

## Collagenous colitis and ileitis under treatment with duloxetine

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### To the Editor,

Collagenous colitis (CC) is a disease that causes chronic diarrhea, that could be diagnosed with a normal colonoscopic examination. Diagnosis is based on the histopathologic examination of the mucosa containing thickened subepithelial collagen layer (1). Etiology and pathophysiology of CC are not known exactly (2). In this article, the first case with CC and CI (Collagenous ileitis) associated with duloxetine [Serotonin norepinephrine reuptake inhibitor (SNRI)] treatment for major depression is presented.

A 66 year-old female patient presented with recurrent diarrhea without mucus and blood but accompanied by cramping abdominal pain. History was unremarkable. The patient has been started with 60 mg of duloxetine par day due to a depression for several weeks before the diarrhea. She had been smoking since the last 20 years and has not been using alcohol or drugs. On physical examination, there was tenderness on the left lower quadrant of the abdomen and bowel sounds with 8/sec. Remarkable laboratory findings were hemoglobin with 11,7 gr/dL, erythrocyte sedimentation rate (ESR) with 45 mm/h, C-reactive protein with 13 mg/L. Stool culture and examination were insignificant. Anti-endomysium, anti-gliadin and anti-tissue transglutaminase antibody tests were negative. There were no villus atrophy and accumulation of intraepithelial lymphocytes in the tissue samples taken from the second part of the duodenum by gastroscopy. Macroscopic examination of the colon mucosa was normal and biopsies were taken from the terminal ileum and from different parts of the colon. Non-specific mononuclear cell infiltration and collagen accumulation in band style were found in the pathological examination of these tissue samples (Fig. 1, 2). Subsequent to cessation of duloxetine, diarrhea decreased to 50% of the admission frequency and budesonid 9 mg/d was initiated. On the second day of treatment, diarrhea ceased and Budesonid was planned to be stopped by decreasing the dose over three months.

Chronic, intermittent, frequent, watery diarrhea without blood may be an unique finding of CC. It is more common in the 5th and 6th decades and in females (3:1-8:1). There are no systemic symptoms, laboratory or radiological findings. Colonoscopic findings are non-specific. Diagnosis is based on the histopathologic examination of the mucosa that contains thickened subepithelial collagen layer (> 15 mic.) and intra-

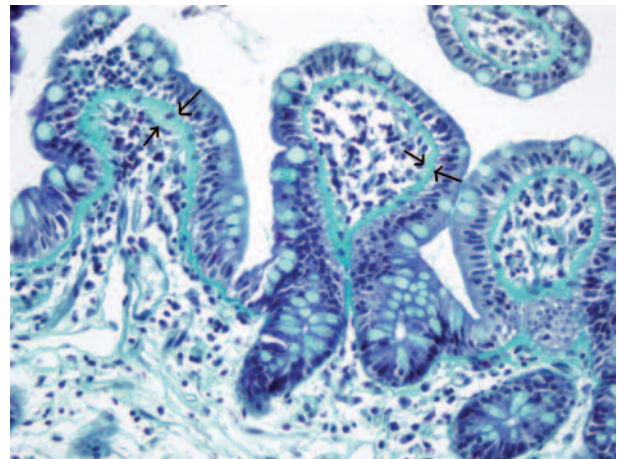


Fig. 1. — Increase of subepithelial collagen in ileum (between black narrows) with Mason-Trichrom staining (×400).

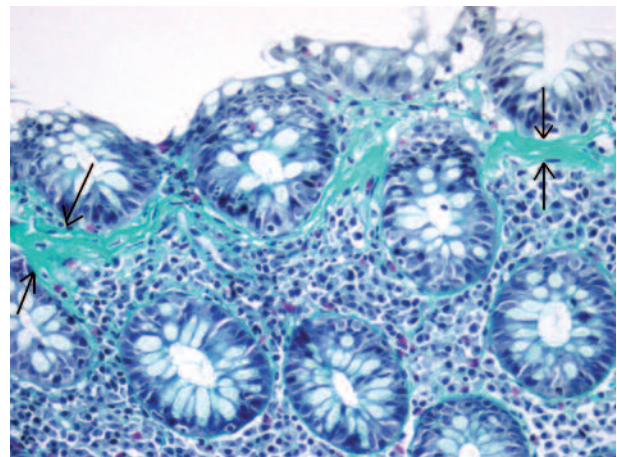


Fig. 2. — Increase of subepithelial collagen in colon (between black narrows) with Mason-Trichrom staining (×400).

epithelial inflammatory cell infiltration. Etiology of CC is not yet exactly known (3). In this article, the first CC and CI case associated with duloxetine treatment for depression is presented.

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Cases of lymphocytic colitis were previously reported to occur under duloxetine treatment and lymphocytic colitis had been linked with it (4). In the case, an accumulation of collagen in the colonic and the ileal mucosa has been demonstrated and the patient's symptoms appeared after the initiation of duloxetine and also diminished after the cessation of treatment. These findings support a relationship between the drug administration and symptoms but this relation could not be confirmed exactly, due to the fact that colonoscopy and biopsy from the colon were not performed after the recovery of diarrhea. It is well known that serotonin induces fibrogenesis, so duloxetine (SNRI), may induce fibrogenesis via increasing the level of serotonin in the gastro-intestinal tract that contains large amounts of serotonin (5).

Sapp and colleagues reported CC cases with sub-epithelial collagen deposition in the ileum and authors suggested that it may be related to similar pathological mechanisms as seen in CC or it may be an extra-colonic manifestation of CC (6).

The incriminated drug should be discontinued for treatment of colitis. Simple anti-diarrhetic drugs should be used as a first-line treatment to relieve the symptoms. If symptoms persist, budesonid (6-9 mg/day for eight

weeks) could be used for remission-induction of the disease and the drug should be continued at 6 mg a day for up to three months (4).

Cases with chronic watery diarrhea should be thoroughly questioned concerning the drug history. Duloxetine should be included into the list of CC and CI associated drugs.

## References

1. GOFF J.S., BARNETT J.L., PELKE T., APPELMAN H.D. Collagenous colitis : histopathology and clinical course. *Am. J. Gastroenterol.*, 1997, **92** : 57-60.
2. LEE E., SCHILLER L.R., VENDRELL D., SANTA ANA C.A., FORDTRAN J.S. Subepithelial collagen table thickness in colon specimens from patients with microscopic colitis and collagenous colitis. *Gastroenterology*, 1992, **103** : 1790-96.
3. CHANDE N., DRIMAN D.K., REYNOLDS R.P.E. Collagenous colitis and lymphocytic colitis : patient characteristics and clinical presentation. *Scand. J. Gastroenterol.*, 2005, **40** : 343-47.
4. KUSNIK B., STOLTE M. Lymphocytic colitis under treatment with duloxetine. *Z. Gastroenterol.*, 2010, **48** (6) : 693-5.
5. SEUWEN K., MAGNALDO I., POUYSSEGUR J. Serotonin stimulates DNA synthesis in fibroblasts acting through 5-HT<sub>1B</sub> receptors coupled to a G<sub>i</sub>-protein. *Nature*, 1988, **335** : 254-256.
6. SAPP H., ITHAMUKKALA S., BRIEN T.P., AYATA G., SHAZ B., DORFMAN D.M. *et al.* The terminal ileum is affected in patients with lymphocytic or collagenous colitis. *Am. J. Surg. Pathol.*, 2002, **26** : 1484-92.