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STUDIUM PRZYPADKU
CASE STUDY

Atypical form of microscopic colitis in 56-year-old patient presenting with long-lasting watery diarrhea

Nietypowa postać mikroskopowego zapalenia jelita grubego u 56-letniego pacjenta z przewlekłą, wodnistą biegunką

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ABSTRACT

Microscopic colitis (MC) is a common cause of unexplainable, chronic diarrhea. The disease is characterized by the presence of clinical symptoms, a normal colonoscopy and typical histopathological changes upon microscopic examination. The aim of the study was to present a case of an atypical histological form of MC.
A 56 year-old man presented with chronic, watery diarrhea. Gastrointestinal infection had been excluded. The colon appeared almost normal on the colonoscopy. Inconsistent histological findings were observed. The pathology of randomly taken colon biopsies showed collagenous colitis (CC; thickness of collagen bands > 10 μm, < 20 IELs). Six months later during a follow-up colonoscopy, colonic specimens revealed typical findings of lymphocytic colitis (LC), namely, no thickened subepithelial collagen bands were identified. The authors analyzed the risk factors, diagnosis, treatment response, clinical course and the atypical histological outcomes.

KEY WORDS

microscopic colitis, budesonide, lymphocytic colitis, collagenous colitis

STRESZCZENIE

Mikroskopowe zapalenie jelita grubego to częsta przyczyna przewlekłej biegunki niewiadomego pochodzenia. Choroba charakteryzuje się obecnością objawów klinicznych, makroskopowo prawidłowym wyglądem błony śluzowej jelita grubego w kolonoskopii i obecnością typowych zmian w badaniu histopatologicznym. Celem pracy jest przedstawienie nietypowego obrazu histologicznego mikroskopowego zapalenia jelita grubego.
Autorzy prezentują przypadek 56-letniego mężczyzny z uporczywą, wodnistą biegunką, z pochopnie rozpoznaną niewydolnością zewnątrzwydzielniczą trzustki. Po wykluczeniu infekcyjnego tła biegunki wykonano kolonoskopię, ukazując makroskopowo niemal prawidłowy obraz jelita grubego. Otrzymano niespójne wyniki badań histopatologicznych. W badaniu mikroskopowym wycinków z okrężnicy potwierdzono rozpoznanie kolagenowego mikroskopowego zapalenia jelita grubego (w preparacie grubość kolagenu podnabłonkowego wynosiła > 10 μm, liczba limfocytów śródnabłonkowych < 20 w przeliczeniu na 100 komórek nabłonka). Tymczasem podczas kontrolnej kolonoskopii w wycinkach z jelita grubego ujawniono cechy zapalenia limfocytowego, w badanych próbkach nie wykazano obecności złogów podna-

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błonkowego kolagenu. Autorzy analizują czynniki ryzyka zachorowania, odpowiedź na zastosowane leczenie, przebieg kliniczny choroby oraz rozbieżne wyniki badań histopatologicznych.

SŁOWA KLUCZOWE

mikroskopowe zapalenie jelita grubego, budezonid, limfocytowe zapalenie jelita grubego, kolagenowe zapalenie jelita grubego

INTRODUCTION

Microscopic colitis (MC) includes two major subtypes known as collagenous colitis (CC) and lymphocytic colitis (LC), which are clinically indistinguishable [1,2]. Histologically, LC is defined as a diffuse increase in the number of intraepithelial lymphocytes (IELs > 20/100 surface epithelial cells). Collagenous colitis is characterized by thick subepithelial collagen bands (thickness > 10 μm). Both entities share a few common histological features, for example, inflammatory hypercellularity in the lamina propria. It is uncertain whether CC and LC remain two separate entities or if they are just different stages of the same disorder. Some researchers suggest that the transformation of one histologic pattern to another is possible [2,3]. Interestingly, there is an increasing number of case reports describing patients with the clinical presentation of chronic watery diarrhea without fulfilling the typical histological criteria for MC. It seems likely that there are more than two histological subtypes of this entity.

