

## Microscopic colitis : a histopathological study of nine cases

P JAYALAKSHMI, MBBS, MRCPATH, AK MALIK, MBBS, MD and NW WONG,\* MBBS, MRCP.

Departments of Pathology and \*Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur.

### Abstract

A retrospective histological analysis of colonic biopsies received by the Department of Pathology, University of Malaya during the 4-year-period between 1990 and 1993 revealed nine cases of microscopic colitis (MC). The ages of the patients ranged from 18 to 53 years. Seven patients were females with a female to male ratio of 3.5 :1. The main clinical symptom was chronic diarrhoea of duration varying from 4 months to 5 years. None of the patients had any systemic illness or were on any prior medication. Colonoscopy and barium enema observations in all the subjects were essentially normal. Colonic biopsies showed diffuse plasmacytic infiltration of the lamina propria, intraepithelial lymphocytic infiltration and normal crypt pattern. To the best of our knowledge, this is the first documented report on MC from Malaysia. It is envisaged that better recognition of this condition by histopathologists would reduce the numbers in the often diagnosed category of "nonspecific colitis".

**Key words:** Microscopic colitis, colonoscopy.

### INTRODUCTION

Microscopic colitis (MC) is a clinicopathological entity where patients present with chronic diarrhoea often watery. Although colonoscopy and barium enema findings are normal, colorectal biopsy reveals an increased inflammatory infiltrate in the mucosa not specific for any established disease.<sup>1</sup> Since the initial report by Read *et al* in 1980,<sup>2-7</sup> at least 58 cases have been reported from the West.<sup>2-7</sup> However there is no documented study on MC in Malaysia. We report the clinicopathological features of nine cases of MC seen at the University Hospital, Kuala Lumpur over a period of 4 years. The aim of this paper is to delineate the pathological features of MC and note the differences between MC and nonspecific colitis.

### MATERIALS AND METHODS

A retrospective histological analysis of all colonic biopsies received by the Department of Pathology, University of Malaya between January 1990 and December 1993 was carried out. There was a total of 221 biopsies from 195 patients. Biopsies of 29 patients showed nonspecific chronic inflammation. Clinical records and endoscopic findings of all these cases were reviewed. There were 9 cases who met the criteria for MC, which were: diarrhoea of unknown origin, normal findings on barium enema and colonic endoscopy, and inflammatory changes in the mucosa on colonic biopsy.<sup>1</sup> All the nine patients presented with diarrhoea with loose to watery stools without

mucus or blood. These patients were referred to the University Hospital, Kuala Lumpur by private practitioners after ruling out infectious colitis. Colonoscopy was performed after bowel preparation with four litres of polyethyleneglycol solution which is chemically inert to the colonic mucosa.

Biopsies were fixed in formalin and embedded in paraffin. Sections were cut at 4µm and stained with Haematoxylin and eosin. Periodic acid-Schiff and Masson's trichrome stains were done to detect microorganisms and collagen band respectively. Histological features studied included surface epithelial changes, crypt distortion and cryptitis, mucus depletion, collagen band and inflammatory infiltrate in the lamina propria. The degree of cellular infiltration was classified as mild (+), moderate (++) and severe (+++).

### RESULTS

There were 9 cases of MC. The patients presented with chronic diarrhoea of duration varying from 4 months to 5 years. There was a preponderance of females with a female to male ratio of 3.5:1. The mean age of the patients was 37.2 years with a range of 18 to 53 years. None of the patients were on any medication prior to endoscopy. Colonoscopy was normal in all the patients.

There was no clinical evidence of malabsorption. The clinical features are summarised in Table 1. Stool examination for parasites, ova and cysts were negative in all the

**TABLE 1: Clinical features of nine patients with microscopic colitis**

| Case | Race | Age (yrs) | Sex | Clinical features     | Duration (months) | Colonoscopy | Stool culture |
|------|------|-----------|-----|-----------------------|-------------------|-------------|---------------|
| 1    | M    | 31        | F   | Diarrhoea weight loss | 18                | Normal      | Not done      |
| 2    | M    | 27        | F   | Diarrhoea             | 60                | Normal      | Not done      |
| 3    | I    | 39        | M   | Diarrhoea             | 6                 | Normal      | Not done      |
| 4    | CA   | 38        | M   | Diarrhoea             | 12                | Normal      | Normal        |
| 5    | ER   | 44        | F   | Diarrhoea             | 6                 | Normal      | Normal        |
| 6    | C    | 18        | F   | Diarrhoea             | 24                | Normal      | Not done      |
| 7    | C    | 43        | F   | Diarrhoea             | 6                 | Normal      | Not done      |
| 8    | I    | 42        | F   | Diarrhoea             | 6                 | Normal      | Normal        |
| 9    | I    | 53        | F   | Diarrhoea             | 48                | Normal      | Not done      |

C = Chinese; CA = Caucasian; ER = Eurasian; I = Indian; M = Malay

cases. Stool culture was performed in three cases and did not show common pathogens such as *Yersinia*, *Salmonella*, *Shigella* or *Campylobacter*.

