International Journal of Celiac Disease, 2020, Vol. 8, No. 1, 32-34
Available online at http://pubs.sciepub.com/ijcd/8/1/6
Published by Science and Education Publishing
DOI:10.12691/ijcd-8-1-6

Olmesartan-Induced Collagenous Sprue

Hugh James Freeman*

Department of Medicine (Gastroenterology), University of British Columbia, Vancouver, BC, Canada
*Corresponding author: hugfree@shaw.ca

Received January 05, 2020; Revised February 14, 2020; Accepted April 27, 2020

Abstract A 65-yr-old female with diarrhea for 3 months and weight loss was evaluated. There was no travel or family history, but she had been treated with olmesartan for an elevated blood pressure. Fecal studies for an infectious cause were negative and serological studies for celiac disease were negative. A small bowel biopsy showed changes of collagenous sprue. The drug was discontinued. Diarrhea ceased and she regained her weight. Repeat biopsies of the small bowel were normal. Except for cessation of the olmesartan, no other dietary (eg., gluten-free diet) or treatment medication (eg., steroids) was provided. Long-term follow-up revealed no recurrence of symptoms in patients with sprue-like intestinal disease or collagenous sprue, consideration should be given to a drug-induced cause. This may limit the need for further clinical studies, restrictive diets or powerful prescribed medications, including steroids and immunosuppressive agents.

Keywords: *collagenous sprue, celiac disease, drug-induced small bowel disease, olmesartan, sprue-like enteropathy, angiotensin-II inhibitor*

Cite This Article: Hugh James Freeman, "Olmesartan-Induced Collagenous Sprue." *International Journal of Celiac Disease*, vol. 8, no. 1 (2020): 32-34. doi: 10.12691/ijcd-8-1-6.

1. Introduction

Collagenous sprue (enteritis) is a mucosal disorder of the small intestine characterized by a very distinct histopathological lesion first described over 50 years ago [1,2,3]. Severe and persistent diarrhea occurs accompanied by pan-malabsorption of multiple nutrients, protein wasting and profound weight loss. Initially, the disorder was believed to often be fatal but more recent reports have suggested that the disorder is heterogeneous and some patients may have a more positive outcome [4,5]. In general, published treatments must be considered only anecdotal, largely because most physicians have only acquired a limited management experience, published series are limited to a few patients and no randomized clinical trials have been done.

The disorder was first labeled for its classical small intestinal mucosal biopsy appearance with a sub-epithelial band-like deposit showing histochemical and ultrastructural features of collagen [3] and extensively reviewed later [6]. Other histopathological changes include a "flattened" villus architecture similar to untreated celiac disease that fails to respond to a gluten-free diet, so-called sprue-like intestinal disease. Occasionally, collagen deposition has been documented in other gastrointestinal sites, including gastric and colonic mucosa [6]. In some, celiac disease was thought to be present but evaluation was later pursued because of "refractory" symptoms [3], while in others, the small bowel disease was never shown to respond to a gluten-free diet, important in definition of celiac disease, a gluten-dependent disorder. However, other clinical features in collagenous sprue shared with celiac disease have been noted: hyposplenism or splenic atrophy [7], small intestinal ulceration with free perforation [8], and T-cell lymphoma that may co-exist or complicate the clinical course of collagenous sprue [9,10].

Recently, another twist in this narrative on collagenous sprue has occurred. As in celiac disease, the histopathological changes are not specific and different causes have been recognized. For instance, drug toxicities are well recognized to cause sprue-like changes in small bowel biopsies [11]. In recent years, however, similar drug toxicity concerns have been raised in collagenous sprue. For instance, non-steroidal anti-inflammatory drugs were suspected to play a role in pathogenesis of collagenous sprue and colitis, in part, because these patients commonly have associated arthritic autoimmune disorders. Interestingly, celiac antibodies, including tissue transglutaminase antibodies, may be positive in some, but not all patients. Resolution of collagenous sprue after cessation of non-steroidal anti-inflammatory drugs has been reported [12]. The possible significance of other commonly prescribed medications for hypertension have also been noted, including drugs in the angiotensin II receptor antagonist class, particularly olmesartan [13].

