Pseudomembranous Colitis: Spectrum of Imaging Findings with Clinical and Pathologic Correlation

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Pseudomembranous colitis (PMC) is a potentially life-threatening acute infectious colitis caused by one or more toxins produced by an unopposed proliferation of Clostridium difficile bacteria. PMC is characterized by the presence of elevated, yellow-white plaques forming pseudomembranes on the colonic mucosa. These plaques can be visualized at both pathologic analysis and endoscopy. Plain radiography, contrast enema studies, and computed tomography (CT) are useful in the evaluation of PMC. Plain radiography of the abdomen can demonstrate polypoid mucosal thickening, “thumbprinting” (wide transverse bands associated with haustral fold thickening), or gaseous distention of the colon. A toxic megacolon with distention and occasionally pneumoperitoneum may be seen in the most severe cases of PMC involving perforation. At contrast enema studies, the primary finding in mild cases of PMC is small nodular filling defects representing the mucosal plaques. With more extensive colonic involvement, the plaques are larger and coalesce to form an irregular bowel wall margin. Mural thickening and wide haustral folds caused by intramural edema may also be seen. A contrast enema study is contraindicated in patients with severe PMC due to the danger of perforation. Common CT findings include wall thickening, low-attenuation mural thickening corresponding to mucosal and submucosal edema, the “accordion sign,” the “target sign” (“double halo sign”), pericolic stranding, and ascites. Familiarity with these imaging characteristics may allow early diagnosis and treatment and prevent progression to more serious pathologic conditions.

Abbreviation: PMC = pseudomembranous colitis

Index terms: Colitis, pseudomembranous, 75.2043, 75.263 • Colon, CT, 75.12112


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INTRODUCTION

Pseudomembranous colitis (PMC) is an acute infectious colitis caused by toxins produced by an unopposed proliferation of *Clostridium difficile* bacteria in the colon (1). *C. difficile* infection is responsible for virtually all cases of PMC and for up to 20% of cases of antibiotic-associated diarrhea without colitis (1). Over the past few decades, PMC has emerged as a significant medical problem, largely due to the increased use of prophylactic and broad-spectrum antibiotics. The prevalence of PMC continues to rise steadily in the United States, with recent epidemic outbreaks reported at a number of institutions (2).

PMC can result in significant patient morbidity and mortality, especially if it is not diagnosed early. Overall mortality rates from 1.1% to 3.5% have been reported for patients with PMC (3,4). It is important for radiologists to be aware of this potentially life-threatening condition and its imaging characteristics because they may be the first to suggest the diagnosis.

In this article, we discuss and illustrate the imaging appearances of PMC at plain radiography, contrast enema studies, and computed tomography (CT) and correlate these findings with pathologic and endoscopic findings.

CAUSES OF PMC

*C. difficile* infection is nosocomial and can be epidemic or endemic in hospitals or nursing homes (5). PMC usually occurs as a complication of antibiotic therapy but is also associated with abdominal surgery, colonic obstruction, uremia, or prolonged hypotension or hypoperfusion of bowel. It also occurs with increased frequency in patients with severe debilitating disease such as lymphoma, leukemia (6,7), and advanced human immunodeficiency virus infection (8). PMC is a toxin-mediated disease that requires production of two toxins by the *C. difficile* organisms for clinical expression. Toxin A is an enterotoxin, whereas toxin B is a cytotoxin (5). Although many laboratories assay for only one of these toxins, both are present, and testing for both increases sensitivity (9).

CLINICAL MANIFESTATION AND DIAGNOSIS

The clinical manifestations of *C. difficile* infection include (in increasing order of severity) absence of symptoms, antibiotic-associated colitis without pseudomembrane formation, PMC, and fulminant colitis.

The majority of hospital inpatients infected with *C. difficile* are asymptomatic (1) or are only mildly to moderately ill (10). The clinical features of PMC include diarrhea, abdominal tenderness, fever, dehydration, and leukocytosis. Occasionally, patients with *C. difficile* colitis...
present with or progress to fulminant, life-threatening colitis. Such patients are acutely ill, with signs and symptoms of lethargy, fever, tachycardia, and abdominal pain (1,11), and may progress to toxic megacolon and colonic perforation resulting from full-thickness colonic necrosis (3).

