

IRRITABLE BOWEL SYNDROME OR INFLAMMATORY BOWEL DISEASE: CAN FECAL CALPROTECTIN MAKE THE DIFFERENCE? CASE STUDY

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Abstract: *revue of literature and case study regarding the role of fecal calprotectin in differentiating irritable bowel syndrome from inflammatory bowel disease and monitoring the treatment outcome in IBD.*

Key words: *fecal calprotectin, irritable bowel syndrome, inflammatory bowel disease.*

1. Introduction

Abdominal pain, bloating, diarrhea are common reasons for seeking medical care. Irritable bowel syndrome (IBS), infectious colitis, inflammatory bowel disease (IBD) or even colorectal cancer can have these symptoms [14].

In the day-to-day medical practice the association or the overlap between IBS and IBD symptoms is a frequent finding [3], [13], [14] and often delays the IBD diagnosis [1], [3].

2. Irritable bowel syndrome or inflammatory bowel disease?

Along the time there have been advanced a great number of opinions on the IBS-IBD relationship. The similarity between IBS and IBD seems to be more than coincidence and can reflect the existence of a bowel inflammation [12].

Studies on IBD patients revealed IBS like symptoms before IBD diagnosis,

during the active disease or in the remission period, advancing the hypothesis that IBS could be a low activity inflammatory disease [2], [13].

The low grade inflammation hypothesis is possible in postinfectious IBS where an long-lasting mast cells infiltrate, different of that from IBD, is seen many months after the acute episode. Also in postinfectious IBS and diarrhea predominant IBS it was observed an increased mucosal permeability probable induced by visceral hypersensitivity. If that is causal or an epiphenomenon it is not sure yet. The study of the risk factors for postinfectious IBS shown the importance of both local and microbiological factors, as well as psychological factors (anxiety, depression, adverse life events) [16].

In an attempt to conclude the dispute, in 2010, Drossman advanced an alternative biopsychosocial model where the mutual effect of peripheral and central factors explains the symptoms in IBS and IBD [11].

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At the same time the hypothesis of occult inflammation was advanced looking to the IBD patients in clinical remission with persistent high calprotectin and IBS like symptoms [7].

2.1. Fecal calprotectin

There are different circumstances in clinical practice (children, subclinical flares of IBD, clinician doubts on the origin of the patients symptoms) when we need surrogate markers to assess the bowel inflammation. These markers can be serological markers, like serum C reactive protein (CRP), or fecal markers like calprotectin, lactoferrin, polimorphonuclear elastase. While the CRP is a general marker of inflammation the fecal markers are proteins produced by the neutrophils from the bowel wall and are a direct indicator of local inflammation [19].

Calprotectin is a binding calcium protein, has antibacterial and antifungal action, inhibits the metaloproteinases, and inhibits *in vitro* normal or neoplastic cells [17].

In the actual and permanently dispute "Inflammatory bowel disease, irritable bowel syndrome or what?" [11] the use of fecal calprotectin is trying to be a tool for differentiating these two conditions.

Comparative studies between serologic markers of inflammation (CPR, leucocytes, specific IBD auto antibodies) and the fecal markers of inflammation shown a 89% of calprotectin accuracy in differentiating IBS-IBD. The same results were obtained with lactoferrin and they are better than serologic markers, the association of pANCA (marker for ulcerative colitis) or ASCA (marker for Crohn disease) being without supplementary benefit [9], [13].

It is proven that fecal calprotectin is an efficient tool in IBD screening also a surrogate marker in monitoring IBD treatment [6], [20]. In this second field there are two opinions one admitting the utility as surrogate marker in monitoring the IBD treatment, the other accepting this

role only in association with the endoscopic findings [18].

The use of fecal calprotectin has the advantage to be very easy to perform and, some time, can avoid the colonoscopy, especially in children. Despite the high negative predictive value the positive predictive value is variable.

