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PSEUDOMEMBRANOUS COLITIS

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ABSTRACT
Pseudomembranous colitis is inflammation of the colon that is most often a manifestation of clostridium difficile infection. That predominantly affects the lower gastrointestinal tract. Its main risk factors are antibiotic use, advanced age, and hospitalization. pseudomembranous colitis, clostridium difficile, antibiotics, pseudomembranous, fulminant colitis. If laboratory testing and endoscopic finding for clostridium difficile infection are negative, then other less common etiologies should be sought to identify the correct diagnosis. Ischemic colitis, inflammatory bowel disease, medications, chemicals, vasculitis, and multiple infectious pathogens are responsible for non-clostridium difficile pseudomembranous colitis. Exposure history, chronic medical problems, and a current medication list will aid in narrowing the differential diagnosis. Histology varies significantly with underlying etiology and can establish the diagnosis. Treatment is specific to the underlying etiology. The purpose of this research article increase awareness of clinicians and other healthcare professionals about various etiologies of pseudomembranous colitis along with its histological finding and treatment. Our case was admitted from ER a Ten-year-old male patient with chief complaints of cramping left lower abdominal pain, abdominal distension, and loose stools with the passage of blood and pus per rectum, associated with high-grade fever for 10 days.

KEYWORDS: Myoinositol, metformin, polycystic ovarian disease.

INTRODUCTION
Pseudomembranous colitis is a serious inflammation of the large bowel characterized by elevated yellow-white plaques that coalesce to form pseudomembranes on the mucosal surface. It is commonly attributed to the bacterium clostridium difficile. Long-term use of broad-spectrum antibiotics and a state of immunosuppression are amongst the common risk factors that predispose patients to this condition. The disease commonly affects the middle-aged and the elderly. This condition is fairly common in India with a reported incidence of about 15%-20% among patients taking antibiotics. Before the antibiotic, pseudomembranous colitis was a relatively rare disease and was associated with various risk factors, including surgery especially of the gastrointestinal tract, shock, uremia, sepsis, ischemic cardiovascular disease, heavy metal poisoning, and colon cancer. However, in the past four decades, virtually all cases have been associated with clostridium difficile, an anaerobic, gram-positive, spore-forming bacillus. More than 95% of C. difficile infections occur during or after antibiotic therapy, and almost every antibiotic has been implicated. In contrast, in antibiotic-associated diarrhea and antibiotic-associated colitis, only 10–30% and 60–75% cases, respectively, are associated with C. difficile. The increasing use of broad-spectrum antibiotics is reflected in the increasing incidence of C. difficile infections. The clinical manifestations of C. difficile infection range from asymptomatic carriage to C. difficile-associated diarrhea, to C. difficile-associated colitis, to the most severe form of pseudomembranous colitis. Patients with pseudomembranous colitis usually present with a mild cramping abdominal pain, fever, and diarrhea and few acute cases progress to fulminant colitis (2%-8%) leading to toxic megacolon, perforation, and bleeding pseudomembranous colitis is an acute mucosal necrosis and cellulose exudative inflammation that occurs mainly in the colon but may involve the small intestine. The disease often occurs after the use of antibiotics and may be referred to as antibiotic-associated colitis. Pseudomembranous colitis occurs mainly in adults and reports of children suffering from this disease are rare.

Definition and Etiology
Pseudomembranous colitis refers to swelling or inflammation of the large intestine colon due to an overgrowth of clostridioides difficile bacteria. This infection is a common cause of diarrhea after antibiotic use.

