

Case report

Collagenous colitis: an unrecognised entity

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SUMMARY A patient is reported with chronic abdominal pain, diarrhoea, and associated radiological and endoscopic abnormalities of the sigmoid colon. Light and electron microscopic study of colorectal mucosa showed abnormal collagenous thickening of the subepithelial basement membrane. The authors felt that the clinical and morphological features justified a diagnosis of collagenous colitis. Review of the literature suggested that collagenous colitis was still an unrecognised entity.

Lindström (1976) recorded the first case of an hitherto undescribed entity for which he suggested the term 'collagenous colitis'. Lindström's report concerned a 48 year old woman with chronic watery diarrhoea; a rectal biopsy showed a heavy collagenous deposit in the mucosal basement membrane. To our knowledge, no further description of this singular entity has appeared in the literature.

We report here the case of a 53 year old man with a somewhat similar clinical presentation. Biopsies of colorectal mucosa showed an identical histological appearance. Electron microscopy confirmed the exclusive collagen nature of the basement membrane deposit.

Case report

A 47 year old male first presented in July 1973 with the clinical features of acute abdomen. A plain x-ray film of the abdomen showed fluid levels suggesting intestinal obstruction. However, no intra-abdominal organic lesion was found at laparotomy.

More recently, this patient (now aged 53 years) had been complaining of intermittent colicky abdominal pain for approximately the last two years, associated with drowsiness, stooping, vomiting, and severe diarrhoea. The pain, described as 'torsion-like', was predominantly periumbilical but shifting to the lower abdomen and lasted two to three days with early morning paroxysm. He experienced up to 15 'dark' stools per day without fresh blood or mucus. The patient acknowledged excessive intake of alcohol. He had not been on any drugs recently

and there was no past history of abdominal irradiation.

The patient was admitted to the gastroenterology unit for colonoscopy. Clinical examination showed a distended abdomen, the patient reacting painfully to palpation of both iliac fossae. The liver was slightly enlarged. The patient was not dehydrated.

A barium enema showed some mucosal irregularity of the sigmoid portion. Except for slightly raised serum bilirubin (25.6 μmol/l; N < 17) and gamma-GT (46 U/l; N < 30), all other biochemical and haematological investigations were essentially normal.

During colonoscopy (14 September 1978), and because of incomplete bowel preparation, only 50 cm of colonic mucosa was visualised, including the abnormal sigmoid portion seen with the barium enema. The colorectal mucosa was markedly congested, friable, and with contact bleeding. Mucosal folds appeared to be oedematous and hypertrophic. There was no identifiable ulceration of the mucosa but a diverticulum and a small polyp were noted. Biopsies (HB 9955) were taken at 10 cm, 17 cm, 20 cm, and 25 cm.

The patient was prescribed a mild non-specific treatment which did not include steroids.

A further proctosigmoidoscopic examination (10 October 1978) showed a mild congestion of the mucosal folds of the rectum; several biopsies (HB 10.334) were taken from the rectosigmoid junction. When last seen (July 1979), the patient had not been complaining of significant symptoms but no further colorectal biopsy had been taken.

PATHOLOGY

The four initial biopsies of colorectal mucosa (HB 9955) were processed for conventional light micro-

