

Microscopic colitis

Miles Parkes

Abstract

Microscopic colitis describes a condition of chronic watery diarrhoea in the absence of macroscopic evidence of colonic inflammation but with characteristic microscopic appearances. It comprises the two separate but related conditions of lymphocytic and collagenous colitis. Disease severity ranges from mild and self-limiting to severe and refractory. Whereas mild disease can be managed adequately with loperamide, severe disease requires budesonide over the short term and, occasionally, immunomodulatory therapy with azathioprine. The long-term prognosis is generally good.

Keywords Budesonide; collagenous; lymphocytic; microscopic colitis; MRCP

Introduction

Microscopic colitis should be a differential diagnosis for any individual referred for investigation of chronic watery diarrhoea, particularly where these symptoms occur daily and are persistent or have proved difficult to control. The condition is more common beyond late middle age. It is a histological diagnosis based on biopsies taken at colonoscopy in which the mucosa is macroscopically normal or just manifests subtle abnormalities. It can be patchy in distribution, so biopsies should ideally be taken from both the ascending colon and left colon. Given the debilitating nature of the watery diarrhoea and the satisfying response in most cases to a course of oral budesonide, this is a diagnosis that should not be overlooked.

Epidemiology and pathogenesis

Lymphocytic and collagenous colitis both have an annual incidence of 5–10 per 100,000 population. More recent series tend to report higher numbers, which probably reflects increased awareness of the diagnosis and more widespread availability of colonoscopy. Peak incidence is around 65 years of age, and there is a marked female preponderance, particularly for collagenous colitis (7:1).

The cause of these conditions is unknown, although some important associations can provide a clinical pointer to the diagnosis:

- autoimmune disease – particularly coeliac disease
- drugs – most commonly non-steroidal anti-inflammatory drugs and proton pump inhibitors, but also ranitidine, sertraline, aspirin and ticlopidine. There is also evidence that the check-point inhibitors used in oncology can trigger a particularly severe form of microscopic colitis.

Miles Parkes MA DM FRCP is a Consultant Gastroenterologist at Addenbrooke's Hospital, Cambridge, UK, and Associate Lecturer at the University of Cambridge. Competing interests: none declared.

Key points

- Consider the diagnosis particularly in postmenopausal women with watery diarrhoea
- Microscopic colitis is a histological diagnosis but can be missed on rectal biopsy; at least four biopsies from around the colon should be taken in patients with watery diarrhoea who are undergoing colonoscopy
- Stop possible drug precipitants and look for evidence of coeliac disease
- Loperamide is a good first-line treatment, followed by budesonide for more troublesome cases

- luminal bacteria – their potential importance is evidenced by a response to antibiotics in some instances, and by reports of a symptomatic and histological response to diversion of the faecal stream by ileostomy in rare refractory cases.

Clinical presentation and diagnosis

The classic symptom of microscopic colitis is watery (non-bloody) diarrhoea, which can be sudden or gradual in onset and can remit and relapse. There can be nocturnal diarrhoea, faecal incontinence (often exacerbated, in postmenopausal women, by reduced anal sphincter pressure after previous obstetric injury) and marked abdominal cramps. Many patients become housebound because of these symptoms. As with active inflammatory bowel disease, fatigue is common.

There are usually no abnormal examination findings; dehydration is rare, and the rectal mucosa looks normal on sigmoidoscopy. Stool analysis should be undertaken to rule out infection, but is negative for pathogens in microscopic colitis. Blood test abnormalities are rare, but coeliac serology should be checked. Macroscopic abnormalities are found at colonoscopy in up to 30% of individuals but are subtle and non-specific (except for rare procedure-induced mucosal tears, which look alarming and mandate scope withdrawal but are rarely serious).

The diagnosis is made on histological examination of rectal or colonic biopsies (rectal sparing is relatively common and can mean the diagnosis is missed). Lymphocytic colitis is characterized by a marked and diffuse excess of lymphocytes interspersed within the surface epithelium and lamina propria (Figure 1). These features are also found in collagenous colitis, with the additional finding of a thickened subepithelial collagen band >10 micrometres in width (Figure 2). The differential diagnosis of microscopic colitis is summarized in Table 1.

Treatment

Management decisions should reflect disease or symptom severity and take into account the benign clinical course and good prognosis in most cases. Over half of treated patients with lymphocytic colitis can expect no recurrence of symptoms after 6



Figure 1 Histology showing lymphocytic colitis with increased inflammatory infiltrate and increased intraepithelial lymphocytes on the surface and in the crypts (blue arrow). Slide courtesy of Dr Vicki Save.