CASE REPORT

A 56-year-old man presented to the General Internal Department SPZZOZ in Staszów with severe watery diarrhea lasting two weeks, with no significant relief of symptoms after one week of Rifaximin and Loperamide therapy. He also had a past medical history of surgically treated duodenal ulcera, alcohol-related acute pancreatitis, epilepsy, alcohol abuse, nicotine addiction, psoriasis and was currently using antidepressant medication (Sertraline – selective serotonin reuptake inhibitor antidepressant). The patient had suffered periodically from mild, self-limited watery diarrhea for the past year. Upon admission to the Department of Internal Medicine, the patient reported watery stools eight to twelve times a day, without blood or mucus and the symptoms were relieved by fasting. No weight loss or abdominal pain was reported. Physical examination revealed dehydration without any other abnormalities. Infectious causes of diarrhea were excluded.

Preliminary laboratory investigations showed decreased hemoglobin and folic acid levels and a slightly increased activated partial thromboplastin time (aPTT). C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), thyroid-stimulating hormone (TSH), amylase, calcium, parathyroid hormone level and total protein as well as albumin ratio were within the normal limits and there were no disturbances in the electrolyte panel or normal liver function tests. The content of elastase-1 in the stool was measured. The test excluded exocrine pancreatic insufficiency. The total and allergen-specific immunoglobulin-E blood tests showed no abnormalities.

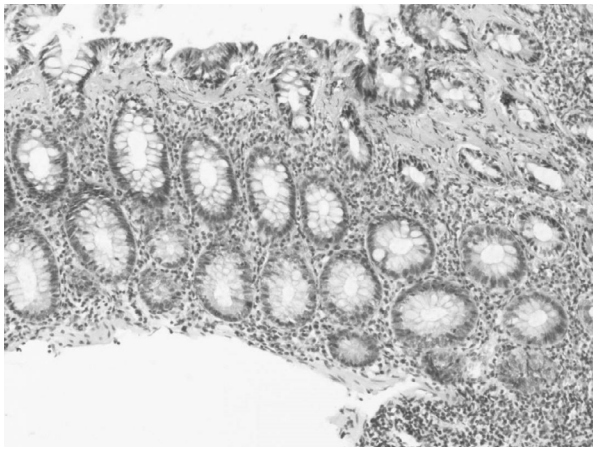

Fig. 1. Colon biopsy taken during first colonoscopy. Histological features of collagenous colitis: increased subepithelial collagenous layer, inflammation of lamina propria. Hematoxylin and eosin staining. Photos courtesy of Head of Department of Pathology NZOZ sp. z o.o. in Kielce, Antoinette Urbaniak PhD.

Ryc. 1. Bioptat okrężnicy pobrany podczas pierwszej kolonoskopii. Widoczne cechy histologiczne kolagenowej postaci mikroskopowego zapalenia jelita grubego: pogrubiona warstwa podnabłonkowego kolagenu, zmiany zapalne w obrębie blaszki właściwej. Barwienie hematoksyliną i eozyną. Zdjęcie udostępnione dzięki uprzejmości Kierownik Zakładu Patomorfologii NZOZ sp. z o.o. w Kielcach, dr n. med. Antoinette-Urbaniak.

The pathology reports showed normal small bowel biopsies. The serologic tests for celiac disease were negative. The colonoscopy revealed macroscopically normal mucosa with a decrease in the vascular-pattern in some areas. When withdrawing the endoscope, mucosal friability was observed. Four samples from the right side and four samples from the left side of the colon were taken, all of which showed CC features (Fig. 1). Treatment with 9 mg of Budesonide daily and osteoporosis prevention was initiated. The patient responded rapidly, symptomatic improvement was seen after a few days. He achieved clinical remission (less than 3 stools daily without any watery stools). After withholding Budeso-

nide, a relapse was reported. We continued the Budesonide therapy, promptly achieving clinical remission.

