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Characterization of *de novo* colonic stricture due to Crohn's disease

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Original Article

ABSTRACT

Background/Aims: The development of colonic stenosis is a rare complication of Crohn's disease (CD) without a surgical anastomosis history. So, the management and long-term follow-up results of colonic stricture due to CD have not been clearly defined. In this study, we aimed to characterize *de novo* colonic stricture due to CD.

Materials and Methods: We evaluated 702 patients with CD to investigate colonic stricture. Colonic stricture was considered to exist when passage of a standard colonoscope was not possible and was diagnosed radiologically and endoscopically in this study.

Results: Of the 702 patients, 14 had colonic stricture according to the definition above. Of the 14, 8 were male. The interval between diagnosis of disease and recognition of the stricture varied from 0 to 13 years. Localization of the strictures differed from the rectum to cecum. Of the 14, 3 patients had more than 1 stricture. Pathological examination of the stricture(s) did not show dysplasia or malignancy initially or during the follow-up.

Conclusion: *De novo* colonic stricture due to CD is a rare condition according to the presented study's results. Distribution of the stricture(s) varied from the rectum to cecum without increased colonic cancer risk. We observed the antifibrotic role of thiopurines and biologic agents in this study.

Keywords: Crohn's disease, stricture, colon, thiopurines, biologics, surgery

INTRODUCTION

Intestinal stricture is one of the main causes of hospitalization and cost in patients with Crohn's disease (CD) (1). It occurs more frequently due to surgical anastomoses (2-4). Although *de novo* colonic stricture is a rare complication of CD (less than 1%), it must be a typical complication over time because of transmural involvement of the bowel wall (1-4). It was reported that shortened tubular colon and colonic stricture are strong risk factors for the development of colorectal cancer (CRC) (5); thus, directed biopsies of strictures are always recommended. We are now aware that development of any stricture is an ongoing dynamic pathological process, which includes both fibrotic and antifibrotic components (6-10). Thus, thiopurines and particularly biologic agents might be good alternatives before giving a surgical decision. However, there is a particular concern about biological agents and their rapid healing effect, which may lead to perforation of the affected bowel segment (8-10). In this study, we aimed to characterize *de novo* colonic strictures due to CD by giving long-term follow-up results.

MATERIALS AND METHODS

We performed a retrospective study among patients with CD at our IBD Center in Ankara, Turkey. In this center, we have been using used a chart review system since 1995. The study was approved by the Ankara Yüksek İhtisas Hospital Ethics Committee, and confidentiality of records was maintained according to the guidelines issued by the health authorities.

The diagnosis of CD was established when clinical, endoscopic, and radiological findings were supported by

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Table 1. Overall results of the patients with colonic stricture due to Crohn's disease (CD). Laboratory results shown at the diagnosis date of the stricure

Number	Sex	Age (yr)*	Type of the disease	Localization of the stricture (s)	#	WBC	PLT count	CRP	ESR
1	F	38	Colitis	Rectum -length: 4 m	3 years	5420	343.000	0.3	14
2	F	33	İleocolitis	ascending	5 years	5300	263.000	1.0	10
3	M	28	İleocolitis	Transverse / left colon/sigmoid	8 years	7500	468.000	128	26
4	M	30	İleocolitis	Rectum/descending	6 months	14,000	789.000	12	19
5	M	28	İleocolitis	Rectum	13 years	9000	645.000	2.5	20
6	F	45	İleocolitis	ascending	1 years	7000	186.000	22	29
7	M	38	İleocolitis	ascending	1 years	10,800	312.000		9
8	M	21	İleocolitis	Splenic flexura	4 years	5000	316.000	0.3	10
9	M	35	İleocolitis	ascending	Presented with stricture and active luminal disease	7700	309.000	4.1	20
10	F	19	İleocolitis	Rectum / ascending /descending	5 months	5300	571.000	0.2	12
11	F	35	Colitis	Rectum	5 years	5900	242.000	1	25
12	M	66	Colitis	Transverse - length: 5 cm	Presented with stricture and active luminal disease	8900	221.000	1.2	7
13	F	42	Colitis	Sigmoid	6 months	8200	518.000	0.3	33
14	M	25	İleocolitis	ascending	2 years	8700	402.000	2.01	5

*age at stricture diagnosis date
#Interval between diagnosis of disease and recognition of stricture
M: male; F: female; WBC: white blood cell count; PLT: platelet; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate

