CASE REPORT

Clinical and histological resolution of collagenous sprue following gluten-free diet and discontinuation of non-steroidal anti-inflammatory drugs (NSAIDs)

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SUMMARY

Collagenous sprue is a rare small bowel enteropathy that has overlapping clinical features with coeliac disease; it is commonly associated with arthritic autoimmune conditions, which often require non-steroidal anti-inflammatory drugs (NSAIDs). In the limited published literature available, there are putative suggestions of a link between NSAID use and collagen deposition in intestinal subepithelia in such patients. The authors present a case of a 43-year-old woman with long-standing NSAID use for autoimmune polyarthropathy and positive coeliac antibodies. However, distal duodenal biopsies revealed a thickened band of subepithelial collagen with villous atrophic appearances consistent with collagenous sprue. The patient was treated with a gluten-free diet and her NSAIDs were discontinued. After 6 months, her gastrointestinal symptoms had resolved with complete histological resolution of the collagenous subepithelial bands and villous atrophy on duodenal biopsy.

BACKGROUND

Collagenous sprue is an extremely rare small bowel enteropathy which shares common clinical and pathological features with coeliac disease; however the condition is often refractory to treatment which, in turn, can lead to severe malabsorption.¹ The exact relationship between coeliac disease and collagenous sprue remains controversial. The pathological hallmark of collagenous sprue is a thickened subepithelial collagen band with villous atrophy detected on distal duodenal biopsy. There is evidence that most patients (63–70%) with collagenous sprue suffer with other autoimmune conditions^{2–3} and that this is 12-fold more likely than in coeliac disease.² Many of the coexisting autoimmune diseases affecting these patients include various types of arthritis, for which patients often require non-steroidal anti-inflammatory drugs (NSAIDs). Interestingly, the largest case series of collagenous sprue in the literature to date reported that 30% of patients with this diagnosis were taking acetylsalicylic acid or NSAIDs.³ It is therefore important to highlight the putative link between the latter medications and collagenous enteropathies,^{4–5} since NSAID cessation may potentially reverse collagen deposition.

CASE PRESENTATION

A 43-year-old female patient with a history of indeterminate autoimmune connective tissue disease and

abdominal symptoms was referred to the gastroenterology clinic having been found to have positive coeliac autoantibodies (tissue transglutaminase antibodies). She had reported that her bowel motions tended to be loose with associated flatus and bloating after eating wheat-containing products in recent years. At the time of review, there were no other specific gastrointestinal symptoms and no history of weight loss. She had been taking NSAIDs regularly for episodic arthritic pains in her hands and feet. Since discontinuing hydroxychloroquine 12 months previously, she had not been on any arthritis-modifying immunomodulatory medication. There was no relevant family history. Clinical examination of the gastrointestinal tract was normal. Blood parameters including haemoglobin, haematinics, liver function tests, inflammatory markers and vitamin D were within the normal range. In view of the strong suspicion of coeliac disease, oesophagogastroduodenoscopy (OGD) with distal duodenal biopsies was arranged.

INVESTIGATIONS

OGD was normal macroscopically. Duodenal biopsies (figure 1) revealed marked blunting of villous architecture, chronic inflammatory cell infiltration within the lamina propria and intraepithelial infiltration by lymphocytes and polymorphs. Additionally, there was an increase in the thickness of basal collagen, suggestive of collagenous sprue. There was no evidence of parasitic infection. She

Figure 1 Distal duodenal histology at diagnosis showing increase in the thickness of basal collagen and marked blunting of villous architecture, chronic inflammatory cell infiltration within the lamina propria and intraepithelial infiltration by lymphocytes and polymorphs.

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later had a bone density scan that proved to be normal.

Rheumatological autoantibody profile demonstrated positive antinuclear antibody and anti-Ro antibodies, with negative rheumatoid factor; furthermore, there were no clinical features of Sjogren's syndrome, systemic sclerosis, rheumatoid arthritis, dermatomyositis or lupus.

TREATMENT

The patient was immediately provided with dietetic advice regarding a gluten-free diet. Given the possible association between NSAID use and collagen deposition in the small and large intestine reported in small case series,^{4 5} NSAID cessation was also advised. A repeat OGD was planned in 6 months.

OUTCOME AND FOLLOW-UP

The patient reported marked improvement in energy levels with significant improvement in her bloating and flatus shortly after starting a gluten-free diet and following NSAID cessation; furthermore, tissue transglutaminase levels normalised at 6-month review. At that juncture, however, the patient reported the novel symptom of bright red rectal bleeding; as such, a colonoscopy was requested in addition to her planned follow-up OGD.