Pseudomembranous colitis results most commonly from C. difficile infections the many bacteria in your colon in

a naturally healthy balance, but antibiotics and other medications can upset this balance. Pseudomembranous colitis occurs when certain bacteria usually C. difficile rapidly outgrow other bacteria that normally keep them in check. Certain toxins produced by C. difficile, which are usually present in only tiny amounts, rise to levels high enough to damage the colon. While almost any antibiotic can cause pseudomembranous colitis, some antibiotics are more commonly linked to including fluoroquinolones, ciprofloxacin cephalosporin, penicillin; other medications besides antibiotics can sometimes cause pseudomembranous colitis. Chemotherapy drugs that are used to treat cancer may disrupt the normal balance of bacteria in the colon certain diseases that affect the colon, such as ulcerative colitis or Crohn's disease may also predispose people to pseudomembranous colitis. C. difficile spores are resistant to many common disinfectants and can be transmitted from the hands of health care professionals to patients. Increasingly, C. difficile has been reported in people with no known risk factors, including people with no recent health care contact or use of antibiotics. This is called community-acquired C. difficile. However, less common etiologies include ischemic colitis, collagenous colitis, inflammatory bowel disease, cytomegalovirus-induced colitis, vasculitis, bacterial and parasitic organisms, Behcet's disease, chemotherapeutic medications, and toxins, such as heavy metal poisoning. Often considered as solely a nosocomial pathogen, C. difficile most commonly causes diarrheal illness in the elderly with histories of antimicrobial utilization or healthcare facility stays. Other C. difficile risk factors include the history of prior C. difficile infection, advanced age, use of gastric acid-suppressing medications, gastrointestinal surgery, feeding tubes, immunodeficiency, chemotherapy, chronic kidney disease, and inflammatory bowel disease. The absence of risk factors does not exclude the presence of C difficile infection.

Signs and symptoms of pseudomembranous colitis

Many episodes of watery diarrhea, abdominal cramps, pain or tenderness, fever, pus or mucus in your stool, nausea, dehydration. Symptoms of pseudomembranous colitis can begin as soon as one to two days after you start taking an antibiotic, or as long as several months or longer after you finish taking the antibiotic. Factors that may increase your risk of pseudomembranous colitis taking antibiotics. Staying in the hospital or a nursing home.

Increasing age, especially over 65 years. Having a weakened immune system. Having a colon disease, such as inflammatory bowel disease or colorectal cancer. Undergoing intestinal surgery. Receiving chemotherapy treatment for cancer.

Epidemiology

C. difficile infections have increased over the last 20 years with almost 500,000 episodes and 29,000 associated deaths reported annually in the United States, which makes it among the most common nosocomial infections. C. difficile colitis in patients without antibiotics and healthcare exposure has led to the recognition of community-associated C difficile infection. The most common cause of infectious diarrhea in healthcare settings, C. difficile causes substantial morbidity and can potentially result in mortality in vulnerable inpatient populations. C. difficile colonization occurs in 13% of hospitalized patients with stays of 2 weeks and up to 50% of patients with stays for more than 4 weeks. C. difficile can colonize the human colon; 2% to 5% of the healthy outpatient community will be colonized and will not manifest signs of infection.

Pathophysiology

The administration of antibiotics, chemotherapeutic drugs, or immunosuppressive therapy disrupts the normal colonic biome, which allows for C. difficile colonization. C. difficile induces colitis via exotoxin production, toxin A, and toxin B. These toxins generate inflammation, colonic cell cytoskeleton disruption, and cellular death. The pseudomembranes of pseudomembranous colitis form as these toxins pathologically hyperstimulate the native immune system by drawing neutrophils to invade the colonic mucosa.

Histopathology

An invasive test not usually performed for the initial diagnosis of C. difficile or antibiotic-induced colitis, colonoscopy aids in confirming the diagnosis of pseudomembranous colitis in the presence of suggestive symptoms, negative testing, and failure to respond to conventional treatment. Colonoscopies of patients with pseudomembranous colitis demonstrate inflamed colonic mucosa characterized by raised yellowish, occasionally hemorrhagic nodules or plaques that congregate into widespread, pseudomembranes on the surface of the colonic mucosa. Up to 2 cm in diameter, these pseudomembranes present in scattered diffusely pattern among areas of normal or healthy mucosa. The most severely affected areas have confluent pseudomembranes covering the entirety of their colonic mucosa.