Because its manifestations may vary, PMC is not always recognized by the attending physician. For example, approximately 5% of patients with PMC may present with signs and symptoms suggestive of acute abdomen or abdominal sepsis (3,12), leading to unwarranted laparotomy (3,13).

The diagnosis of PMC depends on the demonstration of C difficile toxins in the stool or of characteristic adherent yellow plaques 2-10 mm in diameter at proctosigmoidoscopy or colonoscopy (1).

**TREATMENT**

The treatment of PMC consists of oral administration of metronidazole or vancomycin, and most patients respond well within 3–4 days (10). In a study by Morris et al (3), medical therapy failed in 22% of patients prior to initiation of treatment with metronidazole or vancomycin, resulting in the need for surgical intervention. Today, PMC is essentially a “medical” disease with less than 1% of patients requiring surgery (10). However, in patients with a fulminant and toxic form of PMC who fail to respond to medical therapy, surgical intervention (usually partial colectomy with a temporary diverting ileostomy) can be lifesaving (1,14).

**PATHOLOGIC FINDINGS**

PMC caused by C difficile infection is restricted to the colon except in patients with ileostomies or defunctionalized loops of small bowel (5,15). At gross examination, PMC is characterized by multiple elevated, yellow-white plaques on the colonic mucosa forming pseudomembranes (5) (Fig 1). At histologic analysis, these pseudomembranes are typically seen to arise from a point of superficial ulceration and are accompanied by an acute or chronic inflammatory infiltrate in the lamina propria. They are composed of fibrin, mucin, sloughed mucosal epithelial cells, and acute inflammatory cells and can vary from a few millimeters to 20 mm in diameter. With advanced disease, pseudomembranes may coalesce and eventually slough to leave large areas of denudation (5).

In patients with severe acute PMC requiring surgical resection, massive transmural edema has also been observed extending through the submucosa into the muscularis propria of the colon (Fig 2). Although mural edema can be present in acute colitis, it is typically confined to the mucosa and submucosa (16). Therefore, a marked degree of transmural edema involving the colon is probably indicative of severe C difficile colitis.

**ENDOSCOPIC FINDINGS**

Endoscopy can help establish the diagnosis of PMC by demonstrating the characteristic adherent yellow plaques (Fig 3). The rectum and sigmoid colon are typically involved, but in approximately 10% of cases colitis is confined to the more proximal colon and may be missed at sigmoidoscopy (17). In fulminant colitis, sigmoidoscopy or colonoscopy should not be performed due to the risk of perforation. However, proctoscopy with minimal insufflation of air may be a useful diagnostic tool (1).
With the increased use of radiologic examinations today, it is important that the radiologist be aware of the spectrum of imaging findings in PMC and help determine and direct the correct course of patient management. Imaging is typically not the method of choice in the diagnosis of PMC. However, radiologic studies including plain radiography, barium enema studies, and CT may suggest the diagnosis.

**Plain Radiography**

Plain radiographic findings in PMC vary depending on the severity and extent of disease. Boland et al (18) reported radiographic abnormalities in 32% of 152 hospitalized patients with a positive stool toxin assay, including colonic ileus (32%), small bowel ileus (20%), ascites (7%), and nodular haustral thickening (18%). “Thumbprinting” (unusual, wide transverse bands associated with thickening of the haustral folds) and gaseous distention of the colon have also been identified (19–22) (Figs 4, 5). Segmental dilatation of the colon may or may not occur in the same area as the thumbprinting (20). In severe cases, abdominal radiographs can demonstrate polypoid mucosal thickening, presumably representing the plaquelike pseudomembranous plaques protruding into the air-containing lumen (Fig 4). Toxic megacolon with distention (20) and even colonic perforation (22) with pneumoperitoneum may be seen in the most severe cases.
Although plain radiography may suggest the diagnosis of PMC, it is not sensitive. Furthermore, even when radiographs are positive for PMC, the extent and severity of disease may be underestimated (23) (Fig 6).

- **Contrast Enema Studies**

  Since the advent of cross-sectional imaging, contrast enema studies have played a limited role in the diagnosis of PMC (24).

