J KAU: Med. Sci., **Vol. 8,** pp. 109-115 (1420 A.H. / 2000 A.D.)

Collagenous colitis: A Case Report and Review of the Literature

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ABSTRACT. *Collagenous colitis* is a disorder characterized by chronic non-bloody watery diarrhea together with abdominal pain. The diagnosis is only achieved by colonic biopsy, which is required to rule out conditions with similar presentation. Since it was first described in 1976, several similar cases were reported in the literature. We are reporting our first case of *Collagenous colitis* together with review of the literature with emphasis on different presentations, pathogenesis and suggested treatment.

Keywords: *Collagenous colitis*, Diarrhoea, Colonscopy.

Introduction

Collagenous colitis was first described in 1976 by Lindstrom when he reported a case of a 48-year-old woman with chronic watery diarrhoea[1]. Subsequently, more than 500 cases have been reported in the literature. This study reports the first case of *Collangeous colitis* from King Abdulaziz University Hospital, Jeddah, together with review of the literature.

Case History

The patient was a 35-year old female, with a history of intermittent watery diarrhoea and abdominal cramps of 12 years duration. This patient was first seen in our clinic in

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Accepted for Publication after revision: 21 June 1999. Received: 19 November 1997.

1983 when a rigid sigmoidoscopy was performed and revealed normal appearing mucosa. Colonic biopsies at that time reported evidence of lymphocytic infiltration of the lamina propria. She was labeled as having possible ulcerative colitis and was started on sulfasalazine. She had a variable response to sulfasalazine with a slight improvement of her symptoms. A repeat sigmoidoscopy in 1984 revealed a normal macroscopic finding. A sigmoid biopsy showed an increase lamina propria cellularity with preserved crypt architecture compatible with microscopic colitis [Fig. 1, Plates A & B]. The patient continued to have a waxing and waning course with no relation to stress or subsequent pregnancies.

Recently, she was admitted to King Abdulaziz University Hospital with lower abdominal pain and diarrhoea which did not respond to sulfasalazine (3g/day) and a lactose-free diet. She denied having weight loss, hematochezia or fever. Colonoscopy revealed normal looking mucosa up to the cecum. Multiple biopsies were taken which showed preserved crypt architecture with infiltration of lamina propria with lymphocytes, oesinophils, and neutrophils together with subepithelial *collagenous* band of 40 micron thickness [Fig. 1, Plates C & D.]. She was started on Asacol (2.4 g/day) and Predsol enema with a good response.

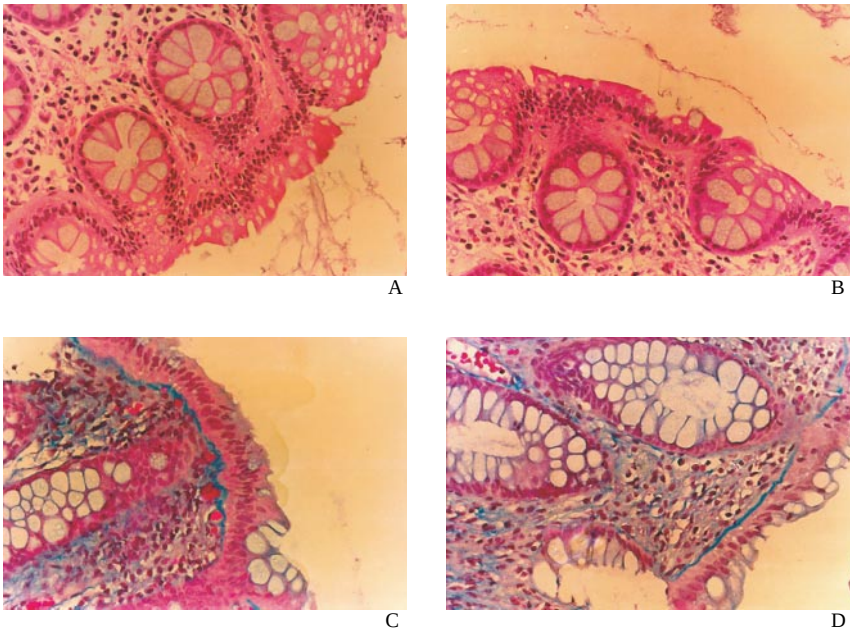

Fig. 1: Plate A & Plate B: Colorectal mucosal biopsy: Mild increase of inflammatory cell, with edema involving lamina propria.
Plate C & Plate D: Colorectal mucosal biopsy: Mild - moderate inflammation with collagenous thickening of surface basement membrane, not extending to crypts (blue color for collagen).

Collagenous colitis is an uncommon disorder characterized by chronic watery non-bloody diarrhoea. It is more common in women (4:1)[2]. However, according to the Mayo Clinic series, there was identical frequency[3] for the two sexes. The patients' ages vary from 23 to 86 years and it has also been reported in children[4]. In addition, the patient may complain of colicky abdominal pain, weight loss, flatulence, dyspepsia [5], polyarthralgia usually affecting peripheral joints[6,7]. Autoimmune diseases (hypothyroidism)[8] as well as celiac disease[9] and very rarely protein-losing enteropathy [10] has been reported. Fever and steatorrhoea are absent with no explanation of diarrhoea despite extensive investigations. Colonoscopy and barium enema are usually normal.

