



# A colorectal mosaic pattern might be an endoscopic feature of collagenous colitis<sup>☆</sup>

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## KEYWORDS

Collagenous colitis;  
Colonoscopy;  
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## Abstract

**Background and aims:** The endoscopic aspect of the colorectal mucosa in those patients with collagenous colitis is usually normal, or with non-specific changes. Until now it had never been related to a mucosal pattern of mosaic type. Our aim was to determine the diagnostic accuracy of the presence of mosaic pattern in the colorectal mucosa for collagenous colitis.

**Methods:** Patients who had undergone a colonoscopy with random biopsies performed in the diagnostic evaluation of chronic diarrhea between 2004 and 2008 were studied. We defined patients with chronic diarrhea and mosaic mucosal pattern as "cases", and patients with chronic diarrhea without mosaic pattern as "controls". The odds ratio (OR) of finding a collagenous colitis in view of a mosaic pattern in colon was determined; as well as sensitivity and specificity; positive and negative likelihood ratios (LR+, LR-), considering this finding as a diagnostic instrument for collagenous colitis.

**Results:** 252 patients who had undergone colonoscopy with biopsy due to chronic diarrhea were analyzed. In 6 patients, a mosaic pattern was identified in the colorectal mucosa. The histological diagnose of 36 of the 252 patients (14%) was microscopic colitis, 27 of which (11%) had collagenous colitis. The colonoscopy was found normal in 21 of these 27 patients; in 2 patients, congestion or petechiae was found in the rectum; and in 4 patients (15%), all women, a mosaic pattern was found in the rectosigmoid mucosa. The OR of this finding was 19.4 (CI95% 3.9–95.4) for collagenous colitis. It had a sensitivity of 14.8% (CI95% 6.8–20), a specificity of 99.1% (CI95% 98.2–99.7), LR+ of 16.6 (CI95% 3.7–76.4), and LR- of 0.86 (CI95% 0.80–0.95) for a collagenous colitis.

**Conclusion:** The mosaic pattern in the colorectal mucosa of patients studied due to chronic diarrhea could be a distinguishing feature of collagenous colitis.

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**Abbreviations:** VCC, colonoscopy; OR, odds ratio; LR+, positive likelihood ratios; LR-, negative likelihood ratios; CI, confidence intervals 95%.

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## 1. Introduction

Microscopic colitis are clinical pathologic entities characterized by secretory-like aqueous chronic diarrhea, in its large majority without hematochezia. Collagenous colitis is a type of microscopic colitis that was first described by Lindstrom<sup>1</sup> in 1976, and numerous cases have been reported since then. It is characterized by a thickening of the subepithelial collagen band, which exceeds the 10  $\mu\text{m}$  diameter. It usually occurs in adults, with a predominance of women, but there have been cases reported in children. In the colonoscopy or in the double-contrast barium enema, the colonic mucosa has a normal aspect or it can present minimum and unspecific abnormalities such as erythema patches, edema or alterations in the vascular pattern.<sup>2,3</sup> The course of the disease can be chronic, intermittent and recurrent. The diagnosis is performed through the biopsy of the colonic and rectal mucosa and the deposit finding of a more than 10  $\mu\text{m}$  diameter collagen band.

From the first descriptions of collagenous colitis, normal endoscopic and radiological findings have been a pathognomonic feature. However, there are few reports of macroscopic endoscopic findings that, when present, suggest this type of colitis. Some of these studies showed that longitudinal ulcerations, erosions and friable mucosa<sup>4–6</sup> have been associated with this colitis. Sato et al.<sup>7</sup> reported slight changes in the vascular texture of the colonic mucosa associated with collagenous colitis which, after the indigo carmine dye, was visualized as an irregular nodular pattern. So far, however, the endoscopic finding of a mosaic pattern has not been associated with this entity.

Our aim was to determine the likelihood of collagenous colitis to present a colorectal mosaic mucosa pattern, and to estimate this finding's diagnostic accuracy by considering it as a diagnostic instrument of collagenous colitis.