  Findings at contrast enema studies also vary depending on the severity and extent of disease. In mild cases, the primary finding is small nodular filling defects representing the mucosal plaques (Fig 7). With more extensive colonic involvement, the plaques are larger and coalesce to form an irregular bowel wall margin (6,7,25). The serrated outline of the barium column represents barium interposed between the plaquelike membranes rather than true ulceration with surrounding edema (26). Mural thickening and wide hastral folds due to intramural edema may also be seen (19,21) (Fig 8). An enema study is contraindicated in patients with severe PMC due to the danger of perforation (6,25). It may be performed only in patients in whom clinical and radiographic findings are equivocal or misleading (25).

- **CT Scanning**

  CT has been used increasingly in recent years for the evaluation of acute abdominal disease and has proved useful in the diagnosis of PMC (27-31), especially when the disease is not suspected clinically. In a study of 26 patients with PMC, Fishman et al (31) found abnormal CT findings in 23 patients. Common CT findings include wall thickening, low-attenuation mural thickening corresponding to mucosal and submucosal edema, the “accordion sign,” the “target sign” (“double halo sign”), pericolonic stranding, and ascites. Although the accordion sign is highly suggestive of PMC, other findings such as wall thickening, pericolonic stranding, and ascites are not very specific and can be seen in a variety of inflammatory or infectious diseases of the colon (32). In addition, approximately 5% of patients with PMC present with signs and symptoms suggestive of acute abdomen or abdominal sepsis (3,12). In these cases, CT can help suggest the diagnosis and thus avoid unwarranted laparotomy.
Wall Thickening.—The most common CT finding in patients with PMC is colonic wall thickening, which usually ranges from 3 mm to 32 mm in diameter (mean, 14.7 mm) (31). Mural thickening may be circumferential (Fig 9), eccentric (Figs 10, 11), smooth, irregular, or polypoid. At CT, wall thickening is often more irregular and shaggy than the typically symmetric and homogeneous thickening seen in Crohn disease (31).

Figures 9–11. CT scan obtained in a 28-year-old woman with acquired immunodeficiency syndrome who developed PMC following antibiotic therapy for pneumonia shows circumferential thickening of the edematous wall of the ascending and sigmoid colon. Note the enhancement of the luminal surface (arrowheads), a finding that indicates mucosal hyperemia. Extensive ascites is also seen. (10) CT scan obtained in a 46-year-old woman with myeloproliferative disorder who developed PMC following antibiotic therapy for pneumonia demonstrates eccentric thickening of the colon with relative sparing of the anterior wall of the transverse colon. (11a) CT scan obtained in a 39-year-old man with a history of pancreatitis with pseudocyst who developed PMC shows eccentric thickening of the transverse colon (arrow) with relative sparing of the anterior wall. (11b) CT scan shows more severe involvement of the ascending colon than of the transverse or descending colon. Note the moderate pericolonic stranding around the ascending colon.
Inflammation of the mucosa and colon wall may enhance markedly following intravenous bolus administration of contrast material (Fig 12). The target sign, which consists of two or three concentric rings of different attenuation, was originally described in ulcerative colitis and Crohn disease and has also been reported in PMC (33) (Fig 13). The target sign indicates mucosal hyperemia and submucosal edema or inflammation (34). The rings of varying attenuation are better appreciated during the arterial phase of enhancement.

Figures 12, 13. (12) Unenhanced (a) and contrast-enhanced (b) CT scans obtained in the same patient as in Figures 1 and 6 demonstrate a thickened colon wall that enhances markedly after administration of contrast material. Note the presence of ascites and diffuse subcutaneous edema. (13) CT scans obtained in a 23-year-old man with cystic fibrosis who developed PMC following antibiotic therapy for pneumonia demonstrate marked thickening of the colon wall with intense enhancement of the mucosa and thickened, low-attenuation submucosa (target sign).
Accordion Sign.—The accordion sign is seen when orally administered contrast material becomes trapped between markedly thickened haustral folds, giving the appearance of alternating bands of high attenuation (contrast material) and low attenuation (edematous haustra) (31, 35) (Figs 14, 15a). The accordion sign is highly suggestive of PMC, although it is usually seen only in advanced cases. Its appearance may vary depending on the degree of edema of the haustral folds and the amount of contrast material trapped between the folds (35). With significant fold enlargement, barium that is deeply entrapped between markedly thickened folds may simulate intramural tracts (23).