History and Physical

Patients with pseudomembranous colitis most commonly report symptomatic diarrhea. C. difficile presents in various ways. Patients may be asymptomatic carriers or present with fulminant pseudomembranous colitis with toxic megacolon. Generally, the presence of pseudomembranes indicates a more severe case of C. difficile infection or antibiotic-associated diarrhea. Other notable symptoms and signs include fever, abdominal cramping, and leukocytosis. Severe pseudomembranous colitis can manifest profound leukocytosis with white blood cell counts up to 100,000/mm3, hypovolemia, hypotension, protein-losing enteropathy, reactive arthritis, and toxic megacolon. About 3% to 8% of pseudomembranous colitis will develop fulminant infection including severe ileus, toxic megacolon,

hypovolemia, hypotension, renal dysfunction, colonic perforation with attendant peritonitis, and septic shock.

Evaluation

Stool testing for C. difficile when patients have positive guaiac diarrhea in combination with radiographic evidence of toxic megacolon or the presence of C. difficile risk factors such as hospitalization, antibiotic or chemotherapy exposure, and marked leukemoid reactions. Screening for C. difficile as the causative agent for pseudomembranous colitis begins with screening for the C. difficile toxins. A common lab algorithm utilizes an enzyme immunoassay (EIA) to screen for glutamate dehydrogenase antigen, present in most C. difficile isolates followed by EIA sampling for C. difficile toxin A and toxin B. Nucleic acid amplification tests, polymerase chain reaction, loop-mediated isothermal amplification for C. difficile have excellent sensitivity and specificity with high positive likelihood ratios; utilization of these assays aids in clarifying discrepancies between glutamate dehydrogenase and EIA toxin results. Nucleic acid amplification test results should be interpreted with caution because they do not distinguish C. difficile colonization from active infection unless testing for concurrent toxin production. Consider initiating testing for C. difficile colitis on inpatients having multiple, liquid consistency stools per day. Avoid sending stool samples to test for a cure because assays remain positive in 60% upon completing therapy.

Diagnosis

Tests and procedures used to diagnose pseudomembranous colitis and to search for a complications Stool sample. There are several different stool sample tests used to detect C. difficile infection of the colon Blood tests. These may reveal an abnormally high white blood cell count (leukocytosis), which may indicate pseudomembranous colitis. Colonoscopy or sigmoidoscopy. In both of these tests, your doctor uses a tube with a miniature camera at its tip to examine the inside of your colon for signs of pseudomembranous colitis raised yellow plaques (lesions), as well as swelling. Imaging tests. If you have severe symptoms, your doctor may obtain an abdominal X-ray or an abdominal CT scan to look for complications such as toxic megacolon or colon rupture.

Management

Stopping the antibiotic or other medication that's thought to be causing your signs and symptoms, if possible. Sometimes, this may be enough to resolve your condition or at least ease signs, such as diarrhea. Starting an antibiotic likely to be effective against C. difficile. If you still experience signs and symptoms, you may use a different antibiotic to treat C. difficile. This allows the normal bacteria to grow back, restoring the healthy balance of bacteria in your colon. You may be given antibiotics by mouth, through a vein or a tube inserted through the nose into the stomach nasogastric tube. Will most often use metronidazole, vancomycin, fidaxomicin, or a combination. Having fecal microbial transplantation (FMT). If your condition is extremely severe, you may be given a transplant of a stool fecal transplant from a healthy donor to restore the balance of bacteria in your colon. The donor stool may be delivered through a nasogastric tube, inserted into the colon, or placed in a capsule you swallow. May use a combination of antibiotic treatment followed by FMT Once you begin treatment for pseudomembranous colitis, signs, and symptoms may begin to improve within a few days. Researchers are exploring new treatments for pseudomembranous colitis, including alternative antibiotics, drugs to reduce recurrence, and a vaccine. Treating recurring pseudomembranous colitis. The natural occurrence of new, more aggressive strains of C. difficile, which are more resistant to antibiotics, has made treating pseudomembranous colitis increasingly difficult and recurrences more common. With each recurrence, your chance of having an additional recurrence increases. Treatment options may include.