Diagnosis is usually established by histopathological examination of the colonic mucosal biopsy, which shows acellular oesinophilic subepithelial collagen layer[7,11] primarily of types II and III collagen and procollagen of variable thickness, usually > 10 microns (10-100) concentrated around small vessels and more often in the proximal colon. Hence, proctosigmoidoscopy may underestimate the diagnosis, especially if a biopsy shows a normal collagen band (< 6 um) and inflamed mucosa, where full colonoscopy may be indicated[12]. Thickness is variable and may be discontinuous with no correlation between the thickness of *Collagenous* band or its continuity and the severity of symptoms[13]. In addition, there is an increased number of intraepithelial lymphocytes mainly Cd-8 positive TCR and β IELS together with accumulation of Cd 4+ T-cells and plasma cells in the lamina propria with few oesinophils and neutrophils. Lamina propria cellularity correlates more with stool weight[14]. A *Collagenous* band could be found also in few cases in the terminal ileum[15].

Pathogenesis: The cause of *Collangeous colitis* remains obscure. There are several theories suggesting a toxic, ischemic insult mediated via prostaglandins[16], autoimmune, as well as infectious agents as a cause[2,17]. The mechanism of diarrhoea also is unknown. It is secretory diarrhoea. Initially Lindstrom suggested that it is due to impaired water transport by the *Collagenous* band. Prostaglandins may play a role also in the pathogenesis of diarrhoea where it has been shown that PGE2 is increased in jejunal aspirate[2] and in stools[18]. In addition, improvement has been shown with NSAID use which has anti-prostaglandin activity, though NSAID may play a role in thickening of the *Collagenous* band and diarrhoea in some patients with *Collangeous colitis*[16,19].

Course and Prognosis: Patients with *Collangeous colitis* may have spontaneous resolution, persistent diarrhoea or waxing and waning course with exacerbation and remission[7], but it seems that it does not have a malignant potential[5].

Differential Diagnosis: *Collagenous colitis* should be considered in patients with chronic diarrhoea together with inflammatory bowel disease, irritable bowel syndrome, infectious *colitis*, and malabsorption disorders.

However, the absence of haematochezia, loss of weight, normal blood, stool and radiological tests, as well as, the ability of the patient to maintain a generally stable

healthy condition may be in favour of spastic colon or *Collangeous colitis* and hence, colonic biopsy will confirm or rule out *Collangeous colitis*. On the other hand, *Collangeous colitis* should be differentiated from other conditions that may be associated histologically with excessive collagen deposition, including idiopathic ulcerative *colitis* where there are disturbed crypt architecture with crypt abscesses and decreased number of goblet cells. Microscopic colitis (lymphocytic colitis) where there is a similar increase in lamina propria cellularity but not *Collangenous* band[11,26]. Ischemic and radiation *colitis* where there is diffuse collagen in lamina propria and is not limited to subepithelial layer. False diagnosis - when diagnosis is focused only on *Collagenous* band without lamina propria cellularity since tangential sectioning of normal colonic mucosal specimen may result in false thickening of the basal membrane[20]. Fibrotic adenocarcinoma and solitary rectal ulcer syndrome.

Treatment: Different regimens have been used, however, results remain unpredictable. Drugs include: Antidiarrhoeal drugs (Loperamide, Psyllium mucilloid). Sulfasalazine, 5 ASA, Metronidazole, Quinacrine, systemic or topical steroids, cholestyramine and NSAID[5,21-23]. Surgical intervention mainly in the form of fecal stream, diversion and split ileostomy may be effective in medically refractory patients [24]. Response may be either clinical and/or histological with decreased thickness of Collagenous band and decreased lamina propria cellularity[24,25].

Discussion

The case described in the present report demonstrated classical clinical presentation of *Collangeous colitis*. The patient had chronic watery diarrhoea with abdominal pain, with absence of fever and hematochezia, in addition her body weight remained stable during her period of follow-up together with persistently normal investigations which included: CBC, ESR, stool analysis and culture, abdominal ultrasound, barium enema, serum albumin, D-xylose test, as well as, gastroscopy and proximal jejunal biopsy. Her diagnosis was established after colonoscopy and multiple biopsies which showed the characteristic histological features of *Collangeous colitis*. However, the proper diagnosis was delayed. Her previous colonic biopsies were consistent with lymphocytic colitis which shares the same clinical features with *Collangeous colitis* but differs histologically. Delay in diagnosis may be due to specimens having been taken from the distal part of the colon which may miss the diagnosis, since the *collagenous* band is more common in the proximal colon[25]. The *Collagenous* band is discontinuous, hence, inadequate samples may be responsible for delayed diagnosis. Finally, it may be possible that *Collangeous colitis* and *Lymphocytic colitis* are different names of the same disease entity or variant of the same condition[27]. In addition, the *Collagenous* band may increase in thickness with time and the affected colon may show combined areas consistent histologically with *Collangeous colitis* and *Lymphocytic colitis* and this may explain why she was diagnosed initially as L*ymphocytic colitis* and recently as *Collangeous colitis*[3].

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التهاب الأمعاء الغليظة الكولاجيني:تقرير حالة ومراجعة أدبية

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المستخلص. إن مريض التهاب الأمعاء الغليظة الكولاجيني عادة ما يشتكي من إسهال مزمن وآلام في البطن وقد يكون مشابهاً لأعراض أمراض عدة عادة ما تصيب الأمعاء الغليظة، وللتأكد من التشخيص لابد من إجراء منظار سفلي للحصول على عينات كافية من الغشاء المخاطي للتأكد من الحالة عبر التغيرات الخاصة في أنسجة الأمعاء الغليظة. منذ عرض الحالة الأولى عام ١٩٧٦ ورد بعدها عدة أبحاث لحالات مشابهة. ونعرض هنا حالتنا الأولى مع مراجعة البحوث السابقة والتركيز على الأعراض المختلفة ومناقشة المسببات، وسبل الوصول للتشخيص، والأدوية المستخدمة علاجياً.