Extent of Disease.—CT may reveal pancolitis or segmental colitis. In the study by Fishman et al (31), abnormal bowel wall thickening most commonly involved the entire colon (12 of 26 patients) (Fig 15b) but also manifested as disease limited to the sigmoid colon (3 of 26) (Figs 16, 17) or either the right or the transverse colon (7 of 26) (Fig 18). More localized involvement of PMC may also be encountered (Fig 19). By helping determine the extent and location of colonic involvement, CT can aid the endoscopist. For example, if the disease is not present in the rectosigmoid colon, proctoscopy and sigmoidoscopy may fail to allow diagnosis.

Pericolonic Stranding.—Pericolonic stranding may be identified (Fig 20) but is usually mild, reflecting the primary mucosal and submucosal nature of PMC (24). The relative paucity of pericolonic inflammation in PMC in combination with marked colonic wall thickening helps differentiate this disorder from other colitides (29).
Figures 16, 17. (16) CT scan obtained in a 67-year-old man who developed PMC 1 week after undergoing surgery for spine infection shows thickening of the colon wall and haustral folds limited to the rectosigmoid colon. (17) CT scan obtained in a 78-year-old woman who developed PMC following antibiotic therapy shows nodular wall thickening limited to the rectosigmoid colon (arrows).

Figures 18, 19. (18) CT scan obtained in a 37-year-old man with acquired immunodeficiency syndrome who developed PMC following antibiotic therapy demonstrates thickening of the ascending and proximal transverse colon with an irregular luminal surface. The distal transverse colon and the descending colon have been spared. (19) CT scan obtained in a 63-year-old man who presented with signs and symptoms of colon obstruction and had a history of sigmoid colon diverticulitis that had been treated with antibiotics shows a well-defined focal thickening of the sigmoid colon simulating colon cancer (arrows). Sigmoidectomy was performed, and pathologic findings were consistent with PMC. After sigmoid colon resection, PMC progressed to involve the entire colon, and the patient underwent partial colectomy.

Ascites. — Ascites is occasionally a direct complication of PMC and tends to occur in severe cases (Fig 9). However, it may also be due to coexisting conditions such as portal hypertension, congestive heart failure, and sepsis (36) (Fig 13). Because ascites is uncommon in other inflammatory bowel disease, it may be a helpful clinical finding. However, ascites has also been reported in patients with Crohn disease, infectious colitis, and vasculitis and is therefore not specific for PMC (32).
Other CT Findings.—Colonic intramural gas or pneumatosis coli with or without air in the intrahepatic portal vein has been reported in severe cases (12,30). Small pleural effusions (Fig 20) and subcutaneous edema are also commonly seen in patients with severe PMC, although both findings may be related to the primary disease or to the patient’s debilitated state.

PITFALLS AND CAUTIONS
Radiologic studies including plain radiography, barium enema studies, and CT may suggest the diagnosis of PMC. However, imaging findings in PMC are not specific and may be simulated by other disorders that also cause focal or diffuse bowel wall thickening. For example, PMC can be confused with the acute stage of ulcerative and granulomatous colitis, inflammatory colitides, and ischemic colitis. Entities that cause thickening of the colon unrelated to colitis (eg, hemorrhage, colonic lymphangiectasia, leukemic infiltration, diverticulitis) should also be considered as part of the differential diagnosis (24).

A retrospective study of 64 patients with C difficile infection and 30 control subjects with diarrhea who tested negative for C difficile infection revealed that the sensitivity and specificity of CT in the detection of colonic abnormalities were 85% and 48%, respectively (37).

Although CT findings do not necessarily correlate with clinical severity and negative CT findings do not exclude PMC (38), it is important to be suspicious for the disease because increased mortality has been associated with delay in diagnosis. Once PMC is suspected, diagnosis can be confirmed by the presence of toxins in stool assays and by direct visualization of the pseudomembranous plaques at endoscopy.

CONCLUSIONS
PMC is an acute infectious colitis caused by one or more toxins produced by an unopposed proliferation of C difficile bacteria and usually occurs as a complication of antibiotic therapy. The clinical manifestation of C difficile infection varies from absence of symptoms to fulminant colitis. Because imaging is being used increasingly in the evaluation of patients with abdominal pain, it is important to recognize the imaging features of PMC that may suggest the diagnosis. Early diagnosis and treatment are essential for preventing progression to more serious pathologic conditions.

REFERENCES