The natural occurrence of new, more aggressive strains of C. difficile, which are more resistant to antibiotics, has made treating pseudomembranous colitis increasingly difficult and recurrences more common. With each recurrence, your chance of having an additional recurrence increases. Treatment options may include repeat antibiotics. You may need a second or third round of antibiotics to resolve your condition Surgery. Surgery may be an option in people who have progressive organ failure, rupture of the colon, and inflammation of the lining of the abdominal wall (peritonitis). Surgery has typically involved removing all or part of the colon (total or subtotal colectomy). A newer surgery that involves laparoscopic creating a loop of the colon and cleaning it (diverting loop ileostomy and colonic lavage) is less invasive and has had positive results fecal microbial transplantation (FMT). FMT is used to treat recurrent pseudomembranous colitis. You'll receive healthy, cleaned stool in a capsule, nasogastric, or inserted into your colon.

Differential Diagnosis

Pseudomembranous colitis from C. difficile needs to be distinguished from other etiologies of infectious and noninfectious dysentery which Diverticulitis Crohn disease. Irritable bowel disease, salmonella infection, Vibrio infections, viral and bacterial gastroenteritis.

Complications

Treatment of pseudomembranous colitis is usually successful. However, even with prompt diagnosis and treatment, pseudomembranous colitis can be life-threatening. Possible complications dehydration. Severe diarrhea can lead to a significant loss of fluids and electrolytes. This makes it difficult for your body to function normally and can cause blood pressure to drop to dangerously low levels of kidney failure. In some cases, dehydration can occur so quickly that kidney

function rapidly deteriorates kidney failure toxic megacolon. In this rare condition, your colon is unable to expel gas and stool, causing it to become greatly distended megacolon. Left untreated, your colon may rupture, causing bacteria from the colon to enter your abdominal cavity. An enlarged or ruptured colon requires emergency surgery and may be fatal.

A hole in your large intestine bowel perforation. This is rare and results from extensive damage to the lining of your large intestine or after toxic megacolon. A perforated bowel can spill bacteria from the intestine into your abdominal cavity, leading to a life-threatening infection peritonitis death. Even mild to moderate C. difficile infections can quickly progress to a fatal disease if not treated promptly. In addition, pseudomembranous colitis may sometimes return, days, or even weeks after apparently successful treatment.