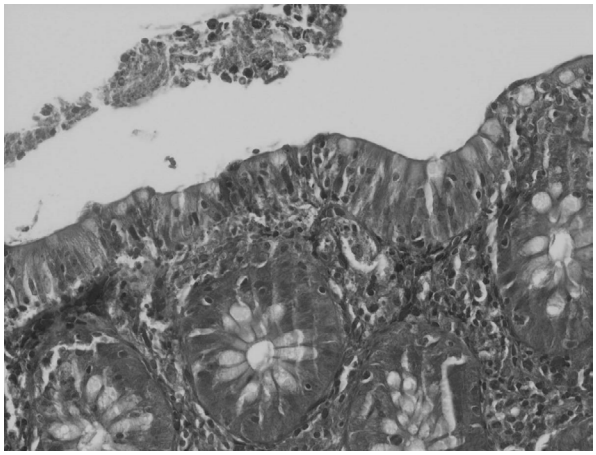

Fig. 2. Biopsy from colon taken during second examination. Characteristic features of lymphocytic colitis: inflammation of lamina propria, lymphocyte infiltration and epithelial pathology. Fontana-Masson staining. Photos courtesy of Head of Department of Pathology of Tumors, Świętokrzyskie Oncology Center in Kielce, Janusz Kopczyński PhD.

Ryc. 2. Bioptat okrężnicy pobrany podczas drugiej kolonoskopii. Widoczne cechy histologiczne limfocytowej postaci mikroskopowego zapalenia jelita grubego: zmiany zapalne w obrębie blaszki właściwej, naciek limfocytowy i cechy uszkodzenia nabłonka. Barwienie Fontana-Masson. Zdjęcie udostępnione dzięki uprzejmości Kierownika Zakładu Patomorfologii Nowotworów Świętokrzyskiego Centrum Onkologii w Kielcach, dr. n. med. Janusza Kopczyńskiego.

Following this treatment, the patient returned six months later for a colonoscopy in order to assess the histological response, although it is not necessary to repeat colonoscopy to evaluate histological remission in the absence of residual symptoms. This time the biopsy revealed histological features of LC (two samples from each: ascending, transverse, descending, sigmoid colon and rectum had been taken). In all the samples, no subepithelial thickened collagenous layers were found (Fig. 2). The patient remained symptom-free on low-dose Budesonide (3 mg daily) continuous therapy.

DISCUSSION

This is a case report of an atypical histologic form of MC. Microscopic colitis was once considered to be a rare condition. The apparent incidence and prevalence of MC is much higher than initially thought. Increases in the reported incidence are observed [4]. Is this a genuine rise in incidence rates or rather the consequence of better detection of the disease? This is still an unanswered question. The authors try to study typical, clinical presentations, the risk factors, appropriate diagnostic algorithms and treatment options. The main focus is to review the analysis of confusing histological outcomes. Long-lasting, watery diarrhea without mucus and blood are typical symptoms of MC. The vast majority of patients feel relief after fasting. Some of them complain of abdominal pain, encopresis and weight loss. This patient had established risk factors independently associated with MC such as concomitant autoimmune disease, cigarette smoking and a history of antidepressant medication (Sertraline).

According to research, there is no significant correlation between alcohol consumption and the prevalence of MC [5,6]. Microscopic colitis is more likely to be seen in patients who already have other autoimmune diseases such as diabetes mellitus type 1, Hashimoto's thyroiditis or celiac disease. A family history of MC is considered to be a risk factor, as well. It is thought that this condition is due to an inflammatory mucosal response in predisposed individuals to unknown luminal factors such as drugs or infectious agents [7]. Three groups of drugs: nonsteroidal anti-inflammatory drugs (NSAIDs), proton-pump inhibitors (PPIs) and selective serotonin reuptake inhibitors (SSRIs) are thought to have the strongest association with MC. Interestingly, most of the drugs associated with MC can also cause diarrhea as a side-effect.

