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REVIEW PAPER

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Inflammatory bowel disease: clinical aspects

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Abstract

Introduction. Inflammatory bowel disease is a complex disease which arises as a result of an interaction between environmental and genetic factors leading to immunological responses and inflammation in the intestine.

Aim. To review medical approaches used in inflammatory bowel disorders.

Materials and methods. An analysis of literature regarding inflammatory bowel diseases, Leśniowski-Crohn's disease, ulcerative colitis and mataloproteinases.

Results. Current evidence suggests that patients with inflammatory bowel disease may have an elevated risk of endothelial dysfunction and coronary artery disease. Over the past two decades, great advances have been made in our understanding of the interplay between the inflammatory bowel disease.

Conclusions. Inflammatory bowel diseases are increasing in Europe. The diagnosis is usually confirmed by biopsies on colonoscopy.

Keywords. inflammatory bowel diseases, Leśniowski-Crohn's disease, ulcerative colitis, mataloproteinases

Introduction

Chronic inflammatory bowel diseases are divided into Leśniowski-Crohn's disease, ulcerative colitis and undetected colitis.[1-5] Inflammatory changes in ulcerative colitis include mucosa and occur continuously from the rectum to the more proximal parts of the colon. In Leśniowski-Crohn's disease, the changes may include the entire digestive tract.[6] The symptoms include diarrhea, frequent bloody stools, and abdominal pain. Most patients with non-specific inflammatory bowel diseases from the moment of diagnosis are treated conservatively. However, a significant group of patients do not undergo such therapy during the course of the disease and require surgical procedures. Indications for surgical treatment depend on the efficacy and success of conservative treatment, the severity of the disease, and associated complications. Due to clinical differences, Leśniowski-Crohn's disease is character-

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ized by a different specialty of surgical treatment than ulcerative colitis.[7]

Material and methods

We reviewed the literature regarding the chronic inflammatory bowel diseases published between 1945 and 2018 (Figure 1). We found more than 500 articles studying this type of chronic inflammatory bowel diseases such as Leśniowski-Crohn's disease, ulcerative colitis and undetected colitis. Our review includes recent studies regarding Leśniowski-Crohn's disease, ulcerative colitis and undetected colitis.

Results

In Leśniowski-Crohn's disease, about 50-80% of patients require surgical treatment during the course of the disease.[1-5] The correct diagnosis of nonspecific inflammatory bowel diseases relies on a multidisciplinary approach based on clinical, laboratory, endoscopic, and histologic examination.

Indications for planned surgery are:[8-10]

- ineffective conservative treatment,
- incomplete occlusion,
- accessing cachexia, intraabdominal abscesses and internal or external fistulas, which cause malabsorption syndrome,
- severe parenteral symptoms,
- perianal lesions (fistulas, perianal abscesses, anal stenosis, anal fissures),
- intestinal epithelium or dysplasia,
- children's developmental delay,

Urgent indications:[11-12]

- hemorrhage,
- occlusion,
- perforation,
- abdominal or perirectal dissemination causing sepsis, fulminant disease or acute phase of disease that does not undergo pharmacological treatment.

In the surgical treatment of Leśniowski-Crohn's disease concerning the small intestine, the rule of economical resections applies, and the resection limits are determined by macroscopic changes and the mesenteric Fazio symptom (assessment of the mesentery infiltration thickness).

In the treatment of colorectal cholangitis, the extent and type of surgery depends on the severity and extent of the disease, the status of the colon and rectal susceptibility, functional sphincter efficiency and the extent of previous resections. It is recommended to perform a colectomy with ileo-rectum anastomosis (in the absence of changes in the rectum) or proctocolectomy with definitive ileostomy (if the rectum is altered diseased).

Surgical treatment of ulcerative colitis is fundamentally different from the surgical treatment of Crohn's disease. In ulcerative colitis, the aim of the operation is to remove the entire large intestine and rectal mucosa. After the procedure, the quality of life of the vast majority of patients improves. The necessity of surgical treatment is in the group of 20-25% of Colits Ulcerosa patients.

Indications for planned surgery are:

- solid symptoms of exacerbation of the disease, despite the optimal conservative treatment
- a large intestine or a pre-cancerous lesion in the large intestine (dysplasia associated lesion or mass-DALM or flat-dysplasia)
- some local complications (occurring rarely in ulcerative colitis) such as narrowing of the colon, or internal fistulas (e.g., recto-stitch) or external
- growth and maturation delay in children

Urgent indications are:

- a severe disease that does not undergo intensive 7-10 days of conservative treatment followed by emergency treatment with cyclosporin or infliximab,
- toxic distension of the colon (megacolon toxicum, when intensive conservative treatment lasting from 24 to 48 hours did not bring any improvement

Emergency indications:

- production of the large intestine with diffuse fecal peritonitis,
- massive bleeding,
- elastic bowel disease,

The surgery of choice for urgent or urgent indications is a colectomy with ileostomy with an occluded stump of the rectum (Hartmann's operation) or sewn into the skin over the pubic symphysis.