2. Case Report

A 65 year old female developed worsening diarrhea up to 5-6 times per day over a 3 month period. During this time, weight loss, estimated to be almost 10 kg was noted. Bloodwork was normal, including a hemogram and iron studies. Antibodies to tissue transglutaminase were negative and serum immunoglobulins were normal. Fecal studies for bacterial and parasitic agents, including

Clostridium difficile, were negative. A colonoscopy with biopsies was normal without findings of colitis or collagen deposits. Upper endoscopy appeared normal except for some non-specific changes including apparent thickening and scalloping of the duodenal mucosa (Figure 1 and Figure 2). Gastric biopsies were normal with no collagen deposits. Duodenal biopsies revealed changes of collagenous sprue (Figure 3).

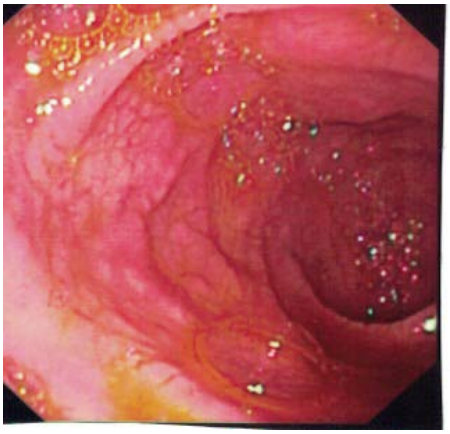

Figure 1. Diffuse hyperaemia with scalloping in duodenal bulb. Macroscopic features are not specific for collagenous sprue and reported in celiac disease and duodenal Crohn's disease.

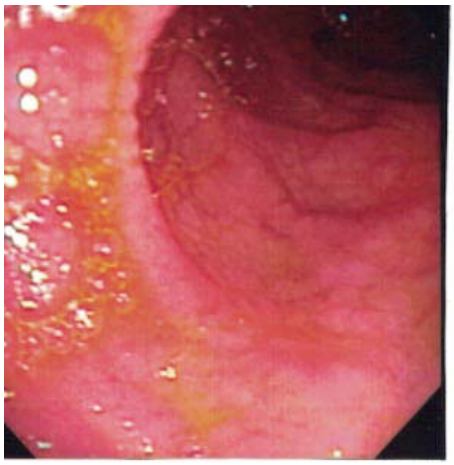

Figure 2. Endoscopic view of descending duodenum showing diffuse hyperaemia, scalloping and nodular folds.

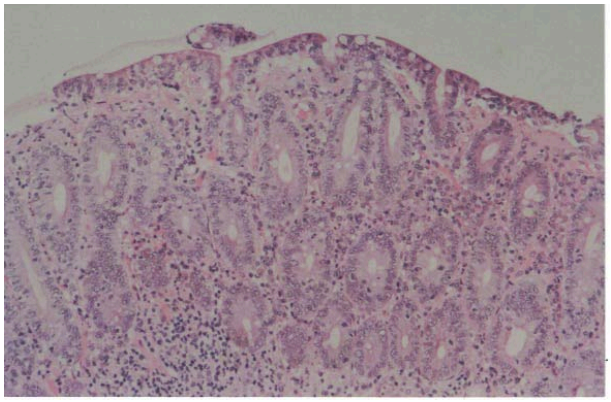

Figure 3. Endoscopic duodenal mucosal biopsy showing mucosal "flattening" with a sub-epithelial band-like deposit typical of collagenous sprue. Increased numbers of intra-epithelial lymphocytes are present and apparent detachment of surface epithelial cells are seen. A trichrome stain for collagen was positive.

The patient also reported that her prior health was normal, except for an elevated blood pressure recording initially self-obtained during a shopping visit in a local food market about a year earlier. This was confirmed by her own physician and she was treated with olmesartan 20 mg daily. A gluten-free diet was not administered. Cessation of drug led to complete resolution of diarrhea and weight gain. After a year, her biopsies were normal. Now, 3 years later, she had remained well and takes chlorthalidone alone for her hypertension.

3. Discussion

Olmesartan enteropathy has been described as a small intestinal sprue-like disease characterized by severe diarrhea, weight loss and pathologic features of untreated celiac disease. In some, the disease has required hospitalization. In the patient here, collagenous sprue was detected after her presentation with diarrhea and weight loss following treatment of her hypertension with olmesartan. There was no other history of intestinal disease, including celiac disease and she was not using other medications. Gastric and colon biopsies were normal.

