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NOTE

Collagenous Colitis in a Patient with Addison’s Disease: A Case Report

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Abstract. Diarrhea is a non-specific symptom which may be associated with Addison’s disease and several causes had been demonstrated in the aetiology. We describe a patient with Addison’s disease who was suffering from chronic diarrhea for three months. She was diagnosed as having collagenous colitis and successfully treated with Sulphasalazine, 2 g/day. Collagenous colitis is an uncommon cause of chronic diarrhea and the association of collagenous colitis with Addison’s disease has not previously been described. We think that collagenous colitis may play a role in the aetiology of diarrhea in patients with Addison’s disease and therefore we suggest a full colonoscopic examination in other patients with Addison’s disease and diarrhea to determine the incidence of collagenous colitis in the aetiology of diarrhea.

Key words: Addison’s disease, Collagenous colitis, Diarrhea

COLLAGENOUS colitis (CC), which was first described in 1976 by Lindström, is a clinicopathologic syndrome that is characterized by chronic watery diarrhea and a distinctive band of collagen deposited beneath the surface epithelium in colonic mucosa [1]. The disease most commonly affects women, and the most frequent presenting symptom is watery diarrhea [2]. Basically, it is an inflammatory disorder of undetermined origin and it is relatively uncommon. The main feature of the disease is a chronic, nonbloody, probably secretory diarrhea which is frequently associated with abdominal pain and the endoscopic and radiographic studies are usually normal and a colonic biopsy should be performed to diagnose this entity [2, 3]. Affected patients are generally well with no evidence of nutritional impairment despite the chronicity of the diarrhea, and nonspecific antidiarrheal therapy is generally ineffective [3]. It has a characteristic histological changes including a thickened, eosinophilic hypocellular subepithelial collagen band and increased inflammatory cells in the lamina propria different from other recognized idiopathic inflammatory bowel diseases [4].

Diarrhea is a common but non-specific symptom in untreated Addison’s disease. It is found in nearly 30% of patients due to malabsorption which is apparently the result of functional defects of enterocytes and generally reversible upon the administration of corticosteroids [5]. In this paper, we describe a woman with primary adrenal insufficiency for three years and chronic diarrhea for three months, who was diagnosed as CC. At least to our knowledge, Addison’s disease associated with CC has not been described previously.

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Case

A 40-year-old woman was admitted to the hospital with a profuse watery diarrhea without blood or mucus for three months. Her medical history and hospital records showed that three years ago she was admitted to our department with nausea and vomiting, progressive fatigue, anorexia, hypotension and hyperkalemia for six months. Besides the routine investigations such as hemogram, urine analysis, chest X-ray, fasting blood glucose, kidney and liver function tests, intravenous ACTH (Synacthen 0.25 mg, Ciba-Geigy) stimulation test was performed. Addison's disease was diagnosed with low baseline cortisol values, high ACTH values and without any cortisol response to ACTH stimulation. There was no secondary cause, such as tuberculosis, which may lead to primary adrenal insufficiency. Polyglandular autoimmune syndrome was also excluded with the absence of insulin-dependent diabetes mellitus (IDDM), autoimmune thyroiditis, hypoparathyroidism and other non-endocrine diseases. She had been discharged with improvement after the initiation of prednisolone (7.5 mg/day) and 9α fluorocortisol (0.1 mg/day) replacement therapy. She was well for three years until three months ago when a watery diarrhea (eight stools per day) without blood or mucus started. She was hospitalized to determine the cause of this complaint. She denied using any medications, including nonsteroidal anti-inflammatory drugs (NSAID), during the last three years except prednisolone and 9α fluorocortisol replacement therapy.

On physical examination, the patient appeared well without evidence of malnutrition or dehydration with 110/60 mm Hg blood pressure, 76 beats/min heart rate, 75 kg body weight and 160 cm height. Her routine laboratory examinations revealed that hematocrit was 42%, the white blood cell count was 4200 per milliliter and ESR was 15 mm/h. Biochemical screening, including blood urea nitrogen, creatinin, Na, K, Ca, P, fasting blood glucose, total protein, albumin, globulin and cholesterol, was normal. She had normal endocrine functions except primary adrenal insufficiency; 10 nmol/l morning cortisol (normal range 200-500) and 52 pmol/l ACTH value (normal range 7-11) with a 40 nmol/l peak cortisol response to 250 µg intravenous ACTH stimulation. Plasma renin activity was 2.7 ng.L⁻¹.s⁻¹ (normal range 0.054-0.756) and the baseline plasma aldosterone level was 41.6 pmol/l (normal range 27-432) without any increase while in the upright position for two h.

