Case Report

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Rare Case of Collagenous Colitis

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Abstract

With an incidence of 5.2 per 100,000, collagenous colitis has a female preponderance and peaks at the age of 50–70 years and female to male ratio of 9:1. It is associated with HLA B8/HLA DR3 and shows increased expression of HLA1. The underlying pathogenesis is decreased levels of interstitial collagenase which leads to reduced matrix degradation which in turn results in accumulation of matrix proteins and this causes defective sodium and chloride absorption. Diagnosis is based upon microscopic analyses of colonic biopsies. The characteristic histopathological finding is the collage band thickening that mainly occurs in the caecum and transverse colon in over 80% cases and in the rectum is lesser than 30%. Blood and urine cultures are usually normal and endoscopy and radiographic evidences are absent. We hereby report a case who presented with a history of intermittent watery diarrhea associated with occasional low-grade fever that spanned over about five years and was finally diagnosed as a case of collagenous colitis.

Keywords: Collagenous colitis; Collagenase; Matrix proteins; Colonic biopsies; Transverse colon.

Introduction

Microscopic colitis (MC) has been subdivided into two forms: collagenous colitis and lymphocytic colitis. The biopsy of the colonic mucosa in collagenous colitis (CC) shows a thickened subepithelial collagen band along with chronic inflammatory changes in the lamina propria and intraepithelial lymphocytosis.[1] However, in lymphocytic colitis (LC) the histologic findings are similar but there are no thickened collagen bands.[1] The condition of microscopic colitis was first described as such in 1982 and collagenous colitis was recognized earlier, in 1976. It was first described by Lindstrom, followed by Lazenby and colleagues who in 1989 described features of lymphocytic colitis.[2] It classically occurs in elderly women since the first description of case of collagenous colitis it has been associated with celiac disease and other autoimmune disorders as well as with certain drugs. Unlike other inflammatory bowel disorders many aspects of the condition's etiology, pathogenesis and natural history remain poorly understood. Most often the clinical course appears to be benign. However serious colonic complications, including death, have been reported although they are rare.

Case Report

A 63-year-old female presented to the Department of General Medicine of IMS and SUM Hospitalon 2nd April, 2018 with complaints of chronic diarrhea for 20 days. She had multiple episodes of watery stools per day associated with a dull aching type of diffuse pain abdomen followed by passage of stool. These episodes lasted for a few days and were self-limiting and were associated with low-grade fever. Previous such histories of multiple loose stools associated with mild fever were diagnosed and treated as typhoid fever on multiple encounters over a period of almost 3 years. Around 2 years ago she had such episodes of watery intermittent loose stools, associated with few episodes of vomitings, but the patient did not develop any fever during this period. About one month back

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she was admitted in Phulvani Government hospital, with similar complaints and after being admitted without any improvement for 15 days she came to our out patient department, and was admitted for further evaluation on 2nd April, 2018 with complaints of watery loose stools, 4 to 5 episodes for one month. She had attained menopause 18 years back. Patient was a known case of thyroid for last twenty years on regular medication of thyroxine 50 mcg per day and a known hypertensive for ten years and was on telmisartan 40 mg. She was admitted to the female medical ward with a working diagnosis of chronic diarrhea for evaluation? IBD ? IBS?

Her general physical examination was unremarkable, vitals were stable, abdominal examination revealed no abnormality.

Investigations

Blood counts, liver function tests, renal function tests, urinary analysis, ultrasound abdomen were normal. Stool showed no parasites and contained mucous.

