A drug-induced microscopic colitis in an older woman: a case report

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We presented a case of a 87-year-old woman hospitalized for chronic watery diarrhea, affected by multimorbidities. After excluding other causes of diarrhea by biohumoral and microbiological tests, endoscopy was performed without revealing any macroscopic abnormalities, but, at histological examination of random biopsies, the characteristic features of collagenous colitis were found. Lansoprazolo and sertraline, chronically taken by the patient, was discontinued, and budesonide was started with prompt clinical improvement.

Collagenous colitis is a rare cause of chronic diarrhea in advanced age, but it should be suspected in patients with polypharmacotherapy, after an accurate differential diagnosis.

Key words: chronic diarrhea, polypharmacy, elderly

INTRODUCTION

Collagenous colitis, a subtype of microscopic colitis, is a relatively rare chronic disease of the colon. Its estimated incidence is 2.0 per 100,000 per year and affects predominantly women (about 52-86% of cases). Pathogenesis is not completely clear and it is likely multifactorial. It is characterized by normal macroscopic picture during endoscopy, so colic biopsy is essential to make a definite diagnosis.

We here report the case of an 87-year-old woman admitted to the hospital for persisting watery diarrhea. The pathological examination was apparent normal, but the colic biopsy revealed the diagnosis.

CASE REPORT

An 87-year-old woman was admitted to Geriatrics Unit with watery diarrhea (over ten episodes per day) lasting about a month without abdominal pain, vomiting or fever. She started to take some symptomatic drugs at home with poor benefit. The patient did not smoke; she did not recently travel to other countries or reported any changes of her eating habits, neither introduced new medications. The patient was chronically affected by major cognitive disorder, depression, hypertensive heart disease, moderate aortic stenosis, paroxysmic atrial fibrillation, HCV-related liver disease, chronic renal failure (stage III), erosive gastritis secondary to Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) chronic use. After her last hospitalization for acute gastritis, she started Proton Pump Inhibitors (PPIs) therapy with lansoprazole. She was also chronically...
taking sertraline for depression. The patient lived with her
daughter and was partially dependent in basic and instru-
mental activities of daily living.
On admission, at clinical examination she appeared alert,
partially oriented, in stable hemodynamic compensation.
The patient reported abdominal distension without any
signs of peritonitis. The skin and oral mucous were hy-
pohydrated. The vital signs were normal.
On blood tests, a modest increase in serum creatinine val-
ues (1.3 mg/dl) was observed; hemoglobin, inflammatory
markers (white blood cells and C-Reactive protein) and se-
rum electrolytes were normal. Abdominal X-Ray revealed
a diffuse and modest distension of intestinal loops, mainly
colon and tenuos, with diffuse air fluid levels (Fig. 1a).
Intravenous rehydration therapy was timely started.
During the hospitalization, the patient continued to pre-
sent multiple episodes of diarrhea daily, so further diag-
nostic investigations were conducted. The chemical and
physical examinations of the stool were normal, as well
as the serum levels of lipase, liver enzymes, total proteins
and thyroid hormones. Microbiological tests (Yersinia,
Salmonella, Shigella, Campylobacter, Clostridium dif-
icile, parasitological, Widal-Wright reaction) were nega-
tive. Celiac disease screening was also negative. Blood
levels of faecal calprotectin were markedly elevated.
Abdominal Computer Tomography (CT) confirmed
the presence of colic distension with minimal parietal
hyperemia (Fig. 1b). In the hypothesis of chronic colic in-
flammation, empiric therapy with mesalazine associated
with lactic ferment and rifaximin was started, with only
modest clinical improvement. A colonoscopy was per-
formed, without revealing any macroscopic abnormalities
(Fig. 1c); nevertheless, random biopsies were performed
in the ascending colon, sigma and rectum. Histological
examination revealed the presence of focal de-epitheli-
ialized colic mucosa with hyperplastic crypts, moderate
lymphoplasmacellular infiltrate of the lamina propria with
eosinophilic component in the ascending colon and in
the sigma extended to the muscolaris mucosa, and a
moderate increase in the subepithelial collagen band. This
finding was compatible with collagenic colitis.
Therefore, oral steroid therapy with budesonide was
undertaken, replacing mesalazine, at a dosage of 9 mg
per day for 6 weeks, followed by progressive recovery
of the patient in 10 days. Moreover, the therapy with
PPIs and Selective Serotonin Reuptake Inhibitors (SS-
RIs) was gradually discontinued.
The patient was discharged at home after three weeks
months.