Her symptoms and small intestinal biopsy changes resolved completely after cessation of olmesartan. No recurrence has occurred during long-term follow-up period over more than 3 years. Further re-evaluation and biopsy after re-introduction of olmesartan was not considered, since other alternatives were readily available to safely manage her elevated blood pressure.

Sprue-like enteropathy associated with olmesartan was previously reviewed [13]. In some, differentiation from underlying celiac disease may difficult, especially if serologic screening studies (eg., tissue transglutaminase) are positive and no response to a gluten-free diet occurs. In the present seronegative patient here, collagenous sprue was defined and olmesartan simply stopped with resolution of her symptoms and normalization of her small intestinal biopsies. Similar histologic recovery or resolution was noted after cessation of the drug by others [14,15,16], however, other forms of treatment were usually provided, including a gluten-free diet and, occasionally, steroids. In one of these reports, however, added evidence for a role of olmesartan was provided with challenge studies [16], not done in the present evaluation. In a similar report to the present case, the authors warned about the possibility of unnecessary exposure to high doses of steroids in this setting where sole cessation of olmesartan alone may be sufficient [16]. There appears to be a wide range of clinical severity of this disorder and, consequently, it is likely to be under-recognized and under-reported.

References

[1] Schein J. Syndrome of nontropical sprue with hitherto undescribed lesions of the small intestine. Gastroenterology 1947; 8: 438-460.

[2] Hourihane DO. Diarrhea of small bowel origin. The histology of intestinal biopsies. Proc R Soc Med 1963; 56: 1073-1977.

[3] Weinstein WM, Saunders DR, Tytgat GN, Rubin CE. Collagenous sprue-an unrecognized type of malabsorption. N Engl J Med 1970; 283: 1297-1301.

[4] Freeman HJ, Davis JE, Myers DM. Complete histological resolution of collagenous sprue. Can J Gastroenterol 2004; 18: 333-336.
[5] Freeman HJ, Berean KW. Resolution of paraneoplastic collagenous enterocolitis after resection of colon cancer. Can J Gastroenterol 2006; 20: 357-360.
[6] Freeman HJ. Collagenous mucosal inflammatory diseases of the gastrointestinal tract. Gastroenterology 2005; 129: 338-350.
[7] Freeman HJ. Hyposplenism, antiendomysial antibodies and lymphocytic colitis in collagenous sprue. Can J Gastroenterol 1999; 13: 347-350.
[8] Freeman HJ, Webber DL. Free perforation of the small intestine in collagenous sprue. World J Gastroenterol 2009; 15: 4446-4448.
[9] Freeman HJ. Collagenous sprue associated with an extensive T-cell lymphoma. J Clin Gastroenterol 2003; 36: 144-146.
[10] Medlicott SA, Beck PL, Loken S, Crabtree T. Synchronous collagenous sprue and enteropathy-type T-cell lymphoma: variants of the same disease. Can J Gastroenterol 2004; 18: 329-332.
[11] Freeman HJ. Sprue-like intestinal disease. Int J Celiac Dis 2014; 2: 6-10.
[12] Vasant DH, Hayes S, Bucknall R, Lal S. Clinical and histological resolution of collagenous sprue following gluten-free diet and discountinuation of non-steroidal anti-inflammatory drugs. BMJ Case Rep 2013. Pie: bcr2013200097.
[13] Freeman HJ. Olmesartan enteropathy. Int J Celiac Dis 2016; 4: 24-26.
[14] Rubio-Tapia A, Herman ML, Ludvigsson JF, Kelly DG, Mangan TF, Wu TT, Murray JA. Severe spruelike enteropathy associated with olmesartan. Mayo Clin Proc 2012; 87: 732-738.
[15] Nielsen JA, Steephen A, Lewin M. Angiotensin-II inhibitor (olmesartan)-induced collagenous sprue with resolution following discontinuation of drug. World J Gastroenterol 2013; 19: 6928-6930.
[16] Desruisseaux C, Bensoussan M, Desilets E, Tran H-K, Arcand R, Poirier G, Wisniewski A, Maniere T. Adding water to the mill: olmesartan-induced collagenous sprue-a case report and brief literature review. Can J Gastroenterol Hepatol 2016.