Multidetector Computed Tomography Features of Positive Endoscopic or Toxin Assay *Clostridium Difficile* Colitis

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Background: *Pancolonic colonic wall thickening is a common CT feature in patients diagnosed with Clostridium difficile colitis (CDC).*

Objective: *To illustrate CT appearances of CDC in hospitalized patients with toxin assay indicant or endoscopic proven CDC.*

Material and Method: *Two reviewers independently evaluated the colonic abnormalities in the retrospectively identified patients with toxin assay indicant or endoscopic proven CDC that underwent abdominal CT between January 2006 and June 2009. The colonic abnormalities included wall thickening, wall enhancement, the "accordion sign, pericolonic stranding, lymphadenopathy, ascites, gut obstruction, and associated findings such as small bowel involvement. They then compared the CT diagnostic findings with lab result and endoscopic findings*

Results: *Fifteen patients (in 897 patients) with toxin assay indicant or endoscopic proven CDC and underwent abdominal CT were included in the study. Colonic wall thickening (0.5 -1.6 cm) and mild degree of pericolonic fat stranding are commonly found in this study. Eleven (73.3%) patients had pancolonic wall thickening and the remaining four (26.6%) had segmental involvement. Accordion sign was demonstrated in 11 (73.3%) patients. No small bowel thickening was detected. Contrast enhanced CT showed superior result to non-contrast enhanced CT for colonic wall thickness evaluation. Accordion sign were not different between contrast enhanced CT in patients that did not received oral/rectal contrast medium administration and non-contrast enhanced CT in patients that received adequate rectal contrast medium administration.*

Conclusion: *Patients taking a broad spectrum of antibiotic were found to have colonic wall thickening, a mild degree of pericolonic fat stranding, and accordion sign on CT scan. The doctor should be concerned with CDC.*

Keywords: *Clostridium difficile colitis, Pseudomembranous colitis, Antibiotic associated colitis*

Pseudomembranous colitis (PMC), also known as antibiotic-associated diarrhea (AAD), is an acute infectious colitis characterized by the formation of an adherent inflammatory membrane (pseudomembrane) overlying sites of mucosal injury. Most important infectious cause of PMC is from *Clostridium difficile*, so called *Clostridium difficile* colitis (CDC)[1].

Clinical manifestations of this condition are varied from mild diarrhea to fulminant colitis, which has serious complications that include perforation and development of toxic megacolon. Other constitutional symptoms include low-grade fever, nausea, vomiting, localized pain, and dehydration[1,2].

Diagnosis of CDC implies a clear history of antibiotic therapy and positive stool examination of Cytotoxin assay toxin A/B or biopsy evidence of colitis with or without formation of pseudomembrane[3].

The prevalence of CDC tends to rise steadily due to increased use of prophylactic and broad-spectrum antibiotics. The prevalence of *Clostridium difficile* isolated from the stools in Thai adult patients with suspected AAD was 18.64%[4]. In addition, CDC can result in patient morbidity and mortality, especially if it is not diagnosed early. Therefore, it is important for radiologists to be aware of this potentially life-threatening condition when an abdominal CT is being performed. The purpose of the present study was to emphasize the CT diagnostic findings of CDC in correlation with lab result and endoscopic findings.

Material and Method
Patients selection
The retrospective single-institution study was approved by the authors' Ethics committee institutional review board of general requirements for informed

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consent. The authors performed a computerized search of the toxin assay and pathology information systems between January 2006 and June 2009. Eight hundred ninety seven patients (452 men; 445 women) were clinically proven CDC based on either positive endoscopic or positive toxin assay findings. Of these patients, sixteen patients, underwent abdominal CT within four weeks of their stool specimen collection date. One of the patients was eliminated from the present study because he had only lower abdomen CT examination. Therefore, 15 patients were enrolled for analysis.

The stool examination for toxin A and B detection was done at Siriraj Hospital using lab Remel Xpect, which have a sensitivity and specificity of 0.82 (0.75-0.89) and 0.96 (0.95-0.98), respectively.

