Diagnosis and Management of Pancolitis in Patient with Ulcerative Colitis

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ABSTRACT

Ulcerative colitis (UC) is a form of inflammatory bowel disease (IBD) that usually affects the rectum and part of the colon, which spreads continuously with no skip area. Pancolitis occurs in 20% of patients with UC. Patients with chronic UC, especially pancolitis, have a higher risk of colon cancer. In patients with pancolitis, the risk of cancer increases by 0.5-1% per year after having 8-10 years of disease.

A 72-year-old man came with complaint of bloody-mucus diarrhea associated with abdominal cramps. The colonoscopic appearance of colitis was observed in whole lumen throughout colon. Histopathological analysis demonstrated dense infiltrates of granulocytes and macrophages formed by severe inflammation. Normal appearances were observed in the remaining epithelial cells. No parasites, specific process, or malignancy were found. Moreover, no acid-resistant bacteria were found. However, atypical cells were found in one of the biopsy specimens.

The patient was diagnosed with extensive type of severe UC. The initial management of treatment included improvement of his general condition along with antibacterial therapy of metronidazole and ciprofloxacin. Specific treatment of sulphasalazine and prednisone were given after pancolitis appearance was revealed, which has similar clinical manifestations in accordance with UC.

Keywords: *pancolitis, ulcerative colitis, chronic diarrhea, inflammatory bowel disease*

INTRODUCTION

Inflammatory bowel disease (IBD) is an idiopathic chronic inflammatory disease involving gastrointestinal tract, with clinical symptoms of chronic diarrhea accompanied with fever, abdominal pain, and weight loss. It consists of ulcerative colitis (UC) and Crohn's disease (CD). Both diseases are common among Caucasians (particularly Jewish), Africans, Americans and Hispanics. However, it is very rare in the Mongoloid race. IBD has peaks of onset at age 15-30 years and 60-80 years.[1] Pathogenesis of IBD may include a combination of environmental factors (such as smoking, diet) and genetic along with the normal intestinal flora or certain unidentified microorganisms triggering intestinal response both of the immune cells (T cells, B cells, eosinophils, neutrophils, monocytes) and non-immune cells (endothelial, epithelial, mesenchymal, neural cells, and matrix).[1,2]

Activated cellular immune response consequently stimulates effectors T cells, macrophages, neutrophils and other leukocytes. In addition, the humoral immune response also stimulates B cells to produce antibodies. Mediator secretion increases activation, amplification and the production of antibodies and autoantibodies, cytokines, growth factors, eicosanoid, neuropeptides, reactive oxygen metabolites (ROMs), nitric oxide (NO), and proteolytic enzymes. Thus, inflammation and tissue damage occur in IBD.[3] In CD, transmural inflammation occurs, whereas in UC it is limited to the mucosa. Genetic factors play a more dominant role in CD when compared to IBD colitis ulseratif.[2] In IBD, there is a mutation in genes IL10RA and IL10RB encoding IL10R1 and IL10R2 subunit proteins, which form a heterotetramer to make up the interleukin-10 receptor and consequently causes

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immune response of intestinal hyperinflammation.[4] Acute exacerbation of IBD can occur because of infection, consumption of non-steroidal anti-inflammatory drugs (NSAIDs), and stress.[1]

Clinical manifestations that can be found in UC include bloody-mucus diarrhea, fever, abdominal pain, tenesmus and weight loss.[5,6] All of these manifestations depend on the severity of the disease spectrum. When it is severe, dehydration, anemia, hypokalemia, and hypoalbuminemia may occur.[1,7] Through sigmoidoscopy/colonoscopy, we can find mucosal redness, granular, exudative and easily bleed mucosa as well as ulcers and pseudopolyp in patients with UC. On biopsy, epithelial damage, inflammation, crypt abscess, as well as loss of goblet cells will be revealed.[1] The management of UC includes providing supportive treatment such as antidiarrhea, sulphasalazine, glucocorticoids, or immunosuppressive agents, which is administered to patients depending on the severity and extent of illness.[7] Further monitoring and continuous follow up is necessary to prevent and perform early detection on colorectal malignancy.[8,9]

UC usually involves the rectum and part of the colon and spreads continuously (no skip areas). Pancolitis only occurs in 20% of patients with UC.[1] Stonnington, et al demonstrated that of all UC cases, pancolitis only occurs in one-third of all cases (4.6/100,000 cases/year), while proctitis and other abnormalities in the distal colon are more common, namely 7.1 and 2/100,000 cases/year in contrast to severe and moderate UC cases which occurs only in 3.8/100,000 cases/year.[10] In addition to IBD, pancolitis also caused by *Escherichia coli* O157 : H7 that produces verotoxin, *Campylobacter jejuni*, penicillin derivatives, cephalosporins and quinolones, *Salmonella*, *Yersinia*, *Shigella*, *Entamoeba*, and *Cytomegalovirus*.[11,12,13]

CASE ILLUSTRATION

A 72-year-old man came with complaint of bloody-mucus diarrhea associated with abdominal cramps since 2 months before admission. The stools were yellow, mucus and mixed with a little amount of fresh red blood. The patient had tenesmus. He also had a history of intermittent diarrhea, slight fever, nausea, loss of appetite, and 10 kg weight loss (more than 10%) in the last 2 months period. In the past week, diarrhea episodes increased (about 10 times per day).