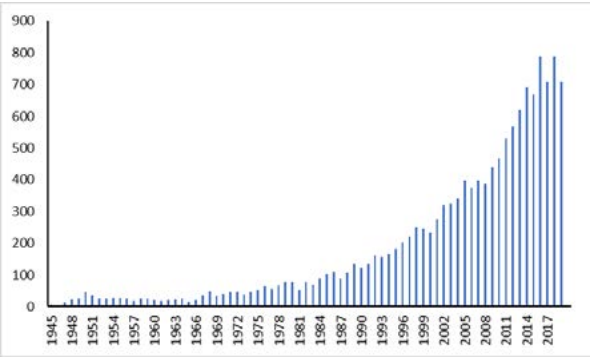

Fig. 1. Number of publications on chronic inflammatory bowel diseases (Leśniowski-Crohn's disease, ulcerative colitis and undetected colitis) from the Library of National Center for Biotechnology Information (NCBI) PubMed Data Base over the years starting from 1945

Currently, is possible to achieve the expected therapeutic results and elimination/reduction of the risk of physical development. The planned indications are: complete proctocolectomy with the final ileostomy using the Brooke method; complete reconstructive proctocolectomy with intestinal ileum (pouch) and anastomosis

of the anal canal (ileo-pouch anal anastomosis - IPAA). The technique of treatment in the case of inflammatory bowel diseases differs from that used in oncology, the wide excision of mesorectum tissues is not justified and the preparation should be conducted close to the rectum wall in order to minimize the risk of postoperative disorders of sexual function, micturition or defecation. However, surgical treatment is not a perfect and final therapeutic solution in non-specific inflammatory bowel diseases. Operations in Crohn's disease are characterized by a large number of adverse effects (e.g. metabolic consequences of short bowel syndrome), complications and relapses, both early and late. Specification of those patients in whom surgical treatment could be characterized by a more severe postoperative course, higher risk of complications and recurrences of the disease would allow more precise selection of qualification criteria, adjust the time of surgical intervention or special surveillance to improve treatment outcomes.

Table 1. Markers for nonspecific inflammatory bowel diseases

Marker	Name	References
TF(+) MPs	*Procoagulant microparticles*	(Palkovits et al. 2013)[13]
PAF	*Platelet activation factor*	(Saluk et al. 2014)[14]
Anti-I2	*Antibodies to Pseudomonas fluorescens-associated sequence I2*	(Zatorski et al. 2015)[15]
PAB	*Pancreatic antibody (an antibody to a trypsin-sensitive protein in pancreatic secretions)*	(Fakhoury et al. 2014)[16]
HLE	*Human leucocytic elastase*	(Fakhoury et al. 2014)[16]
HLE	*Human leucocytic elastase*	(Fakhoury et al. 2014)[16]
Anti-CBir1 flagellin	*Antibodies to bacterial flagellin*	(Cioffi et al. 2015)[17]
ENA-78	*Epithelial neutrophil activating peptide*	(Cioffi et al. 2015)[17]
N	*Neopterine*	(Cioffi et al. 2015)[17]
ASCAs	*Anti-Saccharomyces cerevisiae antibodies*	(Thorsvik et al. 2017)[18]
MRP-8/MRP-14 or S100A8/A9	*Calprotectin*	(Vatn et al. 2015)[19]
L	*Lactoferrin*	(Acevedo et al. 2018)[20]

In the current arsenal of laboratory, imaging and endoscopic examinations there is no marker that would allow such selection of patients. Based on the analysis of over 500 papers described nonspecific inflammatory bowel diseases, endoscopic evaluation is the main diagnostic process. Laboratory tests in the diagnosis of inflammatory bowel diseases play an auxiliary role. The most important currently known markers for nonspecific inflammatory bowel diseases are presented in Table 1.

Although considerable progress in the research has been achieved, there is still a long way to go toward the ultimate goal of an ideal biomarker in nonspecific inflammatory bowel diseases.[21-31]

Inflammatory Markers Belonging to Extracellular Matrix

Inflammatory bowel diseases have biomarkers which can be used to predict disease and treatment outcomes.[32] The Extracellular Matrix components are depolymerized into the small fragments, which are released into circulation.[33] ECM is composed of fibrous proteins and glycosaminoglycans (GAGs) and is involved in proliferation, migration, and adhesion.[34-36] Sulfated GAG types are connected with the intestinal epithelium and regulate its permeability.[37-38]

Marker	Names	References
HA	Hyaluronan	(Petrey et al. 2018)[39]
LN	Laminin	(Koutroubakis et al. 2003)[40]
SDC-1	Syndecan-1	(Koutroubakis et al. 2003)[40]
FN	Fibronectin	(Hundorfean et al. 2010)[41]

Conclusions

Inflammatory bowel diseases are increasing in Europe. The diagnosis is usually confirmed by biopsies on colonoscopy.