Stool specimens were negative for occult blood, ova, parasites, bacterial pathogens, clostridium difficile toxin and tubercle bacilli but positive for leucocytes. There was no sign of malabsorption syndrome. Radiological studies of the gastrointestinal system, including small intestine X-ray and double-contrast colongraphy, were normal. Rectosigmoidoscopy was normal and several biopsies were obtained to determine the aetiology of chronic diarrhea.

Histopathologic specimens of the rectum (Fig. 1) showed evidence of focally detached surface epithelium from the basement membrane, and the crypts were infiltrated by inflammatory cells mainly lymphocytes, plasma cells and eosinophilies. The subepithelial collagen thickening was striking and in some areas the thickness was 40 µm which was measured by light microscopy with a screw micrometer. The histopathologic appearance confirmed CC and sulphasalazine (2 g/day) therapy was added to her hormone replacement therapy. Three days after the initiation of

![Fig. 1. Light microscopic photograph of the rectum biopsy.](image)
sulphasalazine therapy her diarrhea began to remit and within a week the stool, passed once a day, returned to normal appearance with no leucocytes microscopically and she was completely well.

Discussion

Deficient adrenal production of glucocorticoids or mineralocorticoids results in adrenocortical insufficiency which is either the consequence of destruction or dysfunction of the adrenal cortex (primary adrenocortical insufficiency, Addison’s disease). Autoimmune adrenitis is now the leading cause of Addison’s disease and may be associated with other immunologic and autoimmune disorders. Diarrhea may be a symptom of the disease besides the common signs and symptoms such as weakness, fatigue, anorexia, nausea, vomiting, hypotension and hypoglycaemia, and it may be also a preconditioning state in acute adrenal crisis [6].

CC is characterized by chronic watery diarrhea and a thickened band of collagen under the surface epithelium and may be associated with various autoimmune disorders such as rheumatoid arthritis, scleroderma, sicca syndrome, inflammatory arthropaties, atrophic gastritis, chronic hepatitis and primary biliary cirrhosis [7, 8]. Autoimmune thyroiditis may also be associated with CC [8] and as we previously reported from our clinic [9], diabetes mellitus may be associated with CC in some patients suffering from chronic diarrhea. Although it is premature to consider CC as a fully autoimmune disease, the female predominance, the frequent presence with some of the autoimmune diseases, similarity of the surface epithelial changes to those in Celiac disease and therapeutic response to corticosteroids or anti-inflammatory drugs denotes the autoimmune aetiology [10]. To date, most of the patients with CC were not diagnosed solely but associated with various disorders [8]. In this case, the appearance of CC in an adequately treated patient with Addison’s disease may be another feature of this aetiologically unknown disease which has been proposed as an autoimmune process. Addison’s disease may be associated with various disorders, either endocrine or non-endocrine diseases. Although the exact cause is not known, a number of secondary causes of diarrhea may be identified in patients with Addison’s disease such as steatorrhea, functional defects of enterocytes, bacterial overgrowth or parasites [5, 11]. We describe a patient presenting with Addison’s disease and chronic diarrhea who had collagenous colitis. At least to our knowledge, this is the first report of collagenous colitis in a patient with Addison’s disease. Although we could not detect the autoantibodies to the steroidal cell enzymes, it is likely that the adrenal insufficiency was autoimmune in origin since no any other secondary cause had been elucidated and also there was no sign or symptom of any other disease which has been previously reported with collagenous colitis.

The normal collagen band of the large intestine is less than 7 µm thick [4, 10] and in CC the subepithelial collagen thickening is around 15–20 µm in most cases and the thickness of the subepithelial collagen band varies greatly in different parts of the colon [2]. Despite diarrhea, our patient was free of symptoms and signs such as weight loss, dehydration or adrenal insufficiency. Also, as previously reported [4], there was no radiological or endoscopic abnormality except a scant number of leucocytes in the stool. We think that Addison’s disease may be another disease in the broad spectrum of disorders associated with collagenous colitis.

Therefore we suggest that CC should be considered in the differential diagnosis of chronic diarrhea in patients with Addison’s disease, and the incidence and the role of CC in the aetiology of diarrhea in Addison’s disease should be investigated in an adequate number of patients.

References


