A REVIEW OF THE LITERATURE RELATING TO THE DIFFERENTIAL DIAGNOSIS OF FUNCTIONAL AND INFLAMMATORY INTESTINAL DISEASES

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Abstract: *In order to improve the presentation of morphological characteristics and histological findings, we have compiled our own practical experience in everyday pathological and anatomical diagnosis of inflammatory bowel disease (IBD) and the data from the main literature. The microscopic appearance of inflammatory bowel disease (IBD) is frequently depicted by a combination of fundamental histologic characteristics that are occasionally regarded pathognomonic and can be observed in other disorders. It is impossible to diagnose Crohn's disease or ulcerative colitis with a single histologic characteristic by itself.When many symptoms are considered concurrently, when alterations in one or more intestinal segments are examined, and when the detected alterations are contrasted with the illness's clinical manifestation, the diagnostic precision rises.*

Keywords: *irritable bowel syndrome, ulcerative colitis, Crohn's disease, differential diagnosis, calprotectin, lactoferrin*

INTRODUCTION.

The paper addresses issues with the differential diagnosis of functional (irritable bowel syndrome) and inflammatory (ulcerative colitis, Crohn's disease) intestinal illnesses. It was mentioned that these kinds of differential diagnostics are required for certain patient types. The possibilities for doing research using laboratory and instrumental approaches are shown. Particular focus is placed on

fecal testing, which measure lactoferrin and calprotectin. Studies that have been shown to be informative are analyzed.

Given the high incidence of intestinal disorders, the issue of intestinal disease diagnosis is critical and urgent. Furthermore, practicing general profile doctors encounter particular challenges when it comes to diagnosing intestinal disease. Traditionally, there are two main categories into which all intestine illnesses can be placed: organic and functional. The Rome criteria III include the following five conditions as functional bowel diseases: nonspecific functional disorder, functional constipation, functional diarrhea, functional bloating, and irritable bowel syndrome (IBS), which is the most common disease [6]. Infectious enteritis and colitis, ulcerative colitis (UC), Crohn's disease (CD), benign (polyps) and malignant (bowel tumors), intestinal diverticula, unique types of colitis (ischemic, radiation, pseudomembranous), celiac disease, and other conditions are included in the category of organic bowel pathology.

Although organic pathology has a higher number of nosologies, functional disorders are often more prevalent. Bowel pathology is frequently a functional condition that a doctor sees, but it's crucial to recognize organic pathology as well, including potentially harmful pathology.

Differential diagnosis is required in this case. It is crucial to differentiate between Crohn's disease and ulcerative colitis, two conditions that are associated with chronic inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). It is related to the following two facts: (1) IBS is the most common intestinal disease, affecting up to 15% of adult populations in developed nations; and (2) UC and CD have significantly increased in frequency in recent decades, with prevalences of 70–150 cases of UC and 50–70 cases of CD per 100,000 people in Europe [2]. These illnesses appear to be very different from one another. Let's look at these illnesses' traditional manifestations of symptoms. Irritable bowel syndrome is a functional disease manifested by intestinal pain or discomfort associated with disturbances in stool frequency and consistency. The main symptoms of this pathology are pain in the bowel area, flatulence, diarrhea

or constipation. In addition, asthenoneurotic phenomena, including anxiety, depression, and hypochondria, are noted in a large proportion of patients with IBS. The disease is characterized by a long recurrent course with periods of exacerbation and remission, without a tendency to progression. The disease has a favorable prognosis for life, but it is difficult to achieve complete recovery [1,2].

Ulcerative colitis is an autoimmune inflammatory disease of the intestine accompanied by inflammation and erosive-ulcerative lesions of its mucosa. The disease is characterized by a shallow, continuous lesion of the intestinal wall of the large intestine with gradual spread from the rectum to the proximal direction. Symptoms of UC include increased stool frequency, blood in stool, pain, flatulence, and, in severe exacerbations, symptoms of intoxication. Some patients have extraintestinal manifestations of UC - lesions of the joints and spine, skin, eyes and liver. The disease may proceed in different ways: as fulminant forms; as continuous relapsing; with rare relapses and long remissions. In a small proportion of patients, complications requiring surgical treatment are possible. In a small proportion of patients with a prolonged course of UC, the risk of intestinal malignization increases. The severity of the disease can also vary: from mild to severe forms [5].