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References

1. Skok P, Skok K. Acute febrile neutrophilic dermatosis in a patient with Crohn's disease: case report and review of the literature. *Acta Dermatovenerol Alp Pannonica Adriat.* 2018;27(3):161-163.
2. Harris KG, Chang EB. The intestinal microbiota in the pathogenesis of inflammatory bowel diseases: new insights into complex disease. *Clin Sci (Lond).* 2018;132(18):2013-2028.
3. Florin THJ, Wright JD, Jambhrunkar SD, Henman MG, Popat A. A well-tolerated and rapidly acting thiopurine for IBD? *Drug Discov Today*. 2018; pii: S1359-6446(18)30290-3.
4. Kaida-Yip F, Deshpande K, Saran T, Vyas D. Biosimilars: Review of current applications, obstacles, and their future in medicine. *World J Clin Cases.* 2018;6(8):161-166

5. Szántó K, Nyári T, Bálint A, et al. Biological therapy and surgery rates in inflammatory bowel diseases - Data analysis of almost 1000 patients from a Hungarian tertiary IBD center. *PLoS One.* 2018;13(7):e0200824.
6. Stawiski K, Strzałka A, Puła A, Bijakowski K. PancreApp: An Innovative Approach to Computational Individualization of Nutritional Therapy in Chronic Gastrointestinal Disorders. *Stud Health Technol Inform.* 2015; 216:325-328.
7. Lu B, Niu LL, Xu XG, Yao SL, Tan XY. Ulcerative colitis in an adult patient mimicking Henoch-Schönlein purpura: A case report. *Medicine (Baltimore).* 2018;97(35):e12036.
8. Aytac E, Ozuner G, Isik O, Gorgun E, Remzi FH. Surgical management of patients with ulcerative colitis during pregnancy: maternal and fetal outcomes. *J Crohns Colitis.* 2015 ;9(1):82-85.
9. Mattioli G, Barabino A, Aloi M, et al. Paediatric ulcerative colitis surgery: Italian survey. *J Crohns Colitis.* 2015;9(7):558-566.
10. Burke KE, Haviland MJ, Hacker MR, Shainker SA, Cheifetz AS. Indications for Mode of Delivery in Pregnant Women with Inflammatory Bowel Disease. *Inflamm Bowel Dis.* 2017;23(5):721-726.
11. Ashton JJ, Ennis S, Beattie RM. Early-onset paediatric inflammatory bowel disease. *Lancet Child Adolesc Health.* 2017;1(2):147-158.
12. Singeap AM, Stanciu C, Cojocariu C, Sfarti C, Trifan A. Capsule Endoscopy in Inflammatory Bowel Disease: Current Applications. *Arch Iran Med.* 2015;18(6):379-383.
13. Palkovits J, Novacek G, Kollars M, et al. Tissue factor exposing microparticles in inflammatory bowel disease. *Journal of Crohn's & Colitis.* 2013;7(3): 222–229.
14. Saluk J, Bijak M, Ponczek MB, Wachowicz B. The formation, metabolism and the evolution of blood platelets. *Postępy Higieny i Medycyny Doświadczalnej.* 2014;68: 384–392.
15. Zatorski H, Sałaga M, Zielińska M, Fichna J. Genetic factors in pathogenesis, course and treatment of inflammatory bowel diseases. *Postępy Higieny i Medycyny Doświadczalnej.* 2015; 69:335–344.
16. Fakhoury M, Negrulj R, Mooranian A, al-Salami H. Inflammatory bowel disease: clinical aspects and treatments. *J Inflamm Res.* 2014; 7:113–120.
17. Cioffi M, Rosa AD, Serao R, Picone I, Vietri MT. Laboratory markers in ulcerative colitis: current insights and future advances. *World J Gastrointestinal Pathophysiol.* 2015; 6(1):13–22.
18. Thorsvik S, Damås JK, Granlund AB. Fecal neutrophil gelatinase-associated lipocalin as a biomarker for inflammatory bowel disease. *J Gastroenterol Hepatol.* 2017; 32(1): 128–135.
19. Vatn MH, Sandvik AK. Inflammatory bowel disease. *Scandinav J of Gastroenterol.* 2015;50(6) 748–762.
20. Acevedo D, Salvador MP, Girbes J, Estan N. Fecal calprotectin: a comparison of two commercial enzymoimmunoassays and study of fecal extract stability at room temperature. *J Clin Med Res.* 2018; 10(5), 396–404.