Imaging acquisition

Scanning was performed according to the routine whole and upper abdomen protocol of Siriraj Hospital, from diaphragm to pubic symphysis and from diaphragm to lower pole of kidney, respectively with 64 slice-MDCT scanners (Lightspeed VCT; GE Healthcare and Somatom definition CT scanner; Siemens). All patients took 800 ml oral contrast material and 11 patients received 150 to 300 ml of rectal contrast material. Thirteen of 15 patients received intravenously administered contrast material in the form of bolus infusion of 100 ml of non-ionic contrast material. Two patients did not received intravenously administered contrast material. Imaging was performed with a slice thickness of 0.5 mm and then were reconstructed in the thickness of 1.2 mm (GE [n = 90] and 1.8 mm (Siemen [n = 6]). The exposure parameters for the CT scans were 120 KVp and 140 to 170 mAs for both the GE Lightspeed and Siemens scanners. Images were transferred to a picture archiving and communication system (PACS) for analysis.

Image analysis

The CT examinations were reviewed by one radiologist with six years experience in abdominal imaging and a third year radiology resident. Both reviewers were aware of the findings that patients had a diagnosis of PMC. Images were reviewed on PACS workstation.

Two reviewers recorded the presence or absence of abnormal colonic wall thickening as greater than or equal to 4 mm, which was based on the criteria from previously published reports[4-9]. Abnormal colonic thickening was categorized into mild (4-10 mm),

moderate (11-15 mm), and severe (>15 mm)[5]. Once the scan was considered positive, more specific assessments were performed. First, the authors determined whether the colon was diffusely or
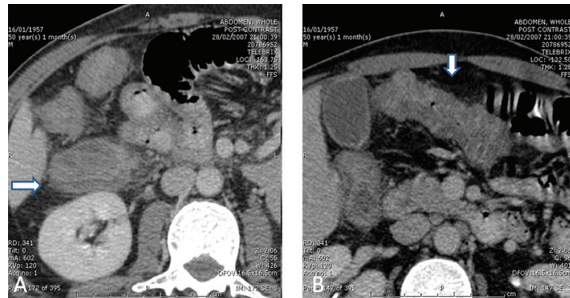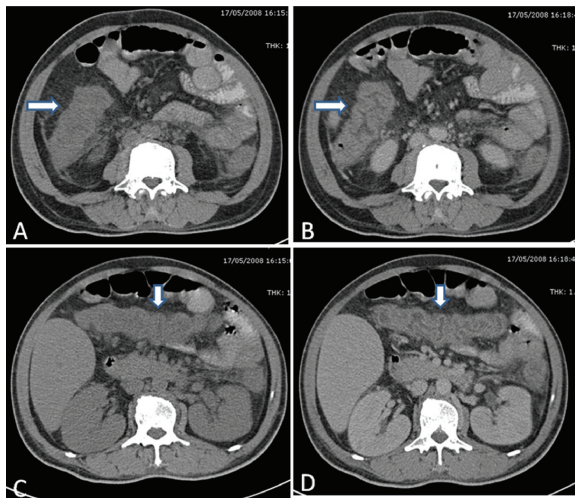

Fig. 1 A 50 year-old man known multiple myeloma, presented with *Clostridium difficile* colitis. Axial contrast enhanced CT scan show colonic wall thickening at cecum (arrow in A) and transverse colon (arrow in B) with mild enhancement. There is minimal pericolonic fat stranding.

Fig. 2 A 71 year-old woman known acute myeloid leukemia, presented with *Clostridium difficile* colitis. Axial contrast enhanced CT scan show pancolonic wall thickening (arrow in A and B), Accordion sign and mark ascites are demonstrated.
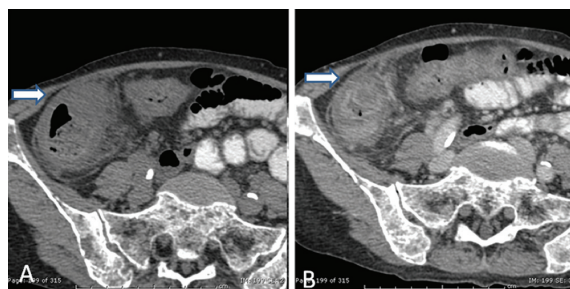
Fig. 3 A 75-year-old woman known multiple myeloma, presented with *Clostridium difficile* colitis. Axial noncontrast enhanced CT scan (A) and contrast enhanced CT scan (B) show right sided colonic wall thickening with mild mucosal enhancement (arrow in B).