*Pathology*

Table 2 summarises the microscopical features. The main histological abnormality in all the cases was a diffuse, heavy plasmacytic infiltration of the lamina propria extending upto the muscularis mucosa (Figs. 1 & 2). This change was noted in all the sites biopsied. There was mild to moderate increase in eosinophils in the lamina propria in eight and one case respectively. In one case occasional polymorphs were noted in the lamina propria. Intraepithelial lymphocytes (Fig. 3) were conspicuous in all. Minimal focal

erosion of the surface epithelium and focal mucus depletion were seen in one case. Surface epithelial flattening (Fig. 4) was observed in four cases. None of the cases revealed crypt loss, distortion or branching. There was no paneth cell metaplasia, hypertrophy of the muscularis mucosa or granuloma formation. No organisms were revealed by the Periodic acid-Schiff stain. The Masson's trichrome stain did not reveal any thickened subepithelial collagen band.

**DISCUSSION**

Microscopic colitis is a distinctive clinicopathological entity first described by Reed in 1980.<sup>1</sup> Lazenby *et al*<sup>7</sup> proposed that the term "lymphocytic colitis" should replace

**TABLE 2: Histological features in nine patients with microscopic colitis**

| Case | Biopsy site | Erosion | Cryptitis | Mucus depletion | IEL | Lamina propria |    |   |
|------|-------------|---------|-----------|-----------------|-----|----------------|----|---|
|      |             |         |           |                 |     | PC             | E  | N |
| 1    | R           | -       | -         | -               | P   | ++             | +  | - |
| 2    | C,R         | Focal   | -         | -               | P   | ++             | +  | - |
| 3    | C,R         | -       | -         | -               | P   | ++             | +  | - |
| 4    | DC,R        | -       | -         | -               | P   | ++             | +  | - |
| 5    | C,TC,DC,R   | -       | -         | -               | P   | ++             | +  | - |
| 6    | C,R         | -       | -         | -               | P   | ++             | +  | - |
| 7    | C,TC,R      | -       | -         | Focal           | P   | ++             | +  | - |
| 8    | C,TC        | -       | -         | -               | P   | ++             | ++ | - |
| 9    | C,TC,SC     | -       | -         | -               | P   | ++             | ++ | - |

C = caecum, DC = descending colon, E = eosinophil, IEL = intraepithelial lymphocyte, N = neutrophil, P = present, PC = plasma cell, R = rectum, SC = sigmoid colon, TC = transverse colon, + = mild, ++ = moderate.