## 2. Materials and methods

The clinical records of patients with chronic diarrhea who underwent a colonoscopy with biopsies between February 2004 and August 2008 were retrospectively analyzed. When a colonoscopy was performed during the evaluation of chronic diarrhea, our diagnostic protocol included random biopsies of normal mucosa in the right colon and rectum, biopsies abnormal mucosal areas, and photographic documentation of the bowel (ileum, cecum, different segments of the colon, rectum, and any mucosal abnormality). When mucosal abnormalities were present, targeted samples were sent to a pathologist on a separate vial. Endoscopic and pathology reports and colonoscopy pictures were reviewed by two of the authors, evaluating the presence of the mosaic mucosal pattern and collagenous colitis.

Collagenous colitis was defined by the finding of colitis (epithelial cell damage and chronic inflammation in the lamina propria) with a basal membrane thickening of  $\geq 10 \mu\text{m}$  of diameter due to the collagen deposit in the histology of the colorectal biopsies taken from patients who consulted for a chronic, aqueous diarrhea with no other attributable causes. Lymphocytic colitis was considered as a relevant differential diagnosis and it was defined by the presence of colitis with surface epithelial damage and increased intraepithelial lymphocytes in the absence of a thickened subepithelial collagen.

Mosaic mucosal pattern was defined as the macroscopic and endoscopic observation, through the conventional colonoscopy, of a "honeycomb" image in the tangential view of the colonic or rectal mucosa (Figs. 1 and 2), with similar characteristics to those of the mosaic found in the duodenum of patients with celiac disease. Colonoscopies were done using endoscopes Karl Storz NKS 13904.

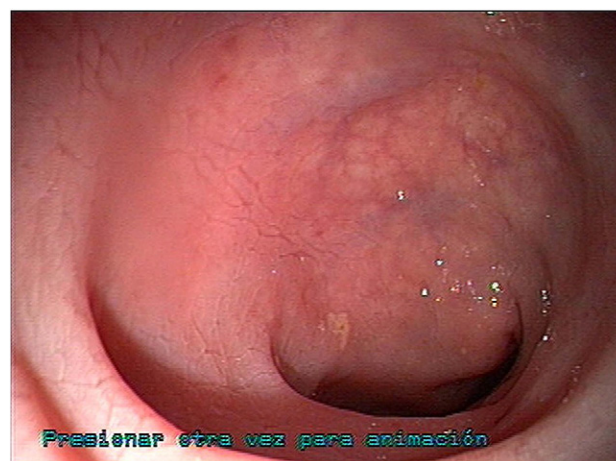
A case-control study was performed, defining patients with chronic diarrhea and mosaic mucosal pattern in the colonoscopy as "cases", and patients with chronic diarrhea without mosaic pattern as "controls". The odds ratio (OR) of finding a collagenous colitis in view of a mosaic pattern in the colon was determined; as well as sensitivity, specificity, positive likelihood ratio and negative likelihood ratio (LR+, LR-), considering this finding as a diagnostic instrument for collagenous colitis.

## 3. Statistics

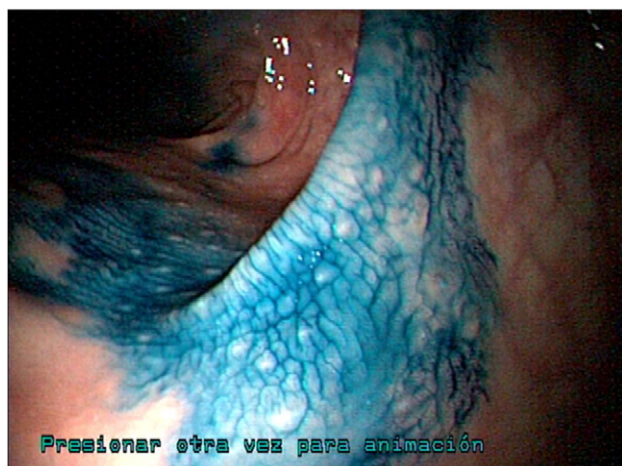
The media was calculated with its corresponding ranges for the ordinal variables. Nominal variables were expressed in percentages with their corresponding confidence intervals of 95% (CI), which were measured using Binomial CI JavaStat. The Fischer test was used for the OR calculation. An OR or a LR+ with confidence interval of 95% that did not go through 1 was considered significant.