Since 2 days before admission, he had less urine output and concentrated yellow-dark colored urine. He also felt dry mouth and throat as well as extreme thirst. There was no history of foreign travel or ingestion of unusual foods. No one had similar disease in his family. The patient had a lack of fruit and vegetables in the diet. There was no history of drugs consumption (analgesics, herbal appetite stimulants, drug addiction). There was no history of pulmonary tuberculosis. The patient was a heavy smoker.

Physical examination revealed a patient with moderate dehydration (compos mentis, dry mucous membrane of mouth and tongue, dry skin, decreased skin turgor). The patient was anemic but hemodynamically stable with pulse rate of 80 beats per minute, febrile (38°C) and tenderness on all four abdominal quadrants (particularly the right lower quadrant). No signs of acute abdomen or appendicitis were observed. Pitting edema was found on the dorsal surface of both feet. On digital rectal examination, no anal fistula, fissures or abscess was found. There was pain in anal canal and yellow liquid stool with a little amount of fresh red blood was found.

The laboratory test showed anemia (hemoglobin 8.9 g/dL), leukocytosis (15,400/μL), and erythrocyte sedimentation rate (ESR) 50 mm/hour, eosinophil 0, basophil 0, segmented neutrophil 2 x 10^9/L, banded neutrophil 83 x 10^9/L, lymphocyte 13 x 10^9/L, monocyte 2 x 10^9/L. Peripheral blood smear demonstrated normocytic-normochromic anemia. The serum iron (SI) level was 37 μg/dL and total iron binding capacity (TIBC) was 188 μg/dL. Hyponatremia 131 mmol/L, hypokalemia 2.4 mmol/L and hypoalbuminemia 1.9 g/dL were also found. His random blood glucose level was 91 mg/dL and his quantitative C-reactive protein (CRP) was 15.8 mg/L. On microscopic stool analysis, mucus and blood were present in the stool, leukocytes 3-4/high power field (HPF), erythrocytes 4-6/HPF. Parasitological stool examination demonstrated negative result of parasites (no amoeba was found neither in trophozoites or cysts form; eggs, larva or adult worms were not found).

On chest X-ray, no appearance of pulmonary tuberculosis was found. The 3-view-abdominal radiograph revealed no appearance of ileus or perforation. Abdominal ultrasonography showed no abnormality. Colonoscopy revealed the appearance of pancolitis (erosive, edematous and hyperemic mucosa with multiple patchy exudative ulcer from rectum to caecum, there was partial loss of haustra in the descending colon, no mass was found). Subsequently, 10 biopsies were taken from various regions, i.e. from rectum to caecum. Histopathological analysis demonstrated dense infiltrates of granulocytes and macrophages formed by severe inflammation. Normal appearances were observed in the remaining epithelial cells. No parasites, specific process, or malignancy were found. Moreover, no acid-resistant bacteria were found. However, atypical cells were found in one of the biopsy specimens.

Based on these findings, the diagnosis of extensive type of severe UC was made. The management of treatment included improvement of patient's general

condition along with initial antibacterial therapy of metronidazole and ciprofloxacin. Specific treatment of sulphasalazine and prednisone were given after

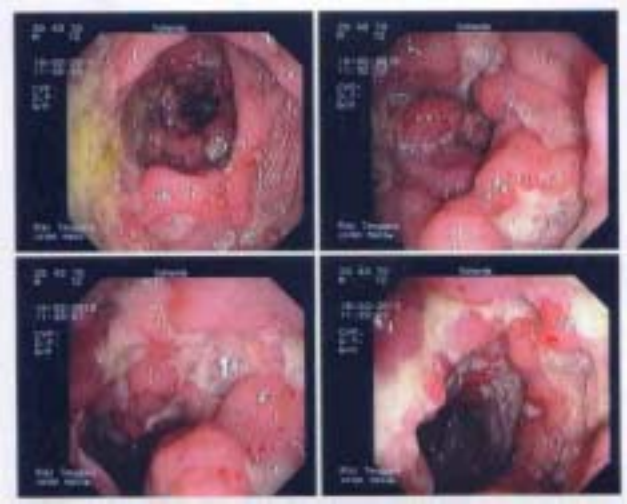

Figure 1. Colonoscopy showed UC with pancolitis

pancolitis appearance was revealed, which has similar clinical manifestations in accordance with UC.

DISCUSSION

Diarrhea is a loose, watery and frequent stool. It is considered chronic when it had last for more than four weeks. Generally, chronic diarrhea may arise by non-infectious causes.[6]

In patients with chronic diarrhea, there are various possible mechanisms of pathophysiology such as a variety of pathophysiological mechanisms, including secretoric, osmotic, steatorrheal, inflammatory, dysmotile, and factitial mechanism.

