Gluten-free Diet for Refractory Inflammatory Bowel Disease; A Case Report

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Abstract
Some factors include environmental triggers have role in development of intestinal inflammation in inflammatory bowel disease (IBD). A number of patients with IBD, experience improvement in their gastrointestinal symptoms and disease course when avoiding gluten. To highlight this issue we present a 28years old male patient, known case of ulcerative colitis, was admitted to the hospital for a flare-up of his disease. He presented with bloody diarrhea despite the fact that he was on long term variable dose of oral and topical Asacol since 4 years ago and azathioprine 2.5mg/kg/day prescribed for his persistent symptoms since last year. In spite of drug adherence, he experienced 3 flare-ups during past year and refused receiving prednisolone. Colonoscopy demonstrated severe erythema, multiple erosions and friability through the left colon from rectum up to splenic flexure. Histopathological evaluation revealed crypt architecture distortion with moderate increase in lymphoplasmacytic infiltration as well as neutrophilic activity in the form of cryptitis and crypt abscess formation. Upper GI endoscopy followed by duodenal biopsies and serological evaluation were negative for celiac disease. Before considering anti-TNF agents, patient underwent a gluten-free diet (GFD) and with a positive response, it continued for 6 weeks. After 6 weeks GFD his bloody diarrhea was nearly resolved and 12 weeks later most of his symptoms disappeared and entered to the full clinical remission. He stopped the diet and 12 weeks later his symptoms returned and experienced another relapse that again improved on GFD. As an environmental factor, gluten represents a strong antigen that might be implicated in the pathogenesis of at least a number of patients with IBD. Dietary restriction of gluten might be useful in some IBD patients during the exacerbation of their disease.

Keywords: inflammatory bowel disease, improvement, non-celiac gluten sensitivity


1. Introduction
Inflammatory bowel disease (IBD) results from a combination of genetic predisposition and environmental factors like infections and diet/lifestyle [1]. Refractory ulcerative colitis is defined as persistence of symptoms and colo-rectal inflammation despite oral/topical steroids and 5-aminosalicylic acids (5-ASA) [2]. The management of patients with moderate to severe ulcerative colitis remains challenging [3]. In this study we discuss the role of dietary intervention in case with refractory ulcerative colitis.

2. Case Report
A 28-year-old male patient, known case of ulcerative colitis (UC), have undergone treatment with variable dose of Asacol tablets, corresponding to his symptoms, and intermittent use of enemas and suppositories of Asacol since 4 years ago was admitted to our clinic. From one year ago he reported a history of bloody diarrhea that was treated with Asacol tablets 4-6 gr daily and azathioprine 2.5mg/kg/day but the symptoms including dysentery 5 to 6 times a day and tenesmus were persistent. The patient had a history of good compliance with treatment. He underwent a flexible sigmoidoscopy that showed severe erythema, multiple erosions and friability through the left colon from rectum up to splenic flexure and several biopsies were taken. The biopsies revealed presence of moderate to severe inflammation. No obvious viral inclusion, granuloma and dysplasia were seen. On admission day the level of Hb, ferritin, PLT were low but he had slightly higher level of AST and ALT than normal range (Table 1). Also the patient underwent upper GI endoscopy to rule out other malignancies. The endoscopy was normal and 4 samples from D1 along with 2 samples from bulb were taken in order to assess celiac disease, and all of them showed normal results. Serological survey tests for tTG (IgA) and EMA (IgA) and total IgA were normal prior to starting a gluten-free diet (GFD).
Table 1. The laboratory data before and after gluten free diet

<table>
<thead>
<tr>
<th>Test</th>
<th>Before diet (at admission)</th>
<th>After GFD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>9.5</td>
<td>12.8</td>
</tr>
<tr>
<td>ESR</td>
<td>33</td>
<td>21</td>
</tr>
<tr>
<td>WBC</td>
<td>4400</td>
<td>4800</td>
</tr>
<tr>
<td>PLT</td>
<td>187000</td>
<td>287000</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.1</td>
<td>3.8</td>
</tr>
<tr>
<td>Ferritin</td>
<td>10</td>
<td>39</td>
</tr>
<tr>
<td>ALT</td>
<td>44</td>
<td>35</td>
</tr>
<tr>
<td>ALP</td>
<td>39</td>
<td>30</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>105</td>
<td>96</td>
</tr>
</tbody>
</table>

At the next step, a microbiological examination was performed on three consecutive stool samples including bacterial enteropathogens, enteric viruses (Astro-, Adeno-, Rota- and Norovirus CMV), Shiga and Clostridium difficile toxins, helminthes and intestinal protozoans. No established or potential bacterial, viral, or parasitic pathogens or any toxins were detected microscopically, by culture and/or PCR methods.