## 4. Results

252 patients who had undergone colonoscopy with biopsies for chronic diarrhea were analyzed (Table 1), from a total of 9990 colonoscopies performed in the period between February 2004 and August 2008. Of the 252 patients, 6 represented the group of cases and 246 the group of controls. The media age was 52 years old (range, 11–89), and 59% were women. The quality of the colonic cleansing was acceptable in 96% of the patients: excellent or good in 70% (CI 64–75) and fair in 26% (20–32). The colorectal mucosa showed a normal aspect in 74% (CI 68–79) of



**Figure 1** Mosaic pattern in colorectal mucosa. Collagenous colitis was shown in the biopsies.



**Figure 2** Indigo carmine staining highlights the mosaic pattern in rectal mucosa.

the patients, and in 6 (2.4%, CI 0.9–5.1), a mosaic pattern of the mucosa was identified, with a rectosigmoid location in all these cases. The histological diagnosis of 36 of the 252 patients (14%, CI 10–19) was microscopic colitis, 27 (10.7%, CI 7–15) of which had collagenous colitis, and 9 (3.5%, CI 2–7) lymphocytic colitis. The media age of the patients with collagenous colitis was 56.2 years old (range, 24–82), with a predominance of females (63%, CI 42–80). Colonoscopies were normal in 21 (81%, CI 62–94) out of these 27 patients; in 2, congestion or petechiae was found in the rectum; and in 4 patients (15%, CI 4–33) a mosaic pattern was found in the rectosigmoid mucosa.

Among the patients defined as cases, the media age was 57.8 (range, 24–77) years old, and 67% (22–95) were women. In all cases, the mosaic pattern was identified in the rectal and/or sigmoid mucosa. The guided biopsies of the mosaic mucosal pattern confirmed the diagnosis of collagenous colitis in 4 (67%, CI 22–95) out of the 6 patients (Table 2); and 2 out of these 4 patients showed collagenous colitis as a finding on other segments of the bowel biopsied.

The two remaining patients evidenced minor non-diagnostic inflammatory changes and unspecific alterations (such as

**Table 1** Characteristics of the patients with chronic diarrhea who underwent a VCC with biopsies.

n = 252	
Characteristics of the patients	
Age in years (media, range)	52 (11–89)
Sex (% women, CI 95%)	59% (52–65)
Endoscopic findings (% , CI 95%)	
Normal	74% (68–79)
Unspecific inflammation	9% (6–13)
Pattern compatible with ulcerative colitis	5% (3–9)
Mosaic mucosal pattern	2.4% (0.9–5.1)
Specific histological diagnosis (% , CI 95%)	
Microscopic colitis:	10.7% (7–15) / 3.5% (2–7)
collagenous/lymphocytic	
Ulcerative colitis	4.7% (2.5–8)
Infectious colitis	1.2% (0.2–3.5)
Crohn's disease	0.8% (0.1–3)

**Table 2** Cases and controls' characteristics.

Characteristics of the patients	Cases (n = 6)	Controls (n = 246)	Value p
Age years (media, range)	57.8 (24–77)	52.3 (11–89)	0.44 <sup>a</sup>
Sex (% women, CI 95%)	67% (22–95)	58% (52–65)	0.52 <sup>b</sup>
Specific histological diagnosis			
Collagenous colitis (% , CI 95%)	67% (22–95)	0.9% (6–14)	0.001 <sup>b</sup>

<sup>a</sup> Wilcoxon 2 sample test.

<sup>b</sup> Fisher's exact test.

increase in superficial lamina propria mononuclear cells without other diagnostic findings; lymphocytic colitis and inflammatory bowel diseases were taken into account and ruled out). Fig. 3 shows an image of a mosaic pattern in the rectal mucosa. This sector's biopsies reported a collagenous colitis (Fig. 4).

As regards the group defined as controls (246 patients with no mosaic mucosal pattern), the media age was 52.3 (range, 11–89) years old, and 58% (52–65) were women, with no statistically significant differences with the cases (Table 2). No significant differences were evidenced in the cecal intubations rate neither in the quality of colonic cleansings. The collagenous colitis' histological diagnosis was significantly higher in the group of the cases vs. controls (67% vs. 0.9%,  $p=0.001$ ).