Case presentation

F.B.EL, a ten-year-old male patient was presented to the emergency department with diarrhea for 48 hours, with 15 episodes /24 hrs of watery bloody stools and referral admitted to hospital to PICU, a decrease of the level of consciousness, vomiting many times, dehydration, watery diarrhea, severe headache, Fatigue fever since 10 days, severe abdominal cramping, nausea oxygen saturation 95%. On examination HR110 bpm, RR30bpm, Temp39.5C high fever, BP80/50mmhg. He presented clinically with general weakness hypoactive pallor face sever sunken eye, irritable. Patient's Diagnosis was pseudomembrane colitis. Physical assessment skin dry, pale, head and face symmetrical, eye symmetrical, white sclera.no drug allergy reported. Ears symmetrical auricles, nose with patent nostrils, good ability to smell, mouth throat and tongue were dry, pale, teeth regularly spaced, enlarged tonsils, neck full range of motion, carotid pulsation120beat/minute symmetrical, thorax and lung respiratory rate 30breath/minute, on inspection symmetrical chest, heart and blood vessels, apical pulse 100beat/minute regular, strong, peripheral pulse of both dorsal is pedis right and left were normal, posterior tibial RT, LF normal, radial RT, LF normal, abdomen soft and relaxed, motor response obeys commands, sensory response identify fine touch, speech clear diffuse abdominal pain the patient is impaired general condition, with pale skin and mucous membranes with reduced turgidity and elasticity, dry and flat tongue Cardiovascular system rhythmic, high-frequency heartbeat up to 110 bpm, weakened heart tones, no murmurs. Registered hypotension up to 80/50 mmHg at hospitalization. Abdominal status soft elastic abdominal wall allowing deep palpation, without clinical evidence of muscular defense, with palpatory tenderness in the left abdomen, accelerated peristalsis, no manifest hepatosplenomegaly. Rectal digital examination showed no evidence of palpable tumor formations in the rectum, only the presence of a large quantity of bloody-slime stools in the rectal ampulla. Laboratory tests and abdominal ultrasound showed no abnormalities. The patient was given parenteral Ringer infusion therapy inadequate volume and symptomatic spasmolytic therapy. With complaints of cramping left lower abdominal pain, abdominal distension, and loose stools with the passage of blood and pus per rectum, associated with high-grade fever for 10 days. He had no previous history of altered bowel habits. On examination, the abdominal examination revealed tenderness and guarding in the bilateral iliac fossae. On digital rectal examination, the rectum was filled with blood clots, the mucosa was friable, and a doubtful defect obscured by clots in the posterior wall of the rectum was felt, suggesting a perforation. Baseline blood investigations showed anemia with hemoglobin of 9g/dl and an elevated white blood cell count of24,000/mm3.PIT350/, PT, PTT within normal, electrolyte imbalance k2.1, ca7, Na128, urea86, creatine 0.85, RBS60mg/dl, and CRP90. He was stabilized with intravenous fluids, blood products, and was started on broad-spectrum antibiotics. Amikacin160/12hrs IV, fortum950/8hrs IV, calcium carbonate600/6hrs orally, KCL orally 5cc/6hrs.lactalose20cc6/hrs. Orally, G/S500cc8/hrs. IV, omperazol20mg/24hrs IV, metrandazole450/8hrsIV. Contrast-enhanced computed tomography (CECT) abdomen was done, which showed diffuse pan-colonic edema. After one week child discharged from hospital on prednisone tab 20mg/12hrs, Pentasa tab. Colonoscopy revealed a diffuse hyperemic contact and spontaneous sanguineous mucosa with a reduced partially obscured vascular pattern and glare, dotted with multiple flat erosions, single superficial, linear ulcerations covered with dense, hardly separable dirty white membranes (Figure 1)These changes were visualized in all sections of the colon, with the exception of ascending colon and caecum, and the most manifest were in the area of descending and transverse colon.

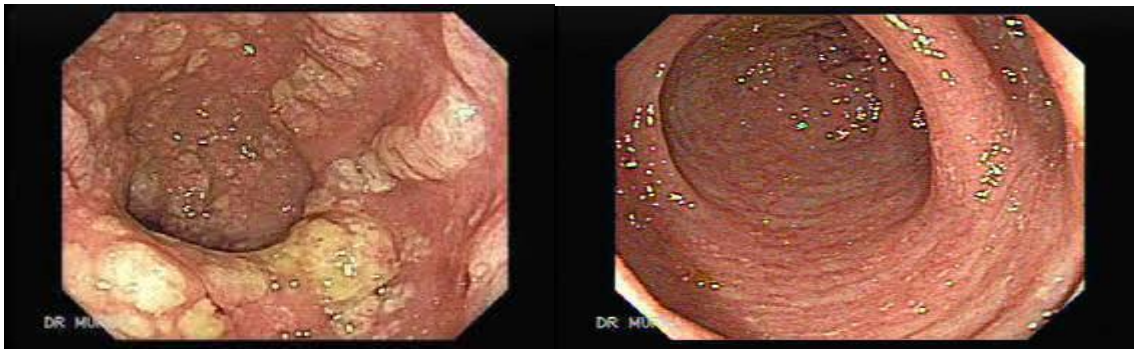
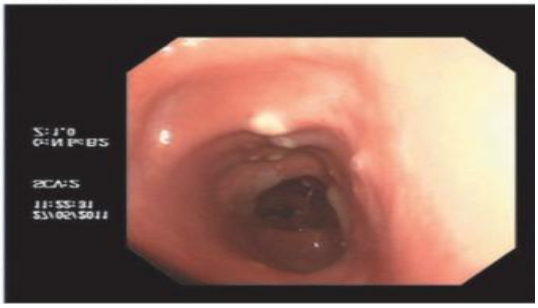


Fig 1a

Fig 1b



The first colonoscopy result after admission: micro-raised patches of varied sizes distributed in the sigmoid colon (a) and descending colon (b). The surface is covered with yellow and white moss-like pseudomembranous material, and difficult to remove. The mucosa between lesions is normal.