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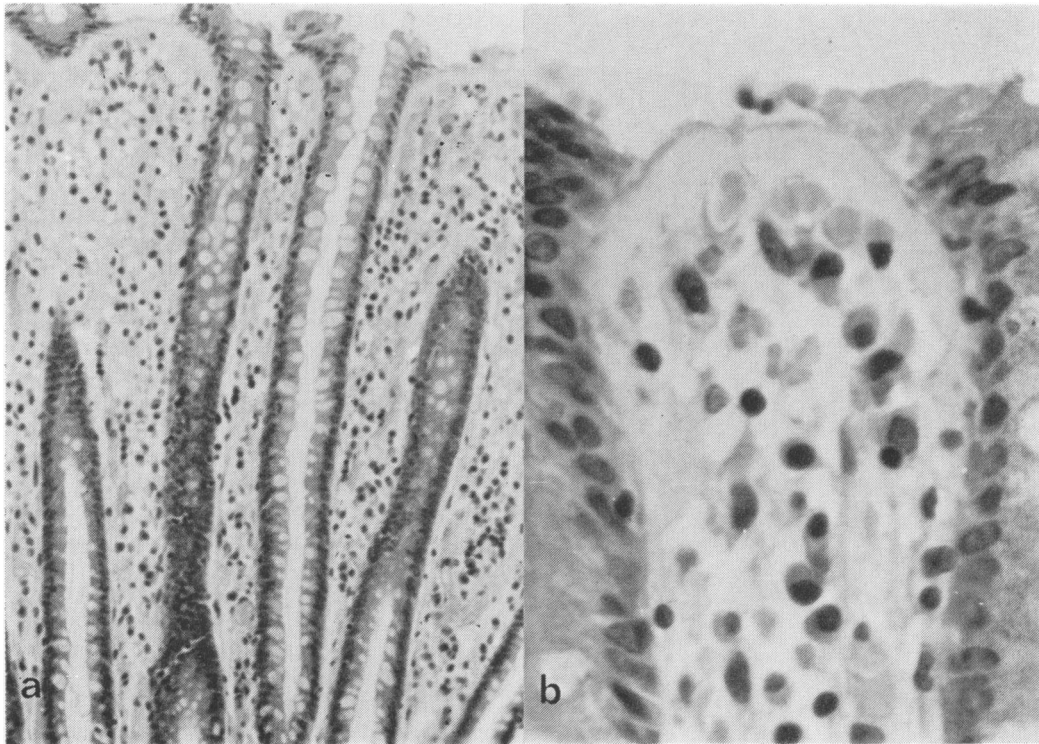


Fig. 1 (a) Biopsy of sigmoid colonic mucosa at 25 cm (HB 9955 A) showing diffuse thickening of the subepithelial basement membrane predominating under the intercryptal or surface epithelium. H and E, $\times 125$ (original magnification). (b) Biopsy of colorectal mucosa (HB 10.334). High power view of epithelial zone with underlying thickened basement membrane. H and E, $\times 625$ (original magnification).

scopy including histochemistry. The repeated rectal biopsies (HB 10.334) were processed partly as above and partly for electron microscopy, histoenzymology and immunofluorescence.

All the biopsies showed similar histological features and histochemical reactions.

The predominant lesion was a diffuse thickening of the subepithelial basement membrane, more pronounced under the intercryptal or surface epithelium than around the crypts (Fig. 1a and b). The thickness of this basement membrane averaged 11.5μ under the surface epithelium, as measured in 20 consecutive step sections from each biopsy and using an eye-piece graticule of scale 10 mm: 100 (total magnification $\times 625$). For comparison, the thickness of the basement membrane was also measured in 30 control biopsies of colorectal mucosa from other patients of similar age group and reported as being within normal limits; it was found on average to be between 4.6μ and 6.9μ .

The basement membrane material was birefringent with polarised light and stained positively as follows:

pale pink with the periodic acid-Schiff reaction (with and without disatase predigestion), green with Masson trichrome, and red with Van Gieson. No positive staining of this material was observed with Alcian blue, Sirius red and Congo red. Gordon and Sweet's method for reticulin revealed a dense condensation of reticulin material throughout the thickened basement membrane (Fig. 2.). Many capillaries and several fibroblasts from the lamina propria appeared to be tightly applied to the under-surface of the abnormal basement membrane. This again was particularly noticeable in the intercryptal zone.

Mild non-specific inflammatory changes were also noted in the mucosa. There was patchy sloughing of the surface epithelium with fibrinous exudate. The lamina propria showed moderate capillary congestion and a slight excess of chronic inflammatory cells with few neutrophils. The lining epithelium of the crypts showed mild decrease of mucus secretion. Some of these changes were probably artefactual and induced by the cleansing isotonic saline enema