Initial approach for patients with chronic diarrhea includes history taking, physical examination and laboratory work-up. When taking history, the onset, duration, triggering and relieving factors as well as stool characteristics should be asked. Further questions should also be asked including the presence of fecal incontinence, fever, weight loss, pain, history of specific exposure (travel, medical treatment, contact with diarrhea patients) and extra-intestinal manifestation (skin changes, arthralgia, oral aphthous ulcer). A question about family history of IBD or sprue should also need to be asked.

On physical examination, we should examine the presence of a thyroid gland, wheezing, murmurs, edema, hepatomegaly, abdominal mass, lymphadenopathy, mucocutaneous abnormalities, perianal fistula or abnormalities of anal sphincter.[6]

Peripheral blood test should be performed to detect leukocytosis, increased erythrocyte sedimentation rate or CRP level indicating active inflammation.[6,8] Anemia suggests nutrient deficiencies or the presence of bleeding; while eosinophilia suggests parasites, neoplasia, connective tissue disease, allergies, or eosinophilia gastroenteritis. Blood chemistry test may reveal electrolyte status, liver function, or other metabolic disorders.[6]

We present a case of a 72-year-old man who had bloody-mucus diarrhea for two months. Other clinical findings include fever, abdominal pain, tenesmus, and weight loss. He also had dehydration, anemia of chronic inflammation, hyponatremia, hypokalemia, and hypoalbuminemia. Chronic diarrhea (over 4-weeks period) accompanied with mucus and bleeding in such patient may be caused by inflammatory mechanisms (which may be due to infection, malignancy, and IBD).

We performed stool microscopic analysis to exclude the possible infection. Based on such test, no amoeba cyst and worm were found. By history taking, physical examination and performing laboratory test upon admission, we considered a working diagnosis of IBD with differential diagnosis of colon cancer and intestinal tuberculosis. In order to confirm the cause of diarrhea, we subsequently proceed to colonoscopy and biopsies.

Treatment provided at that time includes improvement of general condition (fluid resuscitation, correction of hyponatremia, hypokalemia, hypoalbuminemia, and blood transfusion), symptomatic therapy (antipyretic, antidiarrheal, antacids), and antibacterial therapy (metronidazole and ciprofloxacin). After the patient in stable condition, colonoscopy and biopsies were performed. Based on physical and laboratory findings, i.e. bloody-mucus diarrhea, absence of abdominal mass, anal fistula, fissure and abscess, negative signs of gastrointestinal tract obstruction, and positive findings of continuous granulomatous appearance (no skip areas, no rectal sparing) in colonoscopy, we established a confirmed diagnosis of severe UC with extensive type (pancolitis).

The disease was categorized as severe since there was frequent defecation of more than six times a day, fever, anemia with less than 75% of normal value, erythrocyte sedimentation rate more than 30 mm/hour, and the presence of ulceration and spontaneous bleeding in the colon. It was classified as extensive type because it involves part of colon which is more proximal than the splenic flexure (or even classified as pancolitis since the abnormalities were found in all colon, from rectum to caecum).[5,8] Metronidazole and ciprofloxacin were discontinued and sulfasalazine and prednisone were administered orally in accordance with the management of active phase on the extensive type of severe UC.[7]

UC usually involves the rectum and part of the colon and spreads continuously (no skip areas). Pancolitis only occurs in 20% of patients with UC.[1] Based on

a study conducted by Stonnington, et al, pancolitis UC only occurs in one-third of all cases (4.6/100,000 cases/year), while proctitis and other abnormalities in the distal colon are more common, namely 7.1 and 2/100,000 cases/year in contrast to severe and moderate UC cases which occurs only in 3.8/100,000 cases/year.[10]

Histopathological analysis of biopsy specimens of the patient showed atypical cells in 1 of 10 biopsy specimens. However, it has not been considered further whether these cells were included in the low-grade dysplasia or high-grade dysplasia, according to IBD dysplasia morphology-group (DMG).[5] In addition to both types of dysplasia, there is indefinite type of dysplasia. Indefinite dysplasia may offer findings of cells atypical cytoplasm and nuclei (loss of polarity, larger and hyperchromatic nuclei), but the cause of development of dysplasia is unknown.

Cell damage both caused by inflammation (reparative process) and neoplasia may result in atypical cells. Colonoscopy and more frequent multiple biopsies should be performed, in which cell damage due to inflammatory processes (reparative process) will gradually disappear over the course of therapy. Moreover, biopsy results should be assessed by the pathology anatomy gastroenterologist.[9] When there is evidence that those cells are high-grade dysplasia or colorectal malignancy, surgical treatment such as colectomy would be necessary. Surgical treatment may also be considered for low-grade dysplasia, regarding 54% of low-grade dysplasia would become colorectal cancer within five years.[5]

The risk of malignancy of the colon in chronic UC increases with the duration and extent of disease.[1] Chronic UC (> 10 years), particularly the pancolitis type, has a higher risk of such cancer.[14] In patients with pancolitis, the risk of cancer increases by 0.5-1% per year after having 8-10 years of disease.[1]

Based on colonoscopy and histopathological results, the patient should have annual colonoscopy or two times in a year with multiple biopsies as a screening for dysplasia and colorectal carcinoma by Colitis-Associated Colorectal Cancer (CAC).[1,5]

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