Fig 2a

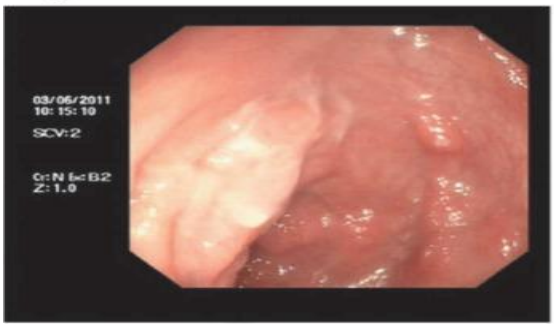
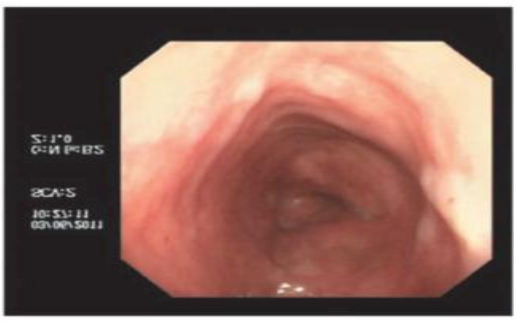


Fig 2b



The second colonoscopy result after treatment of one week: on the surfaces of sigmoid colon (a) and descending colon (b) can be observed micro-raised patches of varying sizes, not covered with yellow and white moss-like pseudomembranous material. The mucosa between lesions is normal.

Fig 3

The second colonoscopy result after treatment of two weeks: the mucosa of the sigmoid colon is normal with no micro-raised patches.

DISCUSSION

Pseudomembranous colitis occurs mainly in adults and caused almost exclusively by toxins produced by Clostridium difficile. Endotoxin detection to be the gold standard for the diagnosis. Discontinuation of antibiotics and supportive therapy usually lead to the resolution of

this disorder. The clinical spectrum of this disease may range from a mild, non-specific diarrhea to severe colitis with toxic megacolon, perforation, and death. Also, 80% to 90% of patients may have dull lower abdominal pain, distending pain and vague pain; a small number of patients do not have pain. The vast majority of patients approximately 80% have a fever and increased white blood cell count. A small number of patients have a severe fulminant onset with symptoms of high fever, severe diarrhea, acidosis, electrolyte imbalance, and shock. Paralytic ileus, intestinal obstruction, and acute renal failure may also be associated with the disease. There is a mortality rate of ≤ 1%– 2%.

The main manifestations of Pseudomembranous colitis Clostridium difficile are observed on colonoscopy with a few millimeters to a few centimeters of bowel mucosal lesions, attached to the surface of yellow-white pseudomembranous lesions. The mucosa between lesions is normal or maybe edematous. It appears to punctuate at the early stage and later fuses into irregular flakes or exfoliative lesions with bleeding occurring in severe cases as the lesions progress Colonoscopy is simple and fast and is the main method of making a diagnosis. Due to mainly involving the distal colon, the rectum and sigmoid were the main object of observation. Colonoscopy can be used as a simple method for follow-up and prognosis.

Irrational use of antibiotics is one of the main causes of pseudomembranous colitis C.difficile and once pseudomembranous colitis C.difficile is suspected, the original use of antibiotics should be immediately suspended. Patients with mild symptoms may recover after stopping antibiotics. In critically ill patients the use of specific drug treatment is often required.

