva O.P., Alekseenko S.A. et al. Socio-demographic characteristics, course features and treatment options for inflammatory bowel disease in Russia. Results of two multicenter studies. Almanac of Clinical Medicine. 2018; 46(5): 445-463.

[3] Seah D, De Cruz P. Review article: the practical management of acute severe ulcerative colitis. Aliment PharmacolTher. 2016 Feb; 43(4): 482-513.

[4] Hindryckx P, Jairath V, D "Haens G. Acute severe ulcerative colitis: from pathophysiology to clinical management. NatRevGastroenterolHepatol. 2016, pp. 65-69.

[5] Shaposhnikov V.I. On the pathogenesis of nonspecific ulcerative colitis // Adv. of modern natural science. - 2013. - № 7. - C. 27-29.

[6] Inflammatory bowel disease: a practical guide / J. Razenak, S.I. Sitkin. - 7th edition revised and supplemented. - Moscow: Forte Print, 2014. - 108 c.

[7] Dorofeev A.E., Dorofeeva A.A. Liver lesions in patients with nonspecific ulcerative colitis. Gastroenterology, vol. 51, no. 2, 2017, pp.36-39.

[8] Nizov A.A. et al. Peculiarities of management of patients with inflammatory bowel disease in the Ryazan region // Pavlov Russian Medical and Biological Bulletin. - 2014. - №. 1, c.47-51.

[9] Varlamova AS, Djametova IL, Salimzyanova RM Extraintestinal manifestations of nonspecific ulcerative colitis and Crohn's disease // International Student Scientific Bulletin. - 2016. - № 4-1, c. 75-81.

[10] MagroF. etal. Third European evidence-based consens uson diagnosis and management off ulcerativ ecolitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders // Journal of Crohn's and Colitis. - 2017. - T. 11. - №. 6. - C. 649-670.

[11] Kornienko E.A. Inflammatory bowel disease in children / Kornienko E.A. - Moscow: Prima Print, 2019. - 228 c.

[12] Tretiakova YI, Antipova AA, Shulkina SG Features of cytokine profile in patients with ulcerative colitis // Modern problems of science and education. - 2017. - № 6, c.88-93.

[13] Kovacs G., Sipeki N., Suga B. et al. Significance of serological markers in the disease course of ulcerative colitis in a prospective clinical cohort of patients. PLoS One, 13 (3) (2018).

[14] Neurath M.F., Leppkes M. Resolution of ulcerative colitis. Semin. Immunopathol., 41 (6) (2019), pp. 747-756.

[15] West N.R., Hegazy A.N., Owens B.M.J. et al. Oncostatin M drives intestinal inflammation and predicts response to tumor necrosis factor-neutralizing therapy in patients with inflammatory bowel disease. Nat. Med., 23 (5) (2017), pp. 579-589.

[16] Kiernan M.G., Coffey J.C., McDermott K. et al. The human mesenteric lymph node microbiome differentiates between Crohn's disease and ulcerative colitis. J. Crohns Colitis., 13 (1) (2019), pp. 58-66.

[17] Sandborn W.J., Panes J., Sands B.E. et al. Venousthromboembolic events in the tofacitinib ulcerative colitis clinical development programme. Aliment. Pharmacol. Ther., 50 (10) (2019), pp. 1068-1076.