**DISCUSSION**

We reported a clinical case of an older woman with
collagenous colitis, presenting with chronic watery diarrhea. The diagnosis was extremely challenging, because of the advanced age of the patient, not typical for collagenous colitis’ onset, and the lack of other major risk factors besides PPIs and SSRIs use. Indeed, she did not report either any autoimmune diseases nor smoking habit.

Collagenous colitis is a subtype of microscopic colitis. It is a relatively rare chronic colic disease with an estimated incidence of 2.0 per 100,000 per year. Unlike our case, it is typically diagnosed in middle-aged patients with a preponderance of female sex (about 52-86% of cases). The pathogenesis is still unclear, but it is likely multifactorial and involves mucosal immune response to luminal factors in genetically predisposed individuals. Indeed, diarrhea is likely caused by mucosal inflammation and its severity correlates with colic inflammation rather than with collagen band thickening.

Several autoimmune diseases have been associated with microscopic colitis, such as autoimmune thyroiditis, type 1 diabetes mellitus, and oligoarticular arthritis and an abnormal collagen metabolism seems to be responsible for the collagen deposition. Some medications have been also implicated as being causative flares, particularly PPIs, specifically lansoprazole, SSRIs and statins (the first two both taken by our patient). Even smoke seems to play a role in collagenous colitis’ pathogenesis, but it was not present in the present case.

Our patient reported the classical clinical presentation of the microscopic colitis. Indeed, it is characterized by chronic, non-bloody, watery diarrhea with usually an insidious onset. Patients have from four to nine watery stools per day, fecal urgency (40%), abdominal pain (50%) and an abnormal stool consistency (70% of cases). The symptom resolution was observed only following the administration of budesonide. Unlike most examined clinical cases, that described the onset of microscopic colitis in adulthood or in younger elderly, our patient presented an atypical age of disease’s onset (late onset). Moreover, our case has the peculiarity that the disease was caused by the contemporary taken of two high-risk medications (e.g. lansoprazole and sertraline), without any other known risk factors, such as the presence of smoking habit or autoimmune diseases. In addition, based on the identified case reports’ examination, the symptoms of microscopic colitis arose after a few weeks after the beginning of the new therapy, in particular with antidepressants (i.e. duloxetine and sertraline), or PPIs (i.e. lansoprazole), or NSAIDs. Similarly, in our clinical case, the characteristic watery diarrhea started a few weeks after the introduction of lansoprazole, while the symptom resolution was observed only following the contemporary discontinuation of both PPIs and sertraline, chronically taken by the patient, in addition to the administration of budesonide.

In conclusions, we reported a case of an older woman with microscopic colitis, which might be underdiagnosed. Finally, according to the literature, our case supports the close association between microscopic colitis and specific medications (e.g. lansoprazole and sertraline) and, unlike the other case reports already described, the disease’s onset in the oldest-old age is peculiar of our patient. However, the problem of polypharmacy (that often including the PPIs and SSRIs use) is extremely widespread in older population, exposing this class of patients to a consequent higher risk of microscopic colitis, which might be underdiagnosed.