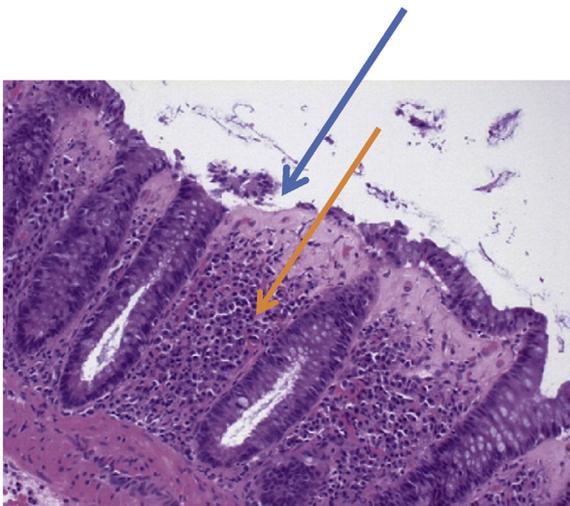


Figure 2 Histology showing collagenous colitis with the characteristic increased lamina propria infiltrate (orange arrow), prominent pink subepithelial collagen band and surface denudation (blue arrow) where the epithelium has sheared off. Slide courtesy of Dr Vicki Save.

months, and over two-thirds of those with collagenous colitis are symptom-free off medication 2–5 years after diagnosis.

In some individuals, identification and withdrawal of drug precipitants and use of anti-diarrhoeal agents, such as loperamide, are sufficient. Treatment of associated conditions such as coeliac disease (with a gluten-free diet) and bile acid diarrhoea (with bile acid sequestrants such as colestyramine or colesevelam) eases the diarrhoea. If symptoms persist despite these measures, the options include a reducing course of budesonide,

Differential diagnosis of microscopic colitis

- Coeliac disease
- Giardiasis
- Small bowel Crohn's disease
- Bile acid diarrhoea
- Post-cholecystectomy syndrome
- Small intestinal bacterial overgrowth
- Lactose intolerance
- Neuro-endocrine tumours
- Irritable bowel syndrome with diarrhoea

Table 1

shown in three randomized controlled trials (RCTs) to be effective in collagenous colitis,^{1–3} or an 8-week course of bismuth subsalicylate. The dose of budesonide is 9 mg/day, reducing by 3 mg decrements every 6 weeks; prolongation of the 3 mg dose for up to 6 months is needed if symptoms return rapidly on drug cessation. A key advantage of budesonide is the relative lack of steroid side effects due to its high first pass metabolism in the liver. In the UK, bismuth is only available as colloidal bismuth subcitrate (De-nol[®]) and can be prescribed for a maximum of 8 weeks. A small uncontrolled trial of bismuth showed histological improvement and sustained clinical response in 9 of 13 patients at 7–28 months.⁴

Other treatment options that can be effective but lack evidence include loperamide (a sensible first-line treatment – high doses up to 24 mg/day can be needed), metronidazole, 5-aminosalicylate (mesalazine), colestyramine and prednisolone. Budesonide was shown to be more effective than mesalazine in an RCT.⁵

There is little literature to guide therapy where symptoms are refractory or relapse frequently. Fortunately, this is uncommon. Repeated courses of budesonide or another corticosteroid can be required, with a prolonged low-dose ‘tail’ to the corticosteroid course; however, many clinicians in this situation opt to use corticosteroid-sparing immunomodulatory agents. Although RCTs are lacking, open-label studies have reported beneficial effects from both azathioprine and methotrexate, and there is anecdotal evidence for benefit from anti-tumour necrosis factor- α therapy. Surgery (either loop ileostomy or colectomy) is required in extreme cases, but advances in medical treatment have made this a very rare event. ◆

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FURTHER READING

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online [here](#).

Question 1

A 64-year-old woman presented with a relatively sudden onset of watery diarrhoea with intermittent incontinence. She had a past medical history of arthritis for which she was taking intermittent naproxen.

Clinical examination was unremarkable.

Which of the following tests is most appropriate?

- A. Barium enema
- B. CT scan of the abdomen/pelvis
- C. Flexible sigmoidoscopy
- D. Coeliac serology
- E. Colonoscopy

Question 2

A 47-year-old man underwent a colonoscopy for watery diarrhoea. During the procedure, air insufflation produced a large mucosal tear at the splenic flexure with visibly intact submucosa.

What should be the next step?

- A. Repair the defect with clips
- B. Withdraw the scope and observe the patient
- C. Continue the colonoscopy
- D. Request surgical intervention
- E. Take biopsies from the site

Question 3

A 72-year-old woman presented with mild watery diarrhoea, with her bowels opening three times a day. She was found to have collagenous colitis. She had a past history of osteoporosis and hypertension. She was taking lansoprazole for Barrett's oesophagus with low-grade dysplasia, and ibuprofen for severe osteoarthritis.

What is the most appropriate first-line treatment?

- A. Withdraw the lansoprazole
- B. Withdraw the ibuprofen
- C. Advise treatment with loperamide
- D. Advise treatment with budesonide
- E. Advise an exclusion diet