The former revealed normal mucosal appearances to the caecum and terminal ileum with no histological evidence of colitis or collagenous deposition in either the right or left colon. OGD was also both macroscopically and microscopically normal now, with resolution of the previous histological features of collagenous sprue (figure 2).

DISCUSSION

Our case describes a patient who presented with clinical features suggestive of coeliac disease (symptoms and positive serology) but was confirmed to have collagenous sprue on distal duodenal biopsy. This is in line with serology data from two published case series of patients with collagenous sprue, where the majority of patients tested (16/21, 76%) had positive coeliac serology.^{2 5} Notably, of those with negative coeliac serology in these series, only two had negative tissue transglutaminase autoantibodies,² whereas the other three patients had only been tested for less sensitive autoantibodies⁶ antigliadin and/or antiendomysial.⁵

There is no uniform consensus regarding the management of collagenous sprue and some conflicting reports of the clinical prognosis of this condition. Historically, it was often felt that the

clinical outcome in these patients was dismal, with progressive malabsorption ultimately leading to inevitable death.⁷ However, recent data suggest clinical improvement can be achieved in most patients after treatment with gluten-free diet and/or immunomodulatory therapies (including corticosteroids).^{2 3 5 8} Histological improvement has been reported on follow-up duodenal biopsies in around two-thirds of patients,^{2 3} with complete histological resolution in 33% of treated cases.³ Indeed, two case series have reported successful clinical outcomes with gluten-free diet alone.^{2 5} In one of these series, 8/19 (42%) patients responded to a gluten-free diet alone, while a further 10/19 required immunomodulatory therapy to induce successful clinical response, with one death due to malnutrition.² In a retrospective study of 30 non-responders to gluten-free diet monotherapy, 26/30 patients received steroids, 2/30 parenteral nutrition, 1/30 octreotide and 1/30 intravenous iron (all treatments in addition to gluten-free diet).³ In this study, 24/30 (80%) patients improved clinically with treatment, 6/30 (20%) remained refractory to the treatment and only 1/30 died from complications of collagenous sprue.³ In the latter study, 9/30 (30%) patients were taking NSAIDs or acetylsalicylic acid.³ Unfortunately there are no data included in the study regarding whether these medications were discontinued during follow-up and therefore it is unknown whether this may have been a factor in the clinical improvement of any of these patients.

In the present case, while it is possible that gluten-free diet alone may have been responsible for her clinical and histological improvement, NSAID cessation may have also played a role. Indeed, there is a reported close temporal relationship between the start of NSAID and development of collagenous sprue⁴ and collagenous colitis.^{4 5} Furthermore, Riddell *et al*⁴ demonstrated that symptoms of collagenous colitis could resolve with NSAID withdrawal but relapse with rechallenge. The mechanism for NSAID involvement in the pathogenesis of collagenous sprue remains unclear. NSAIDs are a well recognised cause of mucosal injury in small⁹ and large bowel (NSAID enteropathy),¹⁰ provoking an inflammatory response, a factor which may therefore be important in the development of collagenous enteropathies. Thus, we would like to highlight the importance of evaluating whether patients with collagenous sprue are taking NSAIDs and if they are, to advise cessation.

Learning points

- ▶ In patients with suggestive clinical features and positive coeliac serology, it is important to perform distal duodenal biopsies to confirm diagnosis and exclude other rare conditions, including collagenous sprue.
- ▶ Collagenous sprue is a rare condition that may be treated with a gluten-free diet and in patients with more severe features, with addition of corticosteroids and immunomodulators.
- ▶ In patients with collagenous sprue, a careful drug history is vital to determine non-steroidal anti-inflammatory drugs (NSAID) use. NSAIDs may be implicated in the aetiology of subepithelial collagen deposition and discontinuation may lead to both clinical and histological improvement in this group of patients.

Figure 2 Follow-up distal duodenal histology 6 months postinitiation of gluten-free diet and discontinuation of non-steroidal anti-inflammatory drugs showing resolution of the features of collagenous sprue.

Contributors DHV obtained consent, researched and wrote the manuscript. SH prepared and interpreted the histological findings and provided figures for the manuscript. RB provided assistance in writing the manuscript. SL conceptualised the case report and provided assistance in writing the manuscript.

Competing interests None.

Patient consent Obtained.

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