Case Report

Sarcoidosis and collagenous colitis - Important clinical association or coincidence?

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ABSTRACT

We present a case of a 57-year-old woman with two rare concomitant diseases: Sarcoidosis and collagenous colitis. The patient was admitted to our hospital with the symptoms of watery diarrhea that intermittently lasted for years because of delayed diagnosis. Despite increasing awareness of microscopic colitis, the delayed diagnosis remains a major problem. The diagnosis was quickly confirmed with flexible proctosigmoidoscopy. Rectal biopsies were sufficient for the diagnosis. Symptoms improved by the 2nd day of the induction therapy with budesonide. The causal relationship between sarcoidosis and microscopic colitis is not yet confirmed, and to the best of our knowledge, this is the first such case report.

Key words: *Budesonide, Calprotectin, Chronic watery diarrhea, Collagenous colitis, sarcoidosis*

Collagenous colitis (CC) was first described in 1976. It classically occurs in the female patients with a peak incidence around 60-70 years. The symptoms of CC are (and not IS) characterized by chronic, watery and nob-bloody diarrhea. Up to half of all, the patients with microscopic colitis will meet the diagnostic criteria for irritable bowel syndrome. In most of the individuals, symptoms resolve with no treatment, or minimal therapy is required for remission [1]. Budesonide is currently the most promising treatment. There are also other drugs that are effective in treating patients with CC. Mesalazine resulted less efficient than budesonide and placebo to induce clinical remission in CC patients; therefore, the current value of mesalazine for the treatment of CC remains unclear. Cholestyramine could be useful in some patients with CC, especially in those with concomitant bile acid malabsorption. In patients who failed to respond and in patients intolerant to budesonide, the use of immunosuppressive therapies should be considered. At the moment, experience with immunomodulators in CC is anecdotal, with no randomized controlled trial available. In some patients, azathioprine has been demonstrated useful. Furthermore, antitumor necrosis factor therapy (adalimumab and infliximab) has been reported in severe refractory CC [2].

CC may be associated with celiac disease and the use of certain medications, particularly non-steroidal anti-inflammatory drugs and proton-pump inhibitors. There are also reports that CG may be precipitated by infections [3]. Sarcoidosis is an inflammatory disease of unknown etiology, the cardinal feature of which are non-caseating granulomas. The incidence of intestinal involvement is not known as there are few reported cases in the literature [4]. Some authors estimate it to <1%. The stomach is the most commonly affected organ, whereas colon is affected less frequently [5]. The causal relationship between sarcoidosis and CC has not been confirmed, which makes this case important to discuss and write about.

CASE REPORT

A 57-year-old Caucasian woman was admitted to the gastroenterology department with persistent watery diarrhea since 2010. Diarrhea was cyclic, and the last episode was the most severe with ten bowel movements per day and night. She complained of fatigue, weight loss, crampy lower abdominal pain, and weight loss of 5 kg in the past 3 months. A week before admission, her calprotectin was checked in an outpatient clinic and was increased (>500 mcg/g; normal levels: <50 mcg/g). Coprocultures were negative. Routine biochemistry, hemogram, and liver functional tests were normal, and physical examination did not reveal abnormalities which were the reason she was initially planned for outpatient diagnostics.

Her medical history was notable for hypothyroidism, migraines, and sarcoidosis of the nose and lymph nodes, which was confirmed by the biopsy from the nasal skin. She was regularly seen by a pulmonologist who suggested corticosteroid therapy, but she was noncompliant to the treatment. She underwent esophagogastroduodenoscopy in 2011 following which celiac disease and Helicobacter pylori infection were ruled out. She was seen by proctologist in 2014 and had a colonoscopy without biopsies as colon mucosa was normal. She was taking sodium levothyroxine, pregabalin, and sumatriptan. Her family history was unremarkable. She worked as a cooking woman. She did not smoke or drink alcohol.

On the 1st day of admission, we performed flexible proctosigmoidoscopy with rectal biopsies. Rectal mucosa was

hyperemic and fragile with touched bleeding. Histopathological examination revealed intraepithelial lymphocytes (15 per 100 epithelial cells) and granulocytes. Trichrome staining revealed 20 μm thick collagen band under the basal membrane, findings suggestive of CC. We started induction therapy with budesonide 9 mg per day and patient experienced dramatic clinical improvement. All other tests were canceled, and the patient was discharged home.