Erythrocyte sedimentation rate of 81; sodium–129; potassium 3.7; chloride 97; calcium 8.3 and magnesium 1.67; serum iron 76.3, serum ferritin 240.7, TIBC 223.4; Vit B12: 461.8. T3: 72.90, T4: 9.02, TSH: 5.12

CT scan of abdomen gave an impression of circumferential abnormal irregular wall thickening

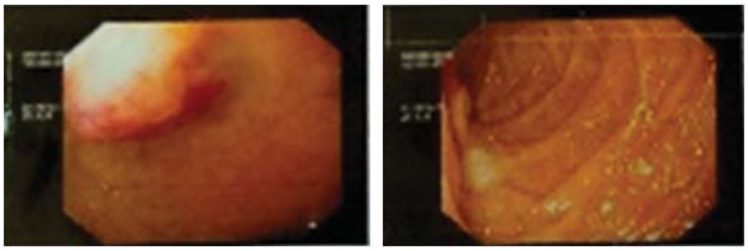

Fig 1: Upper GI Endoscopy showed smooth submucosal elevation of size 1 × 1 cm in the superior wall of D1 with an impression of probably duodenal carcinoid/neuroendocrine tumor. While D2 showed attenuated duodenal folds. Biopsy done from the duodenal folds and also D1 lesion.

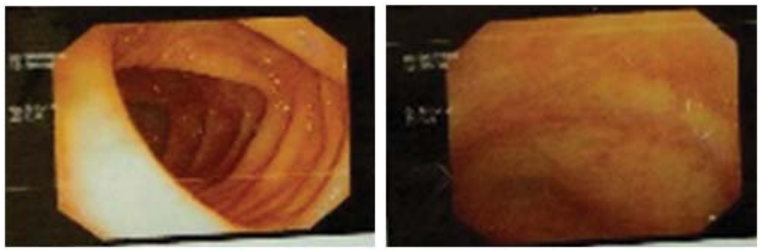

Fig 2: Colonoscopy revealed internal hemorrhoids with sigmoidal diverticulitis. Segmental biopsy done to rule out early IBD.

in GE junction extending to cardia and fundus of stomach without any perigastric lymphadenopathy.

Biopsies were taken from both endoscopy and colonoscopy; sent for HPE. Patient was meanwhile started also on antidepressants, suspecting a functional cause to the complaints of generalized malaise accompanying pain abdomen, to which she did not respond. Patient was discharged (17.4.18), with advice to follow up with biopsy reports.

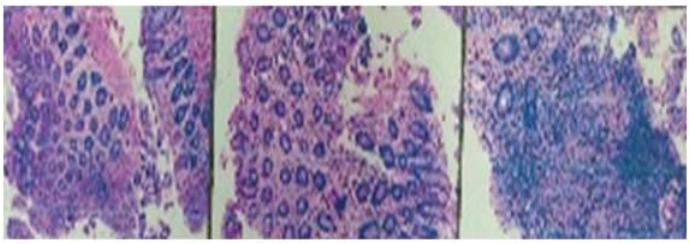

Fig. 3: Shows the tissue sample which on morphological examination favored a resolving collagenous colitis with patchy intraepithelial lymphocytosis, lamina propria fibrosis, and architectural distortion; subepithelial collagen thickening was seen.

Patient returned with the following histopathology report.

Differentials

Urinary 5-hydroxy indole acetic acid was done, and was 0.58 (reference range: 2.0 to 8.0); which ruled out carcinoid. Infectious agents are excluded as the stool doesn't show any parasites ova and enteropathogens. In the absence of characteristic findings, the patient cannot be termed as a case of ulcerative colitis and Crohn's disease. Acute infectious Colitis is characterized by neutrophilic inflammation and decreased intraepithelial lymphocytes, while our case had intraepithelial lymphocytosis.

Management

After poor response to antidiarrheal agents in the previous hospitalization, she was readmitted (with biopsy reports) on 23rd April, 2018 and started on Oral Budesonide and Mesalamine. The goal of therapy is to induce clinical remission, less than 3 stools per day or less than 1 watery stool per day with subsequent improved quality of life. The patient was discharged 7 days later with maintenance therapy of budesonide and mesalamine. Patient continued to remain symptom free till last follow up, that is 4 months after discharge. The treatment is associated with high relapse rates and management of refractory disease is challenging. Clinical response is not always associated with histological improvement.