3. Case study

A 48 years old woman is warded for diffuse abdominal pain, nausea, vomiting, watery diarrhea, symptoms suggesting an acute dyspepsia. She is accountant, is living in town and is divorcee. She is known in our department of gastroenterology about three years with symptoms of IBS (abdominal pain-discomfort, intermittent diarrhea) and depression and she is chronically taking trimebutin, carbamazepin and clonazepam.

At the clinical examination discreet pallor, low blood pressure, afebrile, 50 kg body weight.

Biological moderate anemia (Hb=9.6 g%), hiponatriemia and hipokaliemia (Na=122 mEq/l, K=2.94 mEq/l).

Abdominal ultrasonography was without pathological findings.

Gastroscopy and colonoscopy, including the terminal ileon, showed normal appearance along the all segments.

Initial, the clinical diagnosis was acute dyspepsia on the background of the chronic condition of IBS. The treatment was symptomatic (hydroelectrolitic balancing) and, despite the lack of definite items of IBD (except anemia), anti-inflammatory (hydrocortisone 200 mg/day).

The evolution was very good with quickly relief of symptoms.

After discharge she followed treatment with methylprednisolone 24 mg/day, mesalazine 2 g/day, mebeverine 400 mg/day. The clinical evolution was good until the attempt to reduce the methylprednisolone generate the relapse of diarrhea (10-15 watery stools/day) and fever.

She was rewarded for reevaluation and treatment. The serological markers of inflammation were at high level (CRP=11.07 mg%, ESR 22-150 mm, fibrinogen 927.4 mg%). The fecal calprotectin was at a very high level, 5400 mg/kg (N<50) suggesting an IBD. She continued the anti-inflammatory treatment (Hydrocortisone 200 mg/day) with very good outcome, remission of diarrhea and fever, improvement of general condition. At discharge she continued methylprednisolone 24 mg/day and mesalazine 3 g/day.

On the background of a stable clinical condition with normal stools, no fever, general good status we attempted, after 30 days, to reduce again the methylprednisolone. The result was the relapse of diarrhea. We concluded that we have a corticoid-dependent IBD. We came back to methylprednisolone 24 mg/day and added azathioprine 100 mg/day (2 mg/kg body weight).

After two months we gradually withdrew the methylprednisolone and after that the mesalazine.

We continued the azathioprine 100 mg/day with very good outcome, monitoring the possible secondary adverse events of the drug.

After 12 months we made a general control. The patient was out of symptoms, the biology (BC, CRP, liver and kidney tests) was in normal ranges. The fecal calprotectin was 238 mg/kg (>twentyfold lower than 12 months ago) in concordance with the clinical evolution and the other biologic findings. At the upper and lower endoscopy we find no macroscopic lesions and the biopsies from the terminal ileum and proximal jejunum showed minimal unspecific inflammation. We decide to continue azathioprine at 50 mg/day dosage and clinical and biologic monitoring.

4. Discussions

The particularity of this case consists in the long history of IBS associated with depression high suggestive for functional gastrointestinal disorder.

The lack of endoscopic findings in the segments possible to investigate in classical endoscopy (esophagus, stomach, proximal jejunum, colon, terminal ileum) demanded the use of fecal calprotectin, a surrogate marker of bowel inflammation, to sustain the diagnosis of IBD.

The overlap of IBS and IBD symptoms in this case hold on the actuality the question "IBS, IBD or what?"

4. Conclusions

The long history of IBS symptoms and the association with depression delayed the diagnosis of IBD.

Concerning the dilemma IBS or IBD it is possible that, in this case, we had an IBD with low inflammatory activity till the moment of specific clinical appearance.

The clinical appearance, the endoscopic findings, the high level of fecal calprotectin, the outcome of the azathioprine treatment are suggesting for a Crohn disease of the small bowel. To confirm this diagnosis we need to investigate the entire small bowel (spiralenteroscopy, video-capsule).

In a clinical specific context of IBD with lack of specific endoscopic and histopathologic findings the fecal calprotectin is a helpful diagnosis tool. In the same context fecal calprotectin can be used as surrogate marker in monitoring IBD outcome of treatment.

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