Fig. 4 A 57 year-old man with *Clostridium difficile* colitis. Wall thickening at ascending colon (A and B) and transverse colon (C and D) are illustrated. Contrast enhanced CT (arrow in B and D) improved delineation of wall thickness than that of noncontrast enhanced CT (arrow in A and C).
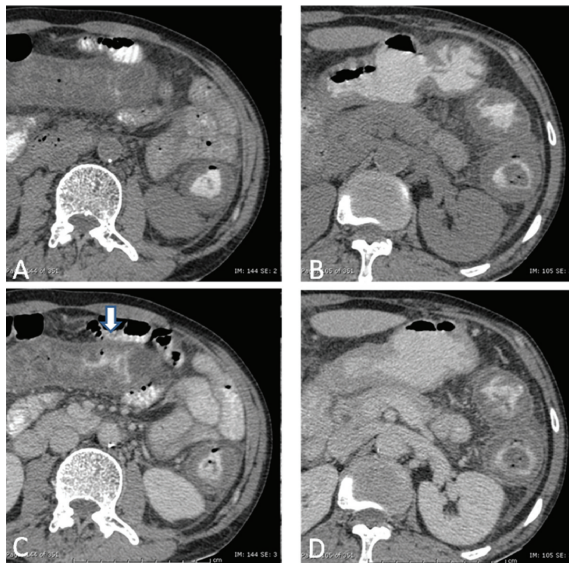

Fig. 5 A 52 year-old man underlying acute myeloid leukemia, presented with *Clostridium difficile* colitis. Axial noncontrast enhanced CT scan (A and B) and contrast enhanced CT scan (C and D) demonstrate contrast medium in descending colon. No transrectal contrast medium in transverse colon is seen. At descending colon, shows no difference between pre- and post-contrast images in wall thickness evaluation. It better demonstrates "Accordion sign" at transverse colon on post-contrast image than that of pre-contrast image (arrow in C).

segmentally involved. To do this, the authors divided the colon into six segments (rectum, sigmoid, descending, transverse, ascending, and cecum), and any affected segments were noted. The small bowel involvement was also recorded. To avoid false-positive findings for colonic wall thickening, the portion of the colonic segment used for these measurements had to have a diameter greater than 1.5 cm (except 2.5 cm for cecum)[5].

In addition, the colonic wall enhancement was assessed as mild, moderate, or mark enhancement and determine usefulness of intravenous enhancement when compared with non-enhancement in assessment wall thickening. The specific finding as Accordion sign represent the contrast trapped within very thick haustra produce alternating bands of high and low density[6,8]. Furthermore, the presence of ascites and its quantity (mild, moderate, and large) were approximated by reviewer as well as the presence of pericolonic stranding, gut obstruction and lymphadenopathy. Lastly, the other CT findings were recorded such as liver lesions, pleural effusion, or gallstone. The reader agreement was assessed with kappa and weighted kappa.

Results (Table 2-4)

Fifteen patients were included in the present study including nine men and six women. The age ranged from 30 to 78 years (average of 60.73 years; median 54 years). All patients had colonic wall thickening. The distribution of colonic wall thickening included pancolonic (11 patients [73.3%]), only the right colon (1 patient [6.7%]), only rectum and rectosigmoid colon (1 patient [6.7%]), and rectal sparing (2 patients [13.3%]). In 13 patients that had intravenous images, all of them had mild to moderate colonic wall enhancement. Furthermore, the authors found nine cases of ascites, 11 cases of accordion sign, 12 cases of pericolonic fat stranding, and four cases of lymphadenopathy, which are 60%, 73.3%, 80%,

Table 1. Kappa and weighted kappa value

Location	Good agreement 0.659 (p-value = 0.011)[a]
Accordion sign	Moderate agreement 0.587 (p-value = 0.013)[a]
Lymphadenopathy	Fair agreement 0.412 (p-value = 0.203)[b]

[a] Kappa value
[b] Weighted kappa value

Table 2. CT findings for *Clostridium difficile* colitis in 15 patients (Reviewer I)