21. Lallemand C, Liang F, Staub F, Simansour M, Vallette B, Huang L, Ferrando-Miguel R, Tovey MG. A Novel System for the Quantification of the ADCC Activity of Therapeutic Antibodies. *J Immunol Res.* 2017;2017:3908289.
22. Abraham BP, Thirumurthi S. Clinical significance of inflammatory markers. *Curr Gastroenterol Rep.* 2009;11(5):360-367.
23. Malícková K, Janatková I, Fucíková T, Adamec S, Lukás M. Initial experience with detection of Saccharomyces cerevisiae antibodies in patients with primary nonspecific inflammatory bowel disease. *Epidemiol Mikrobiol Imunol.* 2001;50(3):131-135.
24. Eda K, Mizuochi T, Takaki Y, Ushijima K, Umeno J, Yamashita Y. Successful azathioprine treatment in an adolescent with chronic enteropathy associated with SLCO2A1 gene: A case report. *Medicine (Baltimore).* 2018;97(41):e12811.
25. Umeno J, Matsumoto T, Hirano A, Fuyuno Y, Esaki M. Genetic analysis is helpful for the diagnosis of small bowel ulceration. *World J Gastroenterol.* 2018;24(28):3198-3200.
26. Derkacz A, Olczyk P, Komosinska-Vassev K. Diagnostic Markers for Nonspecific Inflammatory Bowel Diseases. *Dis Markers.* 2018;2018:7451946.
27. Shivashankar R, Lichtenstein GR. Mimics of Inflammatory Bowel Disease. *Inflamm Bowel Dis.* 2018;24(11):2315-2321.
28. You JY. Features and management of very early onset inflammatory bowel disease. *Zhongguo Dang Dai Er Ke Za Zhi.* 2018;20(5):341-345.
29. Mang T, Scharitzer M. Imaging of gastrointestinal inflammation: Characteristic patterns and signs. *Radiologe.* 2018;58(4):281-291.
30. Gupta AS, Nunley JR, Feldman MJ, Ortega-Loayza AG. Pyoderma Gangrenosum of the Scalp: A Rare Clinical Variant. *Wounds.* 2018;30(2):16-20.
31. Yamada Y, Sugimoto K, Yoshizawa Y, et al. Mesenteric inflammatory veno-occlusive disease occurring during the course of ulcerative colitis: a case report. *BMC Gastroenterol.* 2018; 11;18(1):9.
32. Klimczak K, Lykowska-Szuber L, Eder P, et al. The diagnostic usefulness of fecal lactoferrin in the assessment of Crohn's disease activity. *Eur J Intern Med.* 2015;26(8):623-627.
33. Truffi M, Sorrentino L, Monieri M, et al. Inhibition of Fibroblast Activation Protein Restores a Balanced Extracellular Matrix and Reduces Fibrosis in Crohn's Disease Strictures Ex Vivo. *Inflamm Bowel Dis.* 2018;24(2):332-345.
34. van der Smissen A, Hintze V, Scharnweber D, et al. Growth promoting substrates for human dermal fibroblasts provided by artificial extracellular matrices composed of collagen I and sulfated glycosaminoglycans. *Biomaterials.* 2011;32(34):8938-8946.
35. Nakahara Y, Matsusaki M, Akashi M. Fabrication and enzymatic degradation of fibronectin-based ultrathin films. Fabrication and enzymatic degradation of fibronectin-based ultrathin films. *J Biomater Sci Polym Ed.* 2007;18(12):1565-1573.

36. Matsushima H, Bogenmann E. Modulation of neuroblastoma cell differentiation by the extracellular matrix. *Int J Cancer.* 1992;51(5):727-732.
37. Kliemt S, Lange C, Otto W, et al. Sulfated hyaluronan containing collagen matrices enhance cell-matrix-interaction, endocytosis, and osteogenic differentiation of human mesenchymal stromal cells. *J Proteome Res.* 2013;12(1):378-389.
38. Klimczak K, Lykowska-Szuber L, Eder P, et al. The diagnostic usefulness of fecal lactoferrin in the assessment of Crohn's disease activity. *Eur J Intern Med.* 2015;26(8):623-627.
39. Petrey AC, de la Motte CA. Hyaluronan in inflammatory bowel disease: cross-linking inflammation and coagulation. *Matrix Biology.* 2018; 1461: 4C.
40. Koutroubakis IE, Petinaki E, Dimoulios P. Serum laminin and collagen IV in inflammatory bowel disease. *J Clin Pathol.* 2003: 56(11):817–820.
41. Hundorfean G, Neurath MF, Sitaru C. Autoimmunity against type VII collagen in inflammatory bowel disease. *J Cell Mol Med.* 2010;14(10):2393–2403.