

中文題目：慢性腹瀉的罕見診斷：膠原性結腸炎

英文題目：A rare diagnosis of chronic diarrhea: Collagenous colitis

作者：林千傑¹、王俊偉^{1,2}

服務單位：高雄醫學大學附設醫院¹內科部²胃腸內科

Introduction:

Collagenous colitis, a subtype of microscopic colitis, which belongs to a chronic inflammatory disease of the colon, is associated with abnormal collagen metabolism and inflammation of colon. The incidence of collagenous colitis is only 2.0 to 10.8 per 100,000 and is estimated higher in northern Europe and America. Case numbers are relatively rare in eastern country including Taiwan.

We report a case of 51-year-old male without any known underlying disease, who suffered from watery diarrhea for 2 months and came to our clinic for help. He was initially diagnosed with functional bowel disorder, but was ultimately diagnosed with collagenous colitis.

Case report:

This 51-year-old male without any known underlying disease came to our clinic because he had been having diarrhea for 2 months. The character of stool was brownish and watery, and bowel movement was 4 to 5 times per day. Diarrhea exacerbated especially after meals. He denied abdominal pain, bloody stool, or tarry stool. He also denied any specific travel, occupation, contact, cluster history and any allergy to medication or food. Before this episode, he used to have regular stool passage once to twice per day with normal shape and characters. He denied alcohol and betel nuts consumption. He has cigarette smoked 1 pack per day for 30 years and just quit for 3 months. Besides, he was used to taking Chinese herbal medicine to protect his liver function. Tracing back to his family history, there was neither malignancy nor significant gastrointestinal tract disorder in his family.

Initially, esophagogastroduodenoscopy and colonoscopy were arranged, and reflux esophagitis, chronic gastritis with *Helicobacter pylori* infection and terminal ileum ulcer with non-specific chronic inflammation were impressed. Thus, after *Helicobacter pylori* eradication was executed, we treated him as functional bowel disorder with medication, diet education and life style modification. He had been regularly followed up at our clinic since then. However, after 6-month regular clinic visits and treatment, he had only partial response to our management. Diarrhea still occurred especially under stress. Furthermore, sleep disturbed by diarrhea was complained of. Autoimmune disease laboratory survey revealed normal range of nearly all autoimmune profile including C3, C4, antinuclear antibody (ANA), rheumatoid factor (RF), IgE and erythrocyte sedimentation rate (ESR), except for slightly elevated serum IgA. Therefore, quitting his current Chinese herbal medicine consumption was suggested, and the follow-up colonoscopy was performed after 10 months of treatment.

In this colonoscopic exam, terminal ileum ulcer was still noted, and collagenous colitis was finally diagnosed according to the pathology result which disclosed mucosa with thickened subepithelial collagen over whole colon and terminal ileum. According to our new pathology

evidence, we administered mesalamine for collagenous colitis, and then the patient recovered to normal bowel movement after medication adjustment.

Discussion:

Clinical manifestation of collagenous colitis is characterized by chronic, watery, non-bloody diarrhea. Pathogenesis could be associated with abnormal collagen metabolism which causes increased production of nitro oxide (NO) in the colonic epithelium and induces secretory diarrhea [1]. It typically occurs in middle-aged patients and has a female preponderance 3 times more than male [2]. We herein present a male case though. In general, it appears typically normal or almost normal on colonoscopy in patients with collagenous colitis. The diagnosis is established by biopsy of the colonic mucosa to demonstrate characteristic histologic changes. The initial colonoscopy manifestation of our case revealed mucosal defects over terminal ileum. A total of eleven mucosal specimens were collected at first colonoscopy from terminal ileum, ascending colon, transverse colon, and descending colon. However, these specimens only showed some non-specific ulcerated mucosa, mixed inflammatory infiltration, and bacterial clump. Not until the follow-up colonoscopic biopsy did colonic lesions be identified as subepithelial collagen deposition. This phenomenon could be attributed to patchy distribution in histologic changes of lesions [3]. Also, the different opinions and judgement between pathologists might be another contributing factor. Moreover, clinical manifestation could be easily confused between functional bowel disorder and collagenous colitis. Both conditions could be presented as chronic diarrhea, abdominal pain and bloating. Therefore, tissue proof is exceptionally important to identify them. Some autoimmune diseases could be concomitant with collagenous colitis such as celiac disease, autoimmune thyroid disease, and Sjögren's syndrome [4]. There are neither parenteral symptoms complained nor abnormal laboratory data except IgA found in our case, which has no diagnostic relevance to autoimmune diseases and collagenous colitis [5]. It's worth noting that cigarette smoking is a well-known contributing factor that increases incidence, deteriorates watery diarrhea, and decreases likelihood of achieving clinical remission of collagenous colitis [6][7]. Therefore, quitting cigarette smoking and life style modification are extremely crucial in this case.