| Case | Colon wall thickening | | | Spec finding | | | Other findings (yes/no) | | | | Small bowel involment (yes/no) |
| | Location | Thickness | Describe | Accordion | Enhancement | | Gut | Pericolonic | Lymphadenopathy | Ascites | |
	Diffuse/ segmental	C,A,T,D,S,R	Grade 1-3	(smooth/ nodular)	(yes/no)	Mild, mod, sev	Useful	ob.	fat standing (mild, mod)	(no, few, many)	(mild, mod, large)	(yes/no)
1	Diffuse		2	Nodular	Yes	Mild-mod	No	No	NE	Many	Mod	No
2	Segmental	R,S	1	Nodular	No	NE	NE	No	Mild	No	No	No
3	Segmental	C,A,T	1	Nodular	No	Mild-mod	Yes	No	Mild	Few	No	No
4	Diffuse		1	Nodular	Yes	Mild-mod	Yes	No	Mild	No	No	No
5	Diffuse		2	Nodular	No	Mild-mod	No	No	Mild	No	Mild-mod	No
6	Diffuse		2	Nodular	Yes	Mild-mod	No	No	NE	No	Mod	No
7	Diffuse		2	Nodular	Yes	Mild-mod	Yes	No	Mild	Few	Mild	No
8	Diffuse		1	Nodular	Yes	Mild-mod	Yes	No	Mild	No	No	No
9	Diffuse		1	Nodular	No	NE	NE	No	Mild	No	Mild	No
10	Segmental	A,T,D	1	Nodular	Yes	Mild-mod	Yes	No	Mild	No	No	No
11	Diffuse		1	Nodular	Yes	Mild-mod	Yes	No	Mild	No	No	No
12	Diffuse		2	Nodular	Yes	Mild-mod	No	No	Mild	No	Mild	No
13	Diffuse		1	Nodular	Yes	Mild-mod	Yes	No	Mild-mod	No	No	No
14	Diffuse		2	Nodular	Yes	Mild-mod	No	No	NE	Few	Mod	No
15	Segmental	C,A,T,D	2	Nodular	Yes	Mild-mod	Yes	No	Mild	No	Mild	No

A total of 15 patients in this study (6 women, 9 men) had age range from 30-78 years old mean = 60.73 years, median = 54 years). Colonic wall thickening showed range from 0.5-1.6 cm (mean = 1.05 cm), which 9 of 15 patients had wall thickness greater than 1.0 cm.
C = cecum; A = ascending colon; T = transverse colon; D = descending colon; S = sigmoid colon; R = rectum

Table 3. CT findings for *Clostridium difficile* colitis in 15 patients (Reviewer II)

Case	Colon wall thickening			Spec finding			Other findings (yes/no)				Small bowel involment (yes/no)
	Location	Thickness	Describe	Accordion	Enhancement		Gut ob.	Pericolonic fat standing (mild, mod)	Lymphadenopathy (no, few, many)	Ascites (mild, mod, large)	
	Diffuse/ segmental	C,A,T,D,S,R	Grade 1-3	(smooth/ nodular)	(yes/no)	Mild, mod, sev	Useful					
1	Diffuse		3	Nodular	Yes	Mild-mod		No	NE	Many	Large	No
2	Segmental	R	1	Nodular	No	NE	NE	No	Mild	No	No	No
3	Segmental	C,A,T	1	Nodular	No	Mild-mod		No	Mild	No	No	No
4	Diffuse		2	Nodular	Yes	Mild-mod		No	Mild	No	Mild	No
5	Diffuse		2	Nodular	No	Mild-mod		No	Mod	No	No	No
6	Diffuse		2	Nodular	No	Mild-mod		No	NE	No	Large	No
7	Diffuse		1	Nodular	Yes	Mild-mod		No	NE	No	No	No
8	Segmental	C,A,T,D,S,R	1	Nodular	Yes	Mild-mod		No	Mild-mod	No	No	No
9	Diffuse		1	Nodular	No	NE	NE	No	Mild	No	Mild	No
10	Segmental	C,A,T,D	1	Nodular	Yes	Mild-mod		No	Mild	Few	No	No
11	Diffuse		1	Nodular	Yes	Mild-mod		No	Mild-mod	No	No	No
12	Diffuse		2	Nodular	Yes	Mild-mod		No	Mild-mod	No	Mild	No
13	Diffuse		1	Nodular	Yes	Mild-mod		No	Mild	No	No	No
14	Diffuse		2	Nodular	No	Mild-mod		No	NE	No	Mild-Mod	No
15	Diffuse		2	Nodular	No	Mild-Mod		No	Mild	No	Mild	No

A total of 15 patients in this study (6 woman, 9 men) had age range from 30-78 years old (mean = 60.73 years, median = 54 years). Colonic wall thickening showed range from 0.5-1.6 cm (mean = 1.05 cm), which 9 of 15 patients had wall thickness greater than 1.0 cm.