The patient was very keen to avoid taking medication and asked what he can do to improve his condition. GFD was recommended to him and he started a GFD initially for 6 weeks and continued to further 12 weeks. Surprisingly, after 6 weeks GFD his diarrhea and urgency improved significantly and he was eager to continue with diet for another 6 weeks. After 12 weeks strict GFD all his symptoms disappeared and entered to the clinical remission. For further evaluation he underwent colonoscopy that showed mucosal and vascularis pattern of colon up to splenic flexure was improved slightly. The pathology report also confirmed the colonoscopy finding and reported that crypt architecture was destructed. Usual lymphoplasmacytic infiltration is seen in lamina propria with mild basal plasmacytosis.

3. Discussion

The pathogenesis of IBD including Crohn’s disease (CrD) and UC has not been completely understood. Individual genetic predisposition, influence of the host microbiome and still largely undefined environmental triggers are the most likely factors playing role in development of intestinal inflammation in IBD [4,5]. According to the previous studies high dietary intake of total fats, polyunsaturated fatty acids, omega-6 fatty acids, and meat are the main risk factors for disease development [6].

The majority of patients with IBD believe that diet has continuing effect on worsening the natural course of their disease, exacerbating clinical symptoms, and reducing the quality of life [7,8].

Theoretically more frequent disease flares and the need for more intensified therapies could be triggered by gluten containing diet that makes proinflammatory environment in the intestine, similar to patients with IBD and concurrent celiac disease [9].

Non-celiac gluten sensitivity (NCGS) is characterized by GI and extra GI symptoms following consumption of gluten-containing foods in those who are negative for celiac disease and wheat allergy. The symptoms appear within hours or days following gluten ingestion, disappear with gluten withdrawal, and relapse following gluten challenge [7].

Recent reports have shown that after excluding celiac disease in IBD patients with significant intestinal symptoms, GFD can be a safe that may reduce gastrointestinal symptoms and disease activity [8].

In the study by Aziz et al. characteristics of CrD in patients with self-reported non-celiac gluten sensitivity (SR-NCGS) compared to those without SR-NCGS were demonstrated [9]. They suggest, subjects with SR-NCGS were significantly more likely to have stricture disease and a higher mean Crohn's Disease Activity Index (CDAI) score compared with those without SR-NCGS, whereas moderate-to-severe CDAI score was significantly associated with SR-NCGS and a score of <150 was significantly associated with those who did not reporting non-celiac gluten sensitivity. In contrast, no significant differences were found in UC patients with and without SR-NCGS according to disease extent or severe inflammatory markers.

For further evaluation of the effect of GFD in those IBD patients who have ever followed or were still following a GFD, another large survey on 314 patients in a Western population showed that, 206 (65.6%) had experienced an improvement of at least 1 clinical symptom which has been associated with GFD attempt. Additionally fewer and less severe flares and fewer medications requirement to control the disease were reported in 38.3% and 23.6% respectively [10].

All of the previous studies on the effect of GFD in IBD patients were based on self-reports of symptoms improvement while being on GFD. However by reviewing the literature on IBD and NCGS, we found that investigation in inflammatory responses to gluten in duodenal or colonic biopsies have not been performed up to now. Therefore this is the first case report showing symptoms relief after GFD in a refractory UC. This modality of treatment is not licensed as monotherapy in UC management. It only raise our attention on environmental antigens that are underestimated and yet may open an additional therapeutic modality in treating IBD patients. Manipulating environmental triggering factors like diet might possibly decrease the need of treatment escalation to TNF inhibitors and surgery some patients. Further large studies with large sample size with be required to assess the effect of diet in managing UC as the data related to nutrition therapy in UC are poor and lacking in the current literature.

References