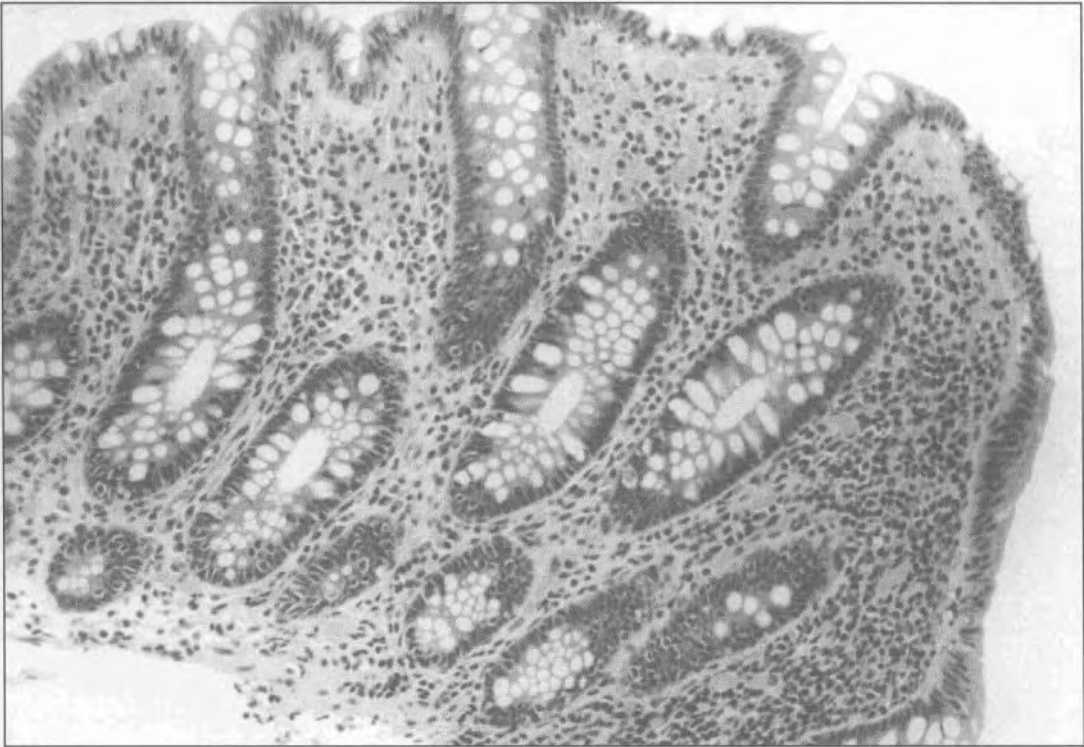


FIG 1: Colonic mucosa with intact surface epithelium, normal glands and crypts. The lamina propria shows a diffuse plasmacytic infiltrate. H&E  $\times$  80.

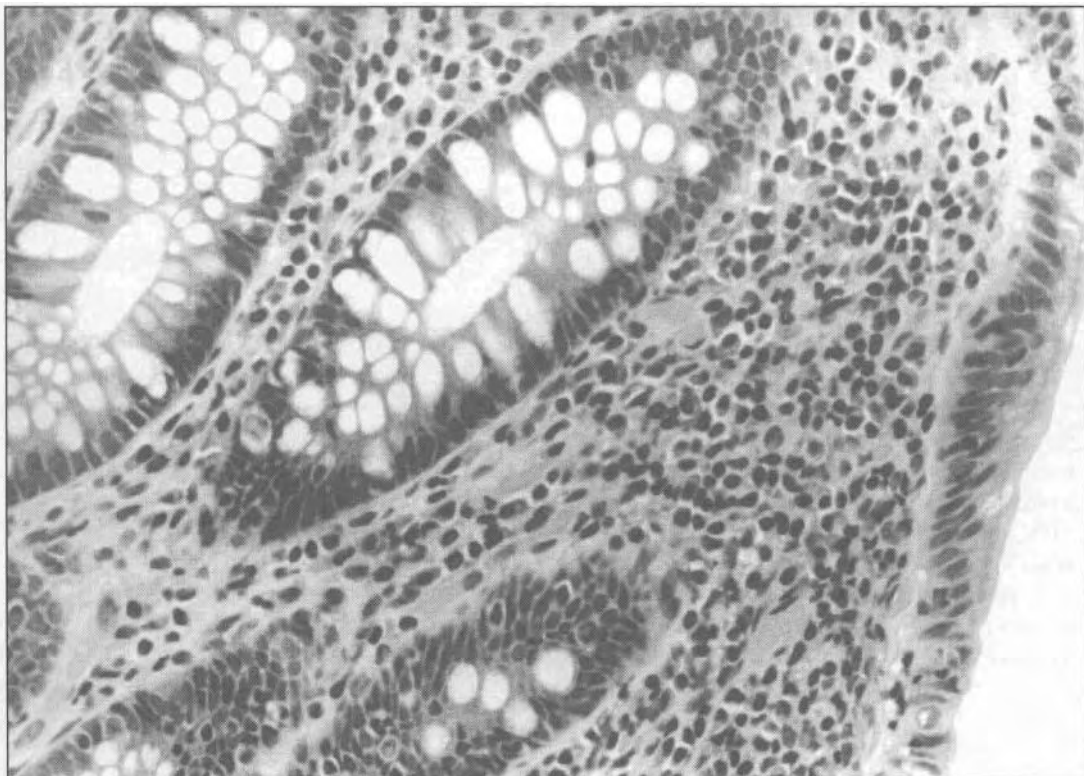
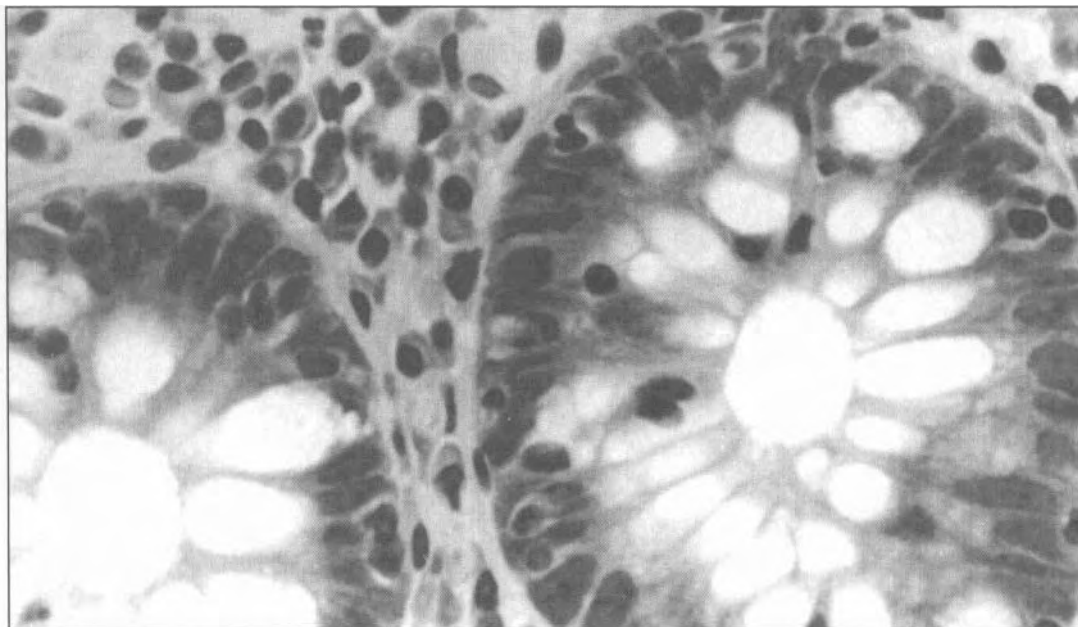