Crohn's disease is also an autoimmune inflammatory disease of the gastrointestinal tract, but unlike ulcerative colitis, it can occur not only in the colon but also in the small intestine and even (rarely) in the upper parts of the digestive tract. Moreover, this lesion is not continuous, but segmental (separate sections), not superficial, but deep, which leads to complications in the form of fistulas and perforations. Symptoms of CD include intestinal pain, flatulence, stool may be normal or frequent, and blood discharge with stool may or may not be present. It is not uncommon for strictures to form, up to and including intestinal obstruction, which may require surgical treatment. Sometimes in ileocecal localization of the lesion, symptoms resembling appendicitis may occur. In CD there may be the same extraintestinal manifestations as in UC, with severe symptoms of intoxication. The course of the disease and its prognosis in CD

resemble those in UC [4], but the therapeutic approach in recent years is different, especially in the choice of surgical treatment.

It would seem, why do we need differential diagnosis between IBS and CP? In classical consideration, they are quite different diseases in clinical manifestations, severity and prognosis.

In practice, however, in the case of a relatively mild course of UC and CD, these diseases can be very similar to IBS. For example, in UC the clinical manifestations may consist of loose and frequent stools up to 3-4 times a day, without blood; spastic pain, flatulence, imperative urge to defecation are possible; symptoms of intoxication are absent. This situation is even more confusing in mild CD: symptoms in such patients may include only intestinal pain and flatulence in the absence of diarrhea, bloody stool and intoxication symptoms. Sometimes extracranial symptoms - fever of unclear genesis, joint pain, anemia, etc. come to the fore, delaying the correct diagnosis for months and sometimes years. In CVD there may also be inherent asthenoneurotic phenomena of IBS, including those of a secondary nature. Thus, as seen from the above examples, differential diagnosis of CPPS and IBS in some patients is of great importance. The logical answer to this question looks like the use of instrumental methods of diagnostics of intestinal diseases. Let's consider them in details. Ideal in terms of informativeness is colonoscopy. This method enables to estimate the mucosa of the whole intestine, to take a biopsy if necessary (which is important to confirm the diagnosis of CD and UC). However, this technique is the most time-consuming and difficult both for the doctor performing it and for the patient himself (most often accompanied by pain in the intestine). Sigmoscopy is a truncated version of colonoscopy, it allows you to visualize the left sections of the intestine. Unlike colonoscopy, it is much easier for patients to tolerate, because the endoscope only reaches the spleen angle. Sigmoscopy is a good way to diagnose UC, because the lesion in UC spreads from the distal parts of the intestine. However, it may not be sufficient to rule out CD because sigmoscopy does not detect mucosal defects in the transverse colon or the right side of the

intestine. Rectomanoscopy provides even less visualization. X-ray examination of the intestine with retrograde barium filling - irrigography - allows to diagnose severe lesions of the intestinal wall, but the informative value of this technique is markedly inferior to endoscopic methods. Besides, the disadvantage of irrigography is poor visualization of rectum. Fractional X-ray examination with oral barium intake is used for diagnostics of small intestine. A special value of this technique is the possibility to examine the terminal ileum. In case of suspected intestinal obstruction, abdominal radiography is performed. Among the newer and more modern methods of bowel examination are virtual colonoscopy and videocapsule endoscopy. Virtual colonoscopy, or CT colonoscopy, is a technique that involves spiral computed tomography with a special technique that allows you to visualize the inner walls of the intestine. The technique is inferior to conventional colonoscopy in informativeness, does not allow you to take a biopsy, but is able to detect gross abnormalities in the intestinal wall. Video capsule endoscopy is a diagnosis of the state of the mucous membrane of the organs of the gastrointestinal tract using a video capsule swallowed by the patient and passed through the entire digestive canal (Figure 1). Video capsule endoscopy makes it possible to diagnose diseases of the small intestine, including lesions in the ileocecal region of the BC, with high informative value. However, video capsule endoscopy is contraindicated in the presence or suspicion of intestinal stricture.