Finally, in patients with symptomatic microscopic colitis, the American gastroenterological association (AGA) recommends treatment with budesonide over mesalamine for the induction of clinical remission. The reason why we chose mesalamine instead of budesonide as first-line treatment was that the payment policy of National health insurance administration (NHIA) regulates budesonide use only when mesalamine treatment is clinically proved failed.

Conclusion:

Plenty of conditions could be associated with chronic diarrhea. Collagenous colitis, a relative rare disease, which needs tissue proof for diagnosis, should be taken into consideration when other common causes are ruled out.

References:

- [1] Andresen L, Jørgensen VL, Perner A, Hansen A, Eugen-Olsen J, Rask-Madsen J. Activation of nuclear factor kappaB in colonic mucosa from patients with collagenous and ulcerative colitis. *Gut*. 2005 Apr;54(4):503-9. doi: 10.1136/gut.2003.034165.
- [2] Tong J, Zheng Q, Zhang C, Lo R, Shen J, Ran Z. Incidence, prevalence, and temporal trends of microscopic colitis: a systematic review and meta-analysis. *Am J Gastroenterol*. 2015;110(2):265. Epub 2015 Jan 27.
- [3] Julia Shor1, Gustavo Churrango, Nooshin Hosseini, Christopher Marshall1. Management of microscopic colitis: challenges and solutions. *Clin Exp Gastroenterol*. 2019; 12: 111–120. 2019 Feb 27. doi: 10.2147/CEG.S165047.
- [4] Lina Vigren 1, Curt Tysk, Magnus Ström, Anders F Kilander, Henrik Hjortswang, Johan Bohr, Cecilia Benoni, Lasse Larson, Klas Sjöberg. Celiac disease and other autoimmune diseases in patients with collagenous colitis. *Scand J Gastroenterol*. 2013 Aug;48(8):944-50. doi: 10.3109/00365521.2013.805809. Epub 2013 Jun 26.
- [5] Andreas Holstein , Joerg Burmeister, Armin Plaschke, Dirk Rosemeier, Adji Widjaja, Eick-Hartwig Egberts. Autoantibody profiles in microscopic colitis. *J Gastroenterol Hepatol*. 2006 Jun;21(6):1016-20. doi: 10.1111/j.1440-1746.2005.04027.x.
- [6] Kristin E Burke, Ashwin N Ananthakrishnan, Paul Lochhead, Ola Olen, Jonas F Ludvigsson, James M Richter, Andrew T Chan, Hamed Khalili. Smoking is Associated with an Increased Risk of Microscopic Colitis: Results From Two Large Prospective Cohort Studies of US Women. *J Crohns Colitis*. 2018 Apr 27;12(5):559-567. doi: 10.1093/ecco-jcc/jjy005.
- [7] Andreas Münch, Curt Tysk, Johan Bohr, Ahmed Madisch, Ole K Bonderup, Ralf Mohrbacher, Ralph Mueller, Roland Greinwald, Magnus Ström, Stephan Miehke. Smoking Status Influences Clinical Outcome in Collagenous Colitis. *J Crohns Colitis*. 2016 Apr;10(4):449-54. doi: 10.1093/ecco-jcc/jjv235. Epub 2015 Dec 30.