FIG 2: Marked plasma cell infiltration of the lamina propria and normal crypts. H&E  $\times$  200.



**FIG 3:** Intraepithelial lymphocytes in the colonic crypts. H&E  $\times$  800.

"microscopic colitis" due to the distinct lymphocytic infiltration of the colonic epithelium. We have retained the term microscopic colitis implying that it is detectable histologically when patients with watery diarrhoea show normal colonic mucosae on colonoscopy.

Although MC is reported at all age groups, it more commonly presents in the sixth decade.<sup>4,6,8</sup> The reason for the higher prevalence of MC among the older age group is not known. In the present study, the mean age of patients was 37.2 years with a range of 18 to 53 years. Extraintestinal manifestation such as arthritis, thyroid disease and the presence of autoantibodies have been noted in patients with MC.<sup>5-7</sup> However none of our cases had any systemic disease at the time of presentation. The major symptom of our patients was chronic diarrhoea, similar to that of other published reports.<sup>1-8</sup>

The histology of all the cases showed a diffuse increase in plasma cells in the lamina propria extending up to the muscularis mucosa. Biopsies from more than one site were performed in eight cases and the inflammation was diffuse in all the areas biopsied. An increase in epithelial as well as crypt lymphocytes were noted in all. No granulomas were observed. There was no crypt distortion or loss thus excluding the possibility of idiopathic inflammatory bowel disease.

Interestingly MC shares many clinical and microscopic features with collagenous colitis. Both disorders present at middle age with symptoms of chronic diarrhoea and normal

endoscopic findings. Recent observations suggest that these two conditions may overlap with time.<sup>6,8</sup> However, they can be distinguished histologically by the presence of a subepithelial collagen band in collagenous colitis demonstrable by the Masson's trichrome stain. Subepithelial collagen thickening may be patchy<sup>9</sup> and tends to be more prominent in proximal biopsies; thus biopsies from multiple sites of the colon should be done. In our study, seven of the nine cases who had biopsies from more than one site did not reveal any increased subepithelial collagen on Masson's trichrome staining, thus ruling out collagenous colitis.

Infective colitis has to be considered in the differential diagnosis of MC histologically. None of the biopsies in the present study showed the characteristic features of infective colitis such as ulceration and acute mucosal inflammation with crypt abscess formation. Ideally, stool examination for parasites and culture should be done in all patients presenting with chronic diarrhoea. In our analysis, no parasites were detected on stool examination. Special stains did not show microorganisms. Stool culture was done for three cases and was negative.