Undoubtedly, instrumental diagnostics is a gold standard in differential diagnostics of inflammatory (i.e.organic) and functional bowel diseases. However, the given analysis of methods of instrumental diagnostics shows that these techniques are rather labor-intensive; besides, most of them require special preparation of a patient. Therefore, it is logical to search for more simple, for example, laboratory methods of differential diagnostics of intestinal inflammation and IBS Indeed, at a classical course of UC or CD exacerbation changes of hematologic parameters are registered: leukocytosis, increased content of neutrophils (especially

stabichocyanurate), increased sedimentation rate, anemia. However, it should be noted that some patients with CD or UC do not have these abnormalities. Another blood parameter that can be used for this purpose is C-reactive protein. There is some correlation between the activity of CD or UC and the degree of C- reactive protein elevation. It is clear that C-reactive protein would not be elevated in a patient with IBS. However, C-reactive protein is known to be a nonspecific index; it can also be elevated in other inflammatory diseases. All this has led to considerable research interest in fecal markers ofintestinal inflammation. It has been noted that patients with inflammatory bowel disease (UC and CD) have significantly increased levels of calprotectin and lacgoferrin in the feces. Calprotectin is a calcium- and zinc-binding protein found in the cytoplasm of neutrophils and macrophages. It is released from cells under stress or damage and enters the feces [1,5].

Lactoferrin, an iron-binding protein that is present in intestinal mucus more than in other body fluids, has a certain antibacterial effect [1,8]. The content of these proteins in the feces is proportional to the leukocyte migration in the gastrointestinal tract. Accordingly, it is logical that calprotectin and lactoferrin will be elevated in patients with CVD, while this increase is not noted in patients with IBS. Thus, the use of these markers is informative and appropriate in the differential diagnosis of inflammatory and functional intestinal pathology.) But this is not the only advantage of these markers. Calprotequin and lacgoferrin content increases during exacerbation of UC or CD and decreases during remission. Thus, it is possible to detect exacerbations of these diseases and evaluate the effectiveness of therapy. There is also an opportunity to use these fecal markers during remission to predict the occurrence of an exacerbation of the disease.

In addition to the most studied and common fecal markers - calprotectin and lactoferrin - lysozyme, myeloperoxidase, polymorphonuclear neutrophil elastase and other markers are also studied.

We would like to dwell on the results of individual studies investigating the diagnostic significance of fecal markers.

One of the first studies on this issue was conducted in Norway, and its data were published in 1997 AG. Roseth et al. evaluated the fecal calprotectin content in patients with active UC, inactive UC and controls. Its content was 68, 11.5 and 6 mg/l, respectively. On this basis, it was concluded that fecal calprotectin can be used as a marker of disease activity [1, 3].

In a study by J. Tibbie et al. found that when using a fecal calprotectin limit of 30 mg/l, this test has 100% sensitivity and 97% specificity in differentiating CD from IBS [6]. In a study conducted in the Netherlands, fecal calprotectin and lacgoferrin were evaluated in 112 patients with a colonoscopy-confirmed diagnosis of RKC and CVC. The sensitivity of the fecal tests was 100% for calprotectin and 78% for lactoferrin; in contrast, the specificity was slightly higher for lacgoferrin. The authors concluded that rapid fecal tests can be good noninvasive methods for excluding CVD, especially in primary care [1].

The sensitivity and specificity of increased fecal calprotectin, increased CRP, increased C-reactive protein, and simultaneous increased C-reactive protein and CRP in the differential diagnosis of CD and IBS were assessed in a study by S. Dolwani et al. its results: sensitivity was 100, 79, 77, 50 %; specificity - 79, 67, 70, 84 %, respectively. The authors of the work concluded that the use of cal-protectin as a laboratory marker was advantageous. [6].

Another study examined the value of the following laboratory markers: fecal cal-protectin, fecal lactoferrin, fecal polymorphonuclear neutrophil elastase, serum C-reactive protein. It was found that in active forms of UC and CD all these parameters were significantly higher than in inactive forms of CP and IBS. The diagnostic value in CVC was as follows: fecal calpro-tectin 80.0 fecal lactoferrin 80.0 %, fecal polymorphonuclear neutrophil elastase 74.1 %, serum C-reactive protein 80.0 %. It was noted that the diagnostic value for CD was highest for calprotectin (81.4%), for UC - for lactoferrin (83.3%) [7]. Another study evaluated the diagnostic value of fecal calprotectin, lactoferrin, lysozyme,

myeloperoxidase, and polymorphnuclear neutrophil elastase in the differential diagnosis of IBS and CVD. The values of polymorphonuclear neutrophil elastase and calprotectin correlated with the severity of inflammation, which allows their use for differential diagnosis of intestinal inflammation and IBS [1,3].