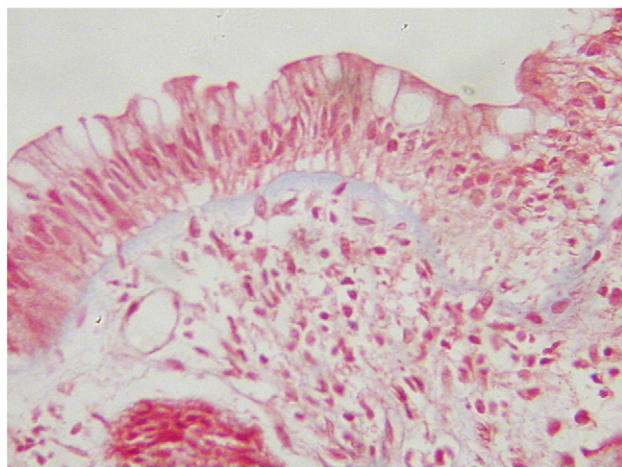
The finding of a colorectal mosaic mucosal pattern had an OR of 19.4 (CI 3.9–95.4) for the collagenous colitis diagnosis. If we consider the visualization of mosaic mucosa as a diagnostic instrument, this characteristic exhibited a sensitivity of 14.8% (CI 6.8–20), a specificity of 99.1% (CI 98.2–99.7), LR+ 16.6 (CI 3.7–76.4) and LR– 0.86 (0.80–0.95) (Table 3).

## 5. Discussion

Collagenous colitis is a clinicopathological entity that is often suspected in patients with chronic diarrhea. Colonoscopy is



**Figure 3** Mosaic pattern in rectal mucosa. A snare is shown taking biopsies from the mucosa with mosaic pattern. Collagenous colitis was shown in the biopsies.



**Figure 4** Collagenous colitis is shown in the histology of biopsies taken.

usually normal, and the diagnosis is made through colonic biopsies.

To our knowledge, mosaic pattern in the colorectal mucosa had never been described in collagenous colitis so far. The observation of this pattern could be an endoscopic finding of collagenous colitis, since, in our study, it has showed a high specificity (S 99%) and a high positive likelihood ratio (LR+ 17), with an increased risk of almost 20 times (OR 19). In this regard, we believe that this finding in a patient with chronic diarrhea can be a positive sign in the diagnostic evaluation of this disease, very useful to suspect it, and therefore, to lead to a biopsy.

The results of this study should alert colonoscopists to search for this colorectal mucosal pattern in those patients with chronic diarrhea who undergo a colonoscopy. On the contrary, the absence of this finding has no value in the collagenous colitis' diagnostic algorithm, which is proved by its low sensitivity and its low negative likelihood ratio (S 15% and LR- 0.86, respectively).

In our study, 67% of the cases had collagenous colitis compared to the 0.9% of the controls ( $p=0.001$ ). Mosaic mucosal pattern was present in 2.4% (Table 1) of the total of patients with chronic diarrhea who underwent a colonoscopy with biopsies, and in 15% of the patients with collagenous colitis; representing the most prevalent endoscopic abnormality in this group, followed by other unspecific signs (3.7%).

Several authors have described colorectal mucosal abnormalities associated with collagenous colitis: erythema patches, edema or alterations in the vascular pattern,<sup>3,4</sup> longitudinal ulcerations, erosions and friable mucosa,<sup>5,6</sup> and

changes in the aspect of the colonic mucosa's vasculature;<sup>7</sup> but no one has reported our finding.

Other authors have associated collagenous colitis with the intake of certain medications, such as non-steroid anti-inflammatories<sup>8,9</sup> or proton pump inhibitors. We have not been able to state whether such association is present in our collagenous colitis population, because such information was not obtained at that time.