Discussion

Collagenous colitis is clinically characterized by watery diarrhea and histologically chronic mucosal inflammation in absence of endoscopic and radiological abnormalities.

Etiology

Inciting agents have been proposed to be bile salts, toxins, infectious agents, NSAIDs (increase the colonic permeability, allowing the intraluminal antigens to enter the lamina propria and promote inflammation). Positive family history, smoking, lansoprazole, omeprazole, Angiotensin receptor blockers, beta blockers and sertraline are also believed to be etiological factors. Hormonal studies like gastrin, vasoactive intestinal peptide, urine 5 HIAA are normal in collagenous colitis. Pathology histopathology reveals flattening of epithelial cells, decrease in the number of goblet cells, Paneth cells hyperplasia and increased number of intraepithelial lymphocytes, other than the increase in plasma cells, CD8+ Tcells.[1] Cryptitis and crypt distortion are unusually seen. Normally the width of the subepithelial collagen band is 4–5 mm and predominantly consists of Type IV collagen; while in collagenous colitis, the width of the collagen band is greater than 10 mm (ranges between 20 and 60 mm) and is mostly made up of Type VI collagen, tenascin and lesser amounts of Type I and III collagen.[3] The thickened collagen layer may be continuous or patchy. Pathology underlying the collagenous colitis is modest increase in mononuclear cells within lamina propria and between crypt epithelial cells that consist of CDD8+ T cells, plasma cells and macrophages.[4] The mechanisms of diarrhea have been said to be pronounced decrease in sodium chloride absorption, active electrogenic chloride secretion, while reduced net Na^+ and Cl^- absorption is the predominant diarrheal mechanism in collagenous colitis, accompanied by a secretory component of active electrogenic chloride secretion. The subepithelial collagenous band as a significant diffusion barrier acts a cofactor.

Celiac disease is a common comorbidity in patients with collagenous colitis and hence should be screened for celiac disease using serology. A gluten free diet often leads to improvement in diarrhea and other symptoms shared by the two disorders.[5]

Treatment

Patients may be managed with intermittent courses of therapy when their disease is most active, relatively few patients require long-term continuous medical treatment. Antidiarrheal therapy with agents like loperamide is the first line of therapy.[6] In patients with symptomatic microscopic colitis in whom budesonide therapy is not feasible, the AGA suggests treatment with mesalamine over no treatment for the induction of clinical remission. Patients with symptomatic microscopic colitis who were treated with budesonide 9 mg daily were nearly twice as likely as those treated with mesalamine 3 g daily to achieve clinical and histological remission, and there was no statistically significant difference in occurrence of adverse events.[7] Bile acid malabsorption can contribute to diarrhea and hence cholysteramine has proven to be effective as monotherapy and when used in conjunction with mesalamine.[6] Diarrhea resolved and resolution maintained over 6 months better with budesonide than mesalamine.[8] Improvement in microscopic inflammation was also found to

better with budesonide.[9] Prednisone is reserved for patients with disease refractory to budesonide therapy. Recent case reports have suggested a role for anti-TNF alpha agents such as infliximab, adalimumab. Therapy with Biologics should be considered before any surgical management.[10] There are ongoing studies of patients being treated with *Boswellia* serrata extract and needs further investigation in larger randomized trials.[11] Surgical interventions like diverting ileostomy, proctocolectomy with ileal J-pouch anal anastomosis are rarely required in patients with collagen colitis and for those who fail all medical therapies.[12] Other agents such as octreotide and verapamil have been studies but with no consistent beneficial outcome.[13] Some of the complications include spontaneous peritonitis with free perforation of the colonic wall, submucosal dissection and colonic fracturing (during endoscopic instrumentation). Colon carcinoma, lymphoma and carcinoid tumors have also been noted in some case studies.[14]

Conclusion

A case of collagenous colitis has been presented in a 63-year-old female and had no family history.

Conflict of Interest: Nil

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