In conclusions, we reported a case of an older woman with collagenous colitis, who presented only medications intake (PPIs and SSRIs) as disease known risk factors. Microscopic colitis should be suspected in a patient with chronic watery diarrhea, particularly in middle-aged women, but also in older women presenting multiple high-risk factors (i.e. smoking habit, medications, autoimmune diseases), after an accurate differential diagnosis. Indeed, a careful evaluation of pharmacological...
Table I. Comparison of identified case reports of collagenous colitis.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Clinical presentation</th>
<th>Age, gender</th>
<th>Main comorbidities</th>
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<tr>
<td>Konijeti et al., 2013</td>
<td>Watery brown diarrhea, dehydration</td>
<td>80 y, male</td>
<td>Henoch-Schonlein Purpura requiring partial jejunal resection, coronary artery disease, CKD, gout, GERD, prior cholecystectomy</td>
</tr>
<tr>
<td>Salter et al., 2017</td>
<td>Watery diarrhea, weight loss, abdominal pain and bloating, nausea</td>
<td>50 y, female</td>
<td>Smoking habit, major depression</td>
</tr>
<tr>
<td>Menon et al., 2015</td>
<td>Watery diarrhea, weight loss</td>
<td>63 y, male</td>
<td>Major depression</td>
</tr>
<tr>
<td>Rammer et al., 2005</td>
<td>Watery diarrhea</td>
<td>57 y, male</td>
<td>Erosive gastritis HP+</td>
</tr>
<tr>
<td>Pelizza et al., 2007</td>
<td>Watery diarrhea, weight loss, abdominal pain, fecal incontinence, fever</td>
<td>37 y, male</td>
<td>Paranoid schizophrenia</td>
</tr>
<tr>
<td>Hawe et al., 2008</td>
<td>Watery diarrhea, dehydration</td>
<td>62 y, female</td>
<td>Bipolar disorder</td>
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<tr>
<td>Chande et al., 2007</td>
<td>Watery diarrhea, weight loss</td>
<td>78 y, female</td>
<td>GERD</td>
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<tr>
<td></td>
<td>Watery diarrhea</td>
<td>65 y, female</td>
<td>NSAIDs-related gastritis</td>
</tr>
<tr>
<td>Bahin et al., 2013</td>
<td>Watery diarrhea, weight loss</td>
<td>75 y, female</td>
<td>GERD, IBD, arterial hypertension, hypercholesterolemia</td>
</tr>
<tr>
<td>Arora et al., 1999</td>
<td>Abdominal pain, dyspepsia, rectorrhagia</td>
<td>79 y, male</td>
<td>Duodenal ulcer, ischemic stroke, aortic stenosis, arterial hypertension, glaucoma, prostate cancer</td>
</tr>
<tr>
<td>Castellano et al., 1999</td>
<td>Watery diarrhea weight loss, anorexia</td>
<td>57 y, female</td>
<td>Non-specific articular pains</td>
</tr>
</tbody>
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Note. CKD: Chronic Kidney Disease; GERD: Gastroesophageal Reflux Disease; CT: Computed Tomography; HP+: Helicobacter pylori positive; IBD: Inflammatory Bowel Disease; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

history can increase the clinical suspicion of the disease, especially in elderly patient who is frequently subjected to polypharmacotherapy, of which should always be considered the potential adverse effects. A close collaboration among geriatrician, endoscopist and pathologist is required to obtain a correct diagnosis and consequent timely treatment of this disease.

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The Authors declare no conflict of interest.

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Authors’ contributions
M, FR, MB, CDG, AZ, SV: conceptualization; IM, FR, MB, CDG: writing-original draft preparation; AZ, SV: writing-review and editing.

Ethical consideration
Written consent was obtained from the participant. The data used in this study were anonymized before its use.
<table>
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<td>Collagenous colitis (thickened subepithelial collagen layer); lymphocytic colitis</td>
<td>Lansoprazole</td>
<td>Balsalazide + prednisone</td>
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<td>Lymphocytic colitis</td>
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<td>Budesonide + duloxetine discontinuation</td>
<td>Resolution in 8 months</td>
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<td>Abdominal CT scan, colonoscopy</td>
<td>Collagenous colitis (increased intraepithelial lymphocytes and thickening of the subepithelial collagen)</td>
<td>Lansoprazole</td>
<td>Lansoprazole discontinuation</td>
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<td>Colonoscopy</td>
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<td>Lymphocytic colitis, mixed inflammatory infiltrate in the lamina propria, focal surface epithelial damage</td>
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<td>Clozapine discontinuation</td>
<td>Resolution in 8 days</td>
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<tr>
<td>Colonoscopy</td>
<td>Collagenous colitis (increased number of plasma cells in the mucosa, a thickened subepithelial collagen band and degenerate surface epithelium)</td>
<td>Lansoprazole</td>
<td>Lansoprazole discontinuation</td>
<td>Resolution in 2 weeks</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>Collagenous colitis</td>
<td>Lansoprazole</td>
<td>Lansoprazole discontinuation</td>
<td>Resolution in 4 weeks</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>Mixed pattern of collagenous colitis and lymphocytic colitis (subepithelial collagen plate prominent, epithelium degeneration, intraepithelial lymphocytes and other inflammatory cells, in the mucosa and in lamina propria, especially plasma cells)</td>
<td>Duloxetine</td>
<td>Duloxetine discontinuation</td>
<td>Resolution in 2 weeks</td>
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<td>No</td>
<td>Colectomy to stop bleeding</td>
<td>Death</td>
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<tr>
<td>Gastroscopy, colonoscopy</td>
<td>Collagenous colitis and gastrobulbitis (thickened subepithelial collagen band in the mucosa of the upper digestive tract)</td>
<td>NSAIDs</td>
<td>Prednisone</td>
<td>Resolution</td>
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References