Very important results were obtained in 2009 in the study of J.P. Gisbert et al. The relapse rate in the following 3 months in patients with CVD in remission made 30.0 % with increased calprotectin and 7.8 % with unexcited calprotectin; 25.0 % with increased lactoferrin and 10.0 % with unexcited lactoferrin. Thus, the use of these biomarkers makes it possible to predict the nearest exacerbation in patients with CVC in remission (Fig. 4) [7].

Figure 4 -- Prediction of the possibility of relapse as a function of increased calprotectin and lactoferrin

A detailed study of the diagnostic value of fecal calprotectin was performed in 2008-2010 at the Department of Gastroenterology and Therapy, FPO, Dnepropetrovsk Medical Academy (Stepanov Y.M., Fedorova N.S.). The average level of fecal calprotectin was 69.8 μg/g in UC, 61.7 μg/g in BC, and 13.7 μg/g in the control group. According to these studies, fecal calprotectin content correlated closely with the phase of the disease and inflammatory activity established according to endoscopic and histological criteria (r=0.65) (Fig. 5) [3].

The importance of using calprotectin and lactoferrin as rapid fecal tests has been studied for a decade and a half by the world's leading specialists. Certainly, to date, we can say that these markers are valuable diagnostic methods. However, it is impossible to say that they can replace instrumental methods of diagnostics, especially at primary establishment of diagnosis of UC, CD or IBS However, there is another very important problem of modern gastroenterology and coloproctology - screening of colorectal cancer and polyps. It is very important to diagnose CGC in time, but it is even more important to detect early colorectal cancer or preceding colorectal polyps in time. In this regard, the value of endoscopic diagnosis is not questioned. Thus, determination of fecal calprotectin and lactoferrin in primary diagnosis is an additional, but not the main method of

diagnosing intestinal diseases. However, the great advantage of assessing these markers is that, as mentioned above, their content correlates with the activity of CDC, allows to evaluate the effectiveness of treatment and predict the nearest exacerbation in patients in remission.

CONCLUSIONS: Thus, we should say that the problem of differential diagnosis of inflammatory and functional intestinal diseases is important and urgent. The gold standard of this differential diagnostics is use of instrumental methods. However, the use of fecal markers of inflammatory process evaluation in intestine becomes more and more popular and widespread.

LIST OF REFERENCES:

1. Zvyagintseva T.D. Irritable bowel syndrome: modern aspects of diagnosis and treatment / T.D. Zvyagintseva // Zdorov'ya Ukrainy. - 2007. - №4. - C. 59.

2. Stepanov Yu.M. Realities and prospects in diagnostics of intestinal diseases / Yu. Stepanov, N.S. Fedorova // Souzhasna gastroenterologii. - 2010. - N° 1. - C. 109-114.

3. Stepanov J.M. Fecal calpro-tectin content in patients with chronic inflammatory intestinal diseases/ J.M. Stepanov, IT. C. Fedorova // Present-day gastroenterology. - 2010. - №2. -

C. 44-48.4. Consensus statement on Crohn’s disease // Materials of 14h ECC0 Educational Workshop. — Donetsk, 2010. — 80p.

4. Consensus statement on ulcerative colitis // Materials of 14h ECCO Educational Workshop.— Donetsk, 2010. — 76p.

5. Diagnostic accuracy of faecal calprotectin estimation in prediction of abnormal small bowel radiology / S. Dolwani, M. Metzner, J.J. Wassell[et al]//Aliment. Phamacol Ther. — 2004. - 20(6). - 615-21.

6. Fecal calprotectin and lactofemn for the prediction of inflammatory bowel disease relapse / J.P. Gisbert, F. Bermejo, J.L. Perez-Calle [et al]//Inflamm. Bowel Dis. — 2009. — Vol. 15. -P. 1190-1198.

7. Modern throid gland diseases clinical laboratory diagnostic methods “Tadqiqotlar jahon ilmiy – metodik” jurnali 128-130 pages,22.05.2024.,