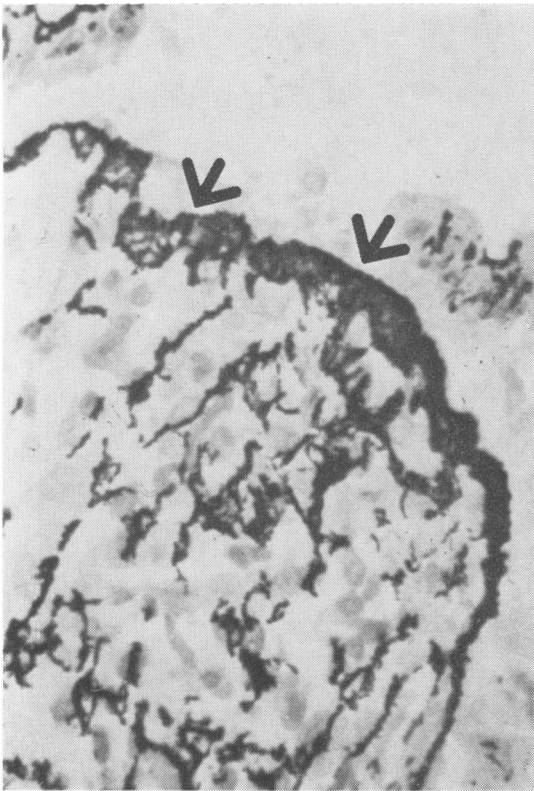


Fig. 2 Biopsy of sigmoid colonic mucosa at 20cm (HB9955 B). Dense condensation of reticulin material within the thickened basement membrane (arrowed). Gordon and Sweet's method for reticulin, $\times 625$ (original magnification).

used (Meisel *et al.*, 1977). The portion of muscularis mucosae included in all the biopsies showed no significant abnormality.

Electron microscopic examination was particularly concerned with the areas of basement membrane under the surface epithelium and around the crypts. Low power micrographs showed an abnormally thickened basement membrane underlying the surface epithelium and measuring approximately 12μ . It consists of a dense and irregular arrangement of fibres embedded in an amorphous granular material. Higher magnification showed considerable variation in size of these fibres and the longest measured 0.10μ . These fibres had a characteristic axial periodicity of 640 \AA and were well demonstrated with silver methanamine (Fig. 3).

The results of light and electron microscopy confirmed the collagen nature of the basement membrane deposit, probably type III collagen (Goldberg and Rabinovitch, 1977).

Sections from unfixed frozen tissue showed no abnormal enzymatic activity or immunoglobulin deposition in the thickened basement membrane.

Discussion

In normal human colorectal mucosa, the basement membrane is a dense acellular layer of collagen, called the 'collagen table' or the 'reticular layer'. There is a close association between the basement membrane and pericryptal fibroblasts (forming the 'pericryptal sheath'), the latter being responsible for the collagen production and deposition within the former. This basement membrane is also directly in contact with the absorptive cells of the surface epithelium. (Donnellan, 1965; Pascal *et al.*, 1968; Kaye *et al.*, 1968; Eidelman and Lagunoff, 1972).

Light and electron microscopic study of several biopsies from our patient's colorectal mucosa shows a non-artefactual, diffuse, and markedly abnormal thickening of the basement membrane due to excessive collagen. Although, this is more pronounced under the intercryptal or surface epithelium, it is found consistently at that level in all the biopsies. The thickened collagenous basement membrane appears to be the only significant histological abnormality in an otherwise slightly inflamed colorectal mucosa.

This lesion of the basement membrane is not described or illustrated, to our knowledge, in the standard published monographs on large bowel pathology (Whitehead, 1973; Morson and Dawson, 1974; Potet 1974). In particular, collagenous thickening of the basement membrane is not mentioned in the literature dealing with the various types of proctocolitis: ischaemic colitis, ulcerative colitis, Crohn's disease, irradiation colitis, pseudomembranous colitis, and specific infections such as tuberculosis or amoebiasis (Mottet, 1971; Tandon and Prakash, 1972; Pittman and Hennigar, 1974; Price and Morson, 1975; Alschibaja and Morson, 1977; Norris, 1977; Yardley and Donowitz, 1977). Furthermore, this lesion is not seen in systemic sclerosis and related collagen tissue disorders (Hoare, 1976); it is not found in mucosa adjacent to carcinoma (Saffos and Rhatigan, 1977). Amyloidosis is perhaps the one condition in which a somewhat similar gross thickening of the basement membrane is observed but then it is entirely due to amyloid deposition, also conspicuous in arterioles (Gilat *et al.*, 1969).

Lindström's case report (1976) appeared to be the first published description of a unique form of colitis, characterised by severe diarrhoea and collagen deposition in the basement membrane.