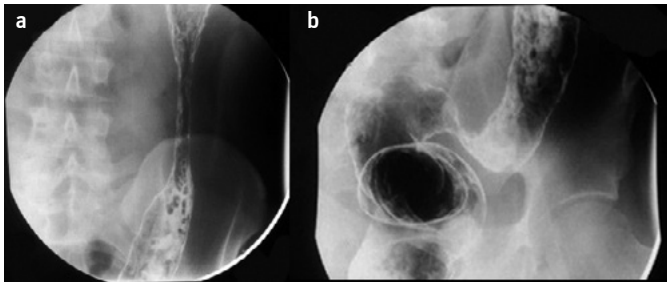

Figure 1. a, b. Double contrast barium enema examination of the colon showed two strictures localized in left and sigmoid colon with prestenotic dilation; the lenght of the strictures were 6 cm and 2 cm, respectively.

histologic evidence and exclusion of other disorders known to cause intestinal inflammation. Mycobacteria were excluded by tissue staining and cultures because of the high incidence of tuberculosis in Turkey.

The diagnosis of colonic stricture was established endoscopically and radiologically. A colonic stricture was considered to exist when passage of a standard colonoscope was not possible. Biopsy and histologic examination of stricture were performed in each patient at the initial diagnosis and during the follow-up. Date of the CD diagnosed; stricture diagnosed; localization of the stricture(s); number, length, and type of the stricture(s); biopsy results; type of the therapy before and after the stricture was diagnosed; and response to therapy were all evaluated in each patient. These patients are still being followed at the IBD center.

RESULTS

Of the 702 patients with CD, 14 had colonic stricture and 6 were female (Table 1). All patients had at least one complaint in his or her history, such as abdominal pain, diarrhea, weight loss, or fever, at the presentation. Mean age was 34.5 years. Time interval between diagnosis of disease and recognition of the stricture varied from 0 to 13 years. Two cases presented with colonic stricture at the initial diagnosis. Strictures were diagnosed to be anywhere ranging from the cecum to rectum. Of the 14 patients, 3 had more than 1 colonic stricture, where 2 patients had 3 colonic strictures and 1 had 2 strictures. Pathological examination of the colonic stricture(s) did not show any dysplasia or malignancy during the follow-up.

Of the 14 patients, 4 had only colitis without ileum involvement: left colon in 2 cases, 1 with sigmoid and 1 with transverse colon involvement. All patients, regardless of dilatation, were put on mainly azathioprine plus shortly oral steroid (with mesalazine) after the diagnosis of colonic stricture (Table 2). Treatment results were as follows: 7 patients showed partial response; 4 had complete resolution; and 3 had no response after at least 6 months of therapy.

One of the nonresponders had 3 colonic strictures, as shown in Figures 1, 2. He had 9 years of disease history and used azathioprine plus steroids irregularly. Abdominal tomography showed that the colonic wall was thickened, particularly in the right

Table 2. Therapy response in IBD patients with colonic stricture(s)

Number	Therapy before the stricture diagnosed	Therapy after the stricture diagnosed	Therapy response for the obstruction to resolve	Maintenance therapy
1	AZA	CS+AZA	relief	AZA
2	AZA	BUD+AZA	Partial response	AZA
3	-	AZA	Non-response	Biologics: Relief at 12 month by endoscopic and MRI enteroclysis
4		CS+AZA	Non-response	Surgery and resection
5	BUD+AZA	CS+AZA	relief	Surgery and resection
6		CS+AZA	Partial response	AZA
7		CS+AZA	Non-response	Surgery and resection
8	AZA	CS+AZA	relief	AZA
9		CS+AZA	Partial response	Biologics: Response at 6 month by, clinical endoscopic, and MRI enteroclysis
10	AZA	CS+AZA	relief	AZA
11	AZA	CS enema plus AZA	Partial response	AZA
12		AZA	Partial response	AZA
13		AZA	Partial response	AZA
14		CS + AZA	Partial response	AZA

All patients were on mesalazine therapy.
MSZ: mesalazine; CS: corticosteroids; BUD: budesonide; AZA: azathioprine; SLZ: salazopyrin; biologics therapy (anti-TNF, tumor necrosis factor)