The patient was seen 2 months after the end of the 8-week therapy with budesonide. Her symptoms deteriorated 1 month after she finished treatment. Due to very high calprotectin concentration and the history of the bloody stools, colonoscopy was later performed to exclude concomitant inflammatory bowel disease (IBD). Colon mucosa appeared endoscopically normal. Pathological examination of colon biopsies again revealed collagenous microcolitis. Upper endoscopy was performed again and was normal. Biopsies of the duodenum showed increased lymphocytic epithelial infiltration (<15 lymphocytes per 100 enterocytes), which were suggestive of nonspecific duodenal lymphocytosis. The maintenance therapy with the budesonide 9 mg was reinduced with the improvement in symptoms and patient scheduled for a follow-up.

DISCUSSION

Sarcoidosis is a multisystemic disorder of unknown etiology and has the potential to affect almost every tissue in the body [6]. Gastrointestinal (GI) involvement is sporadic (<1%). The stomach is most commonly affected and the colon least frequently [4]. The sarcoidosis of the colon is usually asymptomatic [7], but when symptoms occur, the clinical presentation of GI sarcoidosis commonly resembles those of an obstructive colonic disease [4]. A case of an isolated GI sarcoidosis with the diarrhea being the chief complaint was described [8]. Biopsies, in this instance, revealed histological evidence of sarcoidosis and patient improved after the therapy with methylprednisolone, whereas in our case, biopsies of the colon and upper GI tract did not show changes specific for sarcoidosis but CC. The common point with our case is a delayed diagnosis. Both patients presented with chronic watery diarrhea and had prior colonoscopies without biopsies as mucosa was normal. Macroscopic lesions in the colon are seen only in 25% of GI sarcoidosis cases, which warrant low threshold for biopsies despite normal colon mucosa [7]. The main difference is that our patient had a concomitant diagnosis of CC causing diarrhea and was thus diagnosed with two rare diseases: Sarcoidosis and CC. Sarcoidosis itself was not explained as the etiology of diarrhea. The coincidence of both diagnoses captured our attention as such case has not been published yet.

Before performing total colonoscopy, we performed flexible proctosigmoidoscopy with biopsies to exclude ulcerative colitis. Pathohistological examination of rectal mucosa showed changes typical for CC. Precise history revealed that the patient experienced episodes of spontaneous resolutions of watery diarrhea 6 years before admission. Indeed, recent long-term studies have suggested that CC usually runs a benign clinical course, where in some cases, symptoms resolve with no treatment, or remission occurs with minimal therapy. GI symptoms have been reducing the quality of life in this patients for at least 6 years which were dramatically improved after the treatment with budesonide. Recent prospective microscopic colitis registry from the USA revealed that the average duration from the time of diarrheal symptoms to microscopic colitis diagnosis was 2.5 years [9].

Some authors suggest to biopsy all segments of the colon when looking for microscopic colitis [10] because mucosa can have a patchy pattern of histological changes and because changes are more frequently presented in the right rather than in left colon. The fact that typical changes were seen in the rectal mucosa can be explained by the high inflammatory burden, and long-lasting disease and diagnosis in such cases can be achieved by flexible proctosigmoidoscopy. High calprotectin measured in our patient shows that this marker of luminal colon inflammation can be increased in CC despite endoscopically normal mucosa. CC should be differential diagnosis when calprotectin levels are high. We think that endoscopy in patients with sarcoidosis presented with chronic watery diarrhea must not be postponed. Biopsies of the colon mucosa must be obtained to exclude CC and colonic sarcoidosis, which are both possible etiologies of chronic watery diarrhea.

This case may indicate the higher incidence of the CC in patients with sarcoidosis. We are aware that coincidence of these two diagnoses in our patient can also be accidental. It is known that many patients with IBD have concomitant sarcoidosis. A recent study [11] revealed common susceptibility genes that are associated with IBD and sarcoidosis. A similar study with the comparison for genetic background in CC patients has not yet been reported. Cases as ours could foster such further studies.

CONCLUSION

The coincidence of the CC and the sarcoidosis might be of no causal relation. This case demonstrates that watery diarrhea in a patient with sarcoidosis could be caused by CC. To detect CC in patients with chronic diarrhea, biopsies from normal colonic mucosa must be obtained. This practice is still often neglected due to insufficient awareness of microscopic colitis. Fecal calprotectin concentration can be very high in the patients with CC. In severe inflammation of the colonic mucosa, the diagnosis of the CC can be confirmed by the rectal biopsies alone.

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