Pseudomembranous colitis is most commonly caused by C.difficile infection. It is rarely, also caused by other bacteria like Escherichia coli and Klebsiella. Viral colitis by cytomegalovirus, ischemic colitis, collagenous colitis, inflammatory bowel disease, and various drugs are also implicated in the pathogenesis. Usually, patients presenting with this condition have a pre-existing history of chronic drug intake, altered bowel habits, or long-term immunosuppression. However, there has also been few reported cases of pseudomembranous colitis, with none of the above-mentioned factors and wherein, the cause was postulated to be an infection that complicated colonic obstruction or long-standing debilitating disease.

Patients with this disease commonly present with a mild to moderate disease. Their symptoms range from diarrhea, abdominal pain and fever to rarely abdominal distension and rectal bleeding. The latter symptoms are attributed to a more fulminant presentation of pseudomembranous colitis which, if untreated or unresponsive to medical management can lead to a complicated disease with toxic megacolon or colonic perforation. This is a less common presentation of this disease, with an incidence of around 2%-8%. These cases of the complicated disease require colectomy and have high mortality of 38%-80 %, which is more in the elderly age group, and hence early surgical intervention is recommended in these patients.

Pseudomembranous colitis caused by Cl. difficile infection is diagnosed by stool testing. The most commonly used tests are C. difficile cytotoxin neutralization assay and toxin A+B enzyme immune assays. Nucleic acid amplification tests with polymerase chain reaction on rectal swab specimens and glutamate dehydrogenase detection in stools are newer advances in the diagnosis of C.difficile infection. However, these tests are recommended in patients who present with uncomplicated disease. The patient in our scenario had no history predisposing him to C.difficile infection. While his CT imaging showed features of fulminant ulcerative colitis, a possibility of carcinoma rectum was also considered, as there were large firm blood clots on per rectal examination, indicating the probability of an ulcer-proliferative lesion in the rectum or colon. However, the patient was promptly taken up for surgery without causing a delay in the management of his condition.

Cases of pseudomembranous colitis complicating ulcerative colitis have been reported in the past. Reported a case of pseudomembranous colitis in a patient with long term ulcerative colitis, after receiving clindamycin for infectious colitis. A similar case of antibiotic-associated pseudomembranous colitis was also reported in a woman who had received antibiotics for a post-operative infection and was already on steroid treatment for ulcerative colitis. History of immunosuppression and use of antibiotics is common to both these cases, unlike in our patients. The diagnosis of ulcerative colitis in the patient in our report was a clinical and radiological one and it was later disproved after the histopathology report and a negative serum anti-Saccharomyces cerevisiae antibodies report.

The confirmatory diagnosis of pseudomembranous colitis is made by visualization of pseudomembranes on the colonic mucosa. The post colectomy specimen in this patient showed diffuse mucosal exudates and normal serosal surface with the absence of creeping fat. On histopathological examination, mucosal exudates with the clinical practice and indicate that pseudomembranous colitis not associated with antibiotic therapy may develop. Knowledge of the disease and the options for its therapy as well as its inclusion in the differential diagnosis in patients with acute diarrhea especially in immunocompromised patients over 65 years of age and a history of long term NSAIDs or chemotherapeutics is rarely important.

CONCLUSION

Pseudomembranous colitis and can mimic inflammatory bowel disease. The diagnosis is challenging in patients

who do not have previous lower gastrointestinal complaints, especially when they do not have factors predisposing them to pseudomembranous colitis. In cases of persistent bleeding, other sources of bleed should be considered even in the presence of a more obvious pathology to prevent loss of valuable time, and to optimize management cases such as this are rare in the clinical practice and indicate that pseudomembranous colitis not associated with antibiotic therapy may develop. Knowledge of the disease and the options for its therapy as well as its inclusion in the differential diagnosis in patients with acute diarrhea especially in immunocompromised patients over 65 years of age and a history of longterm NSAIDs or chemotherapeutics is rarely important.

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