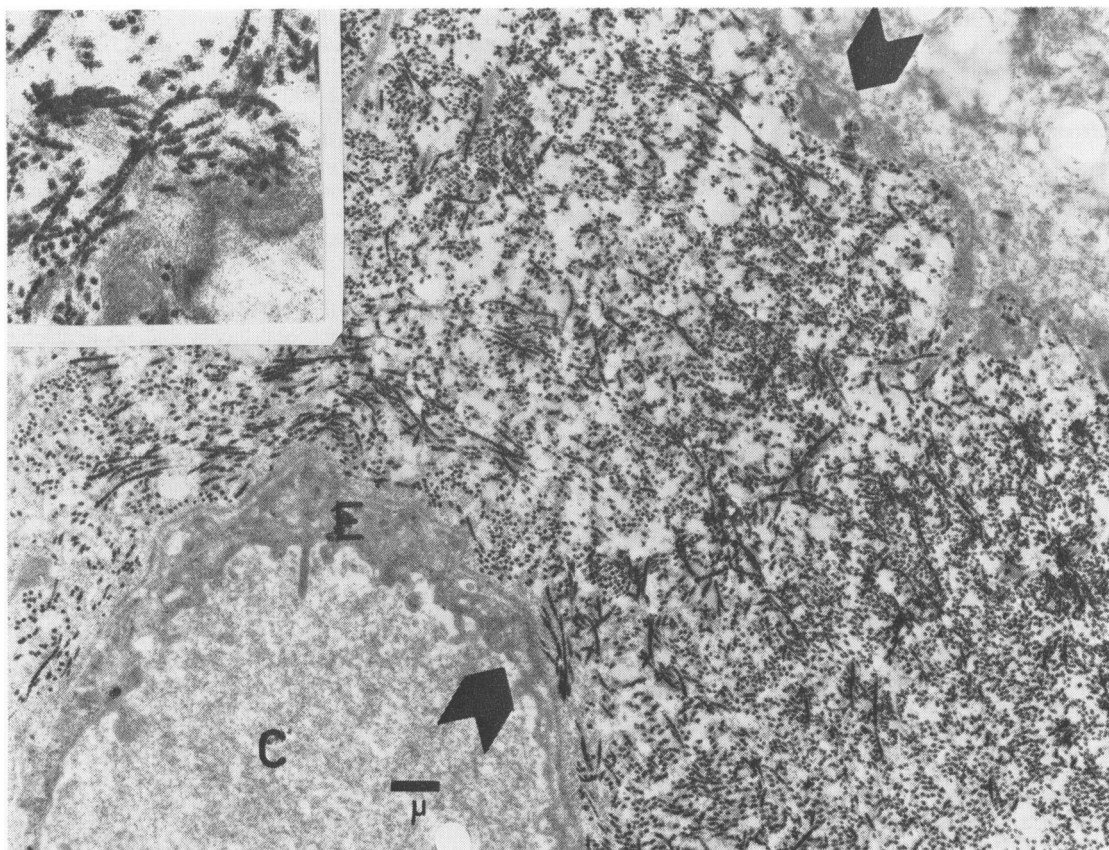


Fig. 3 Biopsy of colorectal mucosa (HB 10.334): electron micrograph. Thickened basement membrane (arrowed) containing numerous collagen fibres of typical appearance and axial periodicity (detail in inset). C: capillary lumen. E: endothelial cell. Silver methanamine, $\times 5000$ (original magnification).

Lindström called this new entity, 'collagenous colitis' and drew a parallel with collagenous sprue.

Collagenous sprue is a rare form of severe malabsorption with subtotal villous atrophy of the small bowel mucosa and a thickened basement membrane consisting entirely of collagen (Weinstein *et al.*, 1970). It has been argued as to whether the presence of excessive collagen in the basement membrane is a specific lesion of collagenous sprue (Perera *et al.*, 1975) or 'makes no difference to the course of the disease' (Thompson, 1976).

Lindström (1976), comparing collagenous colitis with collagenous sprue, inferred that the collagen deposited in the basement membrane of collagenous colitis may be responsible for blocking water resorption with resulting diarrhoea. This was not an altogether speculative hypothesis. Studies on the role of the pericryptal sheath of colorectal mucosa

have indeed suggested that the basement membrane could act as a regulatory barrier for water and electrolytes transport (Kaye *et al.*, 1968).

The peculiar collagenous thickening of the basement membrane observed in our patient is similar in appearances and nature to that of Lindström's case: both patients had severe chronic diarrhoea and abdominal pain. Furthermore, our patient showed no convincing clinical, radiological, endoscopic, or histological features suggestive of Crohn's disease or ulcerative colitis.

We believe that collagenous colitis represents a genuine but unrecognised form or variant of colitis of unknown aetiology. To our knowledge, our case report is the second recorded one in which a diagnosis of collagenous colitis appeared to be appropriate on morphological grounds. In our opinion, its clinical significance cannot be entirely excluded.

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