Lastly, and in reference to our study's methodological design, although we proposed a case-control study, we think our work can be considered as a proper study of diagnostic tests;<sup>10</sup> that is the reason why we also expressed the results as sensitivity and specificity. Our study takes into account and meets the validation criteria suggested by evidence-based medicine of a proper diagnostic test process<sup>10</sup>: there is diagnostic doubt in the analyzed population (chronic diarrhea patients), a gold standard was applied (the colorectal biopsy) to all patients independently of the studied test (mosaic mucosal pattern), and the evaluated results were defined (collagenous colitis).

### 5.1. Limitations

Firstly, it is a retrospective study, and therefore, it has a higher possibility of having bias data. Secondly, the mosaic mucosal pattern is a macroscopic observation of the mucosa of which no interobserver and intraobserver agreement is yet known to inform it. Furthermore, this pattern had not been considered as an "alert sign" in the endoscopy so far, and therefore, it is at risk of being under-diagnosed and under-informed if no special attention is paid. This fact may have over-estimated this finding's specificity.

### 6. Conclusions

The finding of a mosaic pattern in the colorectal mucosa in patients with chronic diarrhea may be characteristic of the collagenous colitis. Prospective studies will be needed to determine the real diagnostic value of this observation.

### 7. Summary. Salient points

- Until now, mosaic pattern in the colorectal mucosa has not been related to collagenous colitis.
- Mosaic pattern in the colorectal mucosa might be characteristic of the collagenous colitis in those patients who undergo a colonoscopy for chronic diarrhea.
- Prospective studies will be needed to determine the real diagnostic value of this observation.

### References

1. Lindstrom CG. "Collagenous colitis" with watery diarrhoea – a new entity? *Pathol Eur* 1976;11:87.
2. Shah RJ, Fenoglio-Preiser C, Bleau BL, Giannella RA. Usefulness of colonoscopy with biopsy in the evaluation of patients with chronic diarrhea. *Am J Gastroenterol* 2001;Apr;96(4):1091–5.
3. Katsinelos P, Katsos I, Patsiaoura K, Xiarchos P, Goulis I, Eugenidis N. A new endoscopic appearance of collagenous colitis. *Endoscopy* 1997;Feb;29(2):135.

**Table 3** Collagenous colitis.

Diagnostic precision of the mosaic pattern	Collagenous colitis
Sensitivity (CI 95% )	14.8% (CI 6.8–20)
Specificity (CI 95% )	99.1% (CI 98.2–99.7)
LR+ (CI 95% )	16.6 (CI 3.7–76.4)
LR- (CI 95% )	0.86 (0.80–0.95)

Diagnostic precision of the mosaic mucosal pattern.

4. Koulaouzidis A, Henry JA, Saeed AA. Mucosal tears can occur spontaneously in collagenous colitis. *Endoscopy* 2006;**38**:549.
5. Wickbom A, Lindqvist M, Bohr J, Ung KA, Bergman J, Eriksson S, Tysk C. Colonic mucosal tears in collagenous colitis. *Scand J Gastroenterol* 2006;Jun;**41**(6):726–9.
6. Umeno J, Matsumoto T, Nakamura S, Jo Y, Yada S, Hirakawa K, et al. Linear mucosal defect may be characteristic of lansoprazole-associated collagenous colitis. *Gastrointest Endosc* 2008;Jun;**67**(7):1185–91.
7. Sato S, Benoni C, Tóth E, Veress B, Fork FT. Chromoendoscopic appearance of collagenous colitis--a case report using indigo carmine. *Endoscopy* 1998;Sep;**30**(7):S80–1.
8. Riddell RH, Tanaka M, Mazzoleni G. Non-steroidal anti-inflammatory drugs as a possible cause of collagenous colitis: a case-control study. *Gut* 1992;**33**:683–6.
9. Giardiello FM, Hansen 3rd FC, Lazenby AJ, Hellman DB, Milligan FD, Bayless TM, Yardley JH. Collagenous colitis in setting of nonsteroidal antiinflammatory drugs and antibiotics. *Dig Dis Sci* 1990;Feb;**35**(2):257–60.
10. Jaeschke R, Guyatt G, Lijmer J. Part 1: The Basics. *Diagnostic Tests. User's guides to the Medical Literature* 1st Edition. Chicago: AMA Press; 2002. Chapter 1–C2.