Microscopic colitis can be distinguished from nonspecific colitis on the basis of clinical and histological features. Patients with MC present with chronic diarrhoea, often watery and no definite causes of diarrhoea are identified clinically or in the biopsy. The colonic mucosa is endoscopically and radiologically normal.

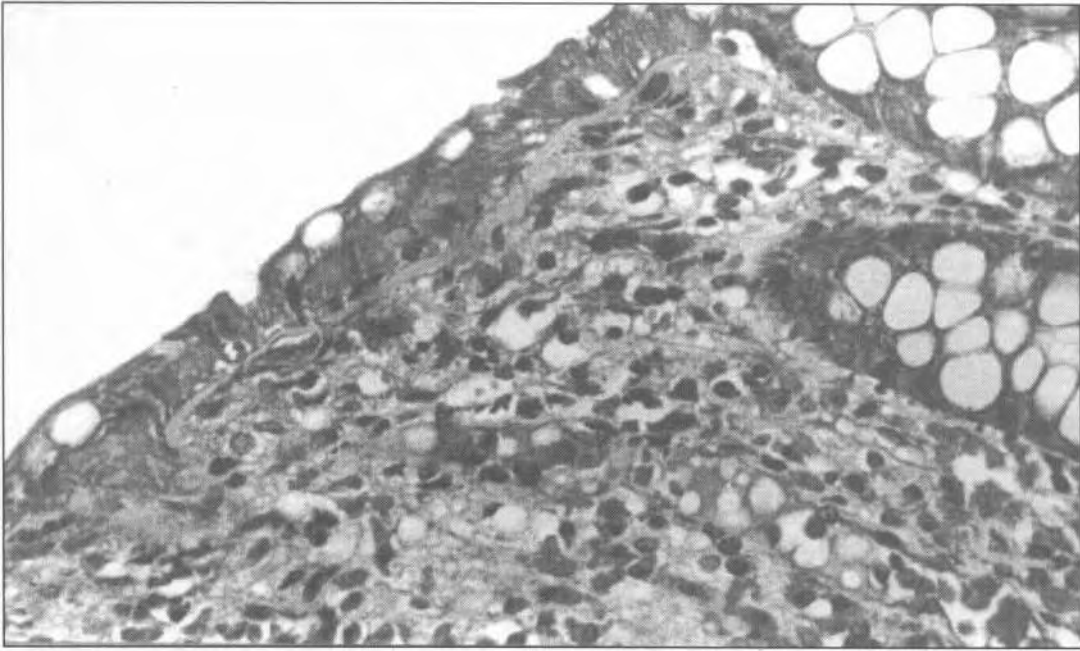


FIG 4: Focal surface epithelial flattening. H&E x 200.

Normal colonoscopic findings may be attributed to the fact that in MC the mucosal surface is intact and the pathological changes are seen mainly in the lamina propria. Multiple biopsies from the colon and rectum aid in the diagnosis. The histological abnormality is **pancolic** and the features are as follows: mild to severe infiltration of the lamina propria by predominantly chronic inflammatory cells, some flattening of the epithelium but minimum crypt distortion, cryptitis and goblet cell depletion and increased intraepithelial **lymphocytes**.<sup>2,4</sup> Patients with nonspecific colitis may not present with diarrhoea. Barium enema and colonoscopy may reveal abnormal findings. The histological abnormality is not **pancolic** and all the changes seen in MC may not be present.

The aetiology of MC remains obscure. Some histological similarities such as surface epithelial irregularity and increased intraepithelial lymphocytes in MC and the small bowel mucosa in coeliac disease have been **highlighted**.<sup>6</sup> Coexistence of coeliac disease and collagenous colitis has been **documented**.<sup>10</sup> Autoimmune dysfunction is believed to be one of the mechanisms in coeliac disease<sup>11,12</sup> and it is reasonable to speculate on the possibility that altered immune function triggered by a viral or bacterial infection might have a role in MC as well.

The treatment of MC is not well established. **Giardiello et al**<sup>6</sup> in their study of 18 cases of MC

reported that eight of the nine patients on antiinflammatory drugs improved. On the other hand four of five patients with nonspecific therapy also had decrease in frequency of diarrhoea. In our study all the patients were advised to take **antidiarrhoeal** therapy if severe diarrhoea exists. We intend to repeat the colonoscopic examination and biopsy if the symptoms persist during the routine follow-up.

We are of the opinion that MC is a characterisable entity. The diagnosis depends on the clinicopathological features. Awareness of this condition might reduce its categorisation into the loose term of "chronic nonspecific colitis."

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