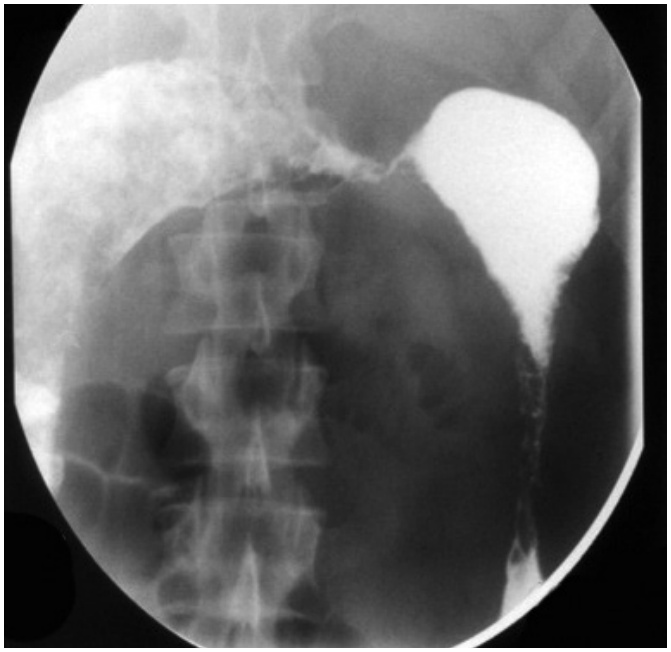

Figure 2. Double contrast barium enema examination of the colon showed a stricture localized in transverse colon with the size 3 cm and prestenotic dilation.

colon, at 22 mm and 12 mm in the transverse and 9 mm in the sigmoid colon. Small bowel contrast examination showed thickened intestinal wall in the distal part of the ileum. Double contrast examination of the colon showed 3 long strictures localized in the transverse, left, and sigmoid colon. The lengths of the strictures were 3 cm, 6 cm, and 2 cm, respectively. Colonoscopy showed active colonic mucosal inflammation with obstructive stenosis. Biopsy and histologic examination showed no dysplasia. After full agreement with the patient and his hesitation to surgery, biological therapy (anti-TNF, tumor necrosis factor) was started. Oral steroid therapy was added according to the guidelines. His condition improved dramatically. Four months later, magnetic resonance imaging enterography was performed and showed significant improvement on the narrowing segments, particularly in the sigmoid and right colon. During the follow-up, his medical condition showed serious disturbances, and total colectomy was performed at the 24th month.

DISCUSSION

Our patients' data were obtained from the records of a tertiary referral center and contained every stage of the disease. Patients were found to have mainly moderate or severe disease in this study. Intestinal stricture is an ongoing dynamic pathologic process and includes fibrotic and antifibrotic components. There is a belief that intestinal fibrosis is preventive against perforation of the affected bowel wall during the natural course of CD. So, the management of colonic stricture due to CD is a controversial issue and has been long debated between gastroenterologists and surgeons (6-10).

The efficacy of biologic agents on stenosing forms of CD has not been established so far. The main concern is that biologic agents might increase the stricture rate and severity because of rapid mucosal healing-induced fibrosis (8-10). Others have

considered that biologic agents might decrease intestinal wall thickness rapidly and lead to colonic perforation. To the best of our knowledge, for the first time, the efficacy and safety of biologic agents were questioned in this study with 2 cases (numbers 3 and 9). We observed that biologic agents might be a safe therapeutic option in patients with colonic stenosing disease due to CD, provided that patients are carefully followed during the biologic therapies.

The incidence of colon cancer in patients with Crohn's colitis was is to be 2% to 7%. Thus, colonoscopy with biopsies and brushing to evaluate malignancy is highly recommended, particularly when the disease is diagnosed at an older age, after longer disease duration, and with more extensive colon involvement (11-13). In our study, we showed that pathologic examination of the stricture(s) revealed no dysplasia or malignancy.

Fifty percent of the patients had elevated C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), which reflected active luminal disease. However, it is still controversial to certainly determine active mucosal inflammation with noninvasive procedures, such as CRP and/or ESR levels and MR or CT enterography. This is of important concern for the preference of biologic agents and surgical therapy, since only strictures with inflammation respond to biological therapy, and surgery is the only effective treatment for chronic fibrotic strictures with mainly proximal dilatation.

The number of patients with CD (702) is not a limitation in this study. So, the 14 patients with colonic stricture due to CD in this study can not be considered a limited number.

In conclusion, *de novo* colonic stricture due to CD is a rare condition, and the distribution of strictures varied from the rectum to cecum. Biologics and thiopurines are reasonable alternatives to surgery before giving a surgical decision.

Conflict of Interest: No conflict of interest was declared by the authors.

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