In this case, drug-induced MC was considered to be a consequence of exposure to Sertraline. Unfortunately, the patient was unable to inform us whether the symptoms appeared before or shortly after starting Sertraline therapy. Sertraline administration was stopped and a tricyclic antidepressant (Tianeptine) had been given instead. It has not been verified, if medications can trigger the recurrence of symptoms. Retrospectively, it was difficult to evaluate if improvement in the symptoms was due to the cessation of serotonin-norepinephrine reuptake inhibitors (SNRIs) therapy. In this case, the role of Sertraline remained uncertain. In patients with a history of chronic non-bloody diarrhea, a full colonoscopy with random colon biopsies has to be performed, even if no endoscopic abnormalities have been observed. Too few samples and missing some parts of the colon are both potential reasons why many patients are overlooked and misdiagnosed.

According to one study, biopsies from the rectosigmoid colon alone will miss even up to 40% of MC cases [5]. Further investigations of effective drugs are still needed. Currently, there are no other evidence-based alternative drugs to Budesonide [3,8]. According to the American Gastroenterological Association Institute Guidelines, Budesonide can be used as intermittent (induction of clinical remission) or continuous therapy. There are high relapse rates following the discontinuation of Budesonide (up to 60–80%) [8], although some

studies reported cases where the clinical course was just a single attack [9]. It has been observed that spontaneous remission is possible, though it is more common in patients with LC than with CC. Interestingly, the course of LC is definitively milder and maintenance therapy is not always required. It should be offered only to patients who had relapses after the cessation of Budesonide therapy (as in this case) [9]. There are some studies reporting good clinical response to methotrexate, thiopurines and anti-TNF therapy in patients with active MC. Unfortunately, the data is insufficient to consider them to be definite therapies [4,5].

The histological findings of MC were inconsistent with repeat endoscopy. The transformation from one type of MC to another one is perhaps due to treatment decisions or just as a natural process of time, should also be considered. Because LC occurs in patients with a lower mean age compared to CC patients, researchers support the statement that LC is an early stage of CC. However, in this case, the opposite transformation of CC to LC had been observed. Is the disappearance of collagen bands possible? Some researchers assume that histologic resolution of CC is probable and it is associated with the disappearance of symptoms [4]. Nonetheless, other research showed that no change in the mean thickness of the collagen band had been reported, even after treatment with Budesonide [1,5,6]. On the other hand, it seems likely that the change of one subtype of MC to another one is quite possible [4].

Researchers from the Karolinska Institutet Marie-Rose Mellander [10] reported such observations during an MC cohort: "Histological change of phenotype over time was not uncommon and was observed in 12% of the patients (10 CC to LC, 13 LC to CC)". Perhaps, the existence of a "mixed form" of MC (coexisting LC and CC in different parts of the colon) should also be taken into consideration [5,7,10]. Interestingly, thickened collagen bands in patients with CC are more commonly seen in the right colon and less frequently in the sigmoid and rectum. Some data suggests that morphologic findings may be patchy [5,6]. Perhaps a sampling error can be suspected (biopsy of the regions with collagen deposit during the first colonoscopy and with lymphocyte infiltration during the second one). This seems unlikely, however, because random biopsies were taken from different parts of the colon during both examinations [5,6,10,11].

In conclusion, a better understanding of the pathophysiology of MC is required. Raising awareness of this entity amongst physicians is needed. The key role of a proper diagnostic approach is crucial to establishing an early diagnosis in order to reduce the number of missed cases of patients with diarrhea who can be treated successfully. Medications are known as environmental risk factors for MC (particularly NSAID, PPI and SSRI) [12,13,14]. In the case of long-lasting diarrhea, it is suggested that two or more biopsies should be obtained from the ascending, transverse, descending, and sigmoid colon during a colonoscopy to increase the diagnostic yield. Pathologists have to be aware that the histological findings in patients with MC are often confusing. Regardless of the histological type of MC, medical management remains the same. Further investigation of effective therapy is essential.

Conflict of interest

The authors declare no conflict of interest.

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Author's contribution

Study design – J. Kiełtucki, J. Zając

Manuscript preparation – J. Kiełtucki, J. Zając

Final approval of the version to be published – J. Kiełtucki

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