C = cecum; A = ascending colon; T = transverse colon; D = descending colon; S = sigmoid colon; R = rectum

Table 4. CT findings in *Clostridium difficile* colitis

CT findings	Patients (n = 15)
Wall thickening >4 mm	15 (100%)
Wall thickening >10 mm	9 (60.0%)
Pericolonic stranding	12 (80.0%)
Accordion sign	11 (73.3%)
Ascites	9 (60.0%)
Lymphadenopathy	4 (26.7%)

and 26.7%, respectively. Pericolonic stranding was demonstrated in 12 patients (80%) with minimal stranding while ascites was present in nine patients (60%). Three patients could not be evaluated for pericolonic stranding due to mark ascites. Nine patients were with ascites, five with minimal amount, and four with minimal to moderate and moderate amount of ascites. No fluid collection is noted in the present study. No small bowel thickening was detected. No gut obstruction in the present study was demonstrated.

The other CT findings included pleural effusion (5 patients), hepatomegaly (2 patients), splenomegaly (2 patients) and thrombus along abdominal aorta (1 patient).

There were two reviewers in the present study, so reader agreement was assessed with kappa and weighted kappa (Table 1). Interobserver agreement for subjective assessment of wall thickening location and Accordion sign was good and moderate[10,11] (kappa value 0.659 and 0.587 respectively). The results of the six-year experienced radiologist were used.

Discussion

CDC is one of the inflammatory process of the bowel mainly affected colon and occasionally distal small bowel[12,13]. Even if the history of antibiotic usage is the essential clue to diagnose this condition, performing further radiologic imaging frequently is required to confirm this disease or exclude other colonic disease[14,15] because of the non-specific clinical signs and symptoms. Colonoscopy is the gold standard to diagnose CDC. It is used to visualize pseudomembrane on the site of mucosal injury. However, colonoscopy cannot be easily done in every case such as in patients with extreme colonic redundancy, comorbidity such as septicemia, and in distal colonic stricture. Furthermore, CT can demonstrate both intraintestinal and extraintestinal findings[16-19]. Owing to aforementioned reasons, the present study was performed to evaluate the CT feature of CDC in correlation with lab chemistry and pathology.

In the present study, the authors found colonic wall thickening in every case ranging from 0.5 to 1.6 cm. Aditionally, 11 of 15 patients (73.3%) had contrast trapped within very thick haustra, producing alternating bands of high and low density. This is called accordion sign. Our observation showed that colonic wall thickening associated with disproportionate mild pericolonic fat stranding are probable key features to diagnose CDC. However, they may be difficult to be implemented in patients with abundant ascites.

When comparing between non-contrast enhanced CT and contrast enhanced CT, colonic wall thickening is much better in contrast enhanced CT because the enhanced mucosal lining is better shown. However, non-contrast enhanced CT helped us to delineate colonic wall thickness much easier, especially in patients with non-distended colonic lumen.

Furthermore, the authors demonstrated the usefulness of rectal contrast in patients with renal impairment or patients who contraindicate to receive intravenous contrast agent. This is because rectal contrast will opacify and distend the lumen that separate one certain wall from the opposed colonic wall, which better define the colonic wall thickness. Therefore, the authors' recommendation is to administer rectal contrast in a patient who has contraindication for iodine contrast medium intravenous injection such as underlying chronic kidney disease or iodine allergy to improve diagnostic accuracy. Limitation of the present study is small sample sizes.

Conclusion

Pancolonic colonic wall thickening is the common CT feature in patients diagnosed with CDC. The authors found disproportionate mild pericolonic fat stranding, colonic wall thickening, and accordion sign. Those may be the helpful sign to indicate this condition. Contrast enhanced CT and/or rectal contrast improve diagnostic performance.

Potential conflict of interest

None.

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ลักษณะภาพเอกซเรย์คอมพิวเตอร์ของผู้ป่วยที่มีภาวะการติดเชื้ออักเสบของลำไส้ใหญ่จากเชื้อ *Clostridium difficile* ที่ได้รับการตรวจจากวิธี *toxin assay* หรือ จากการส่องกล้องทางลำไส้ใหญ่

สิทธิพงศ์ ศรีสัจจากุล, พัชรินทร์ ประไพศิลป์, นิศากร กิจสวัสดิ์

ภูมิหลัง: *ภาวะการติดเชื้ออักเสบของลำไส้ใหญ่จากเชื้อ Clostridium difficile หรือ Clostridium difficle colitis พบได้ใน ผู้ป่วยในของโรงพยาบาลที่ได้รับยาปฏิชีวนะ broad spectrum*

วัตถุประสงค์: *เพื่อดูลักษณะภาพเอกซเรย์คอมพิวเตอร์ของผู้ป่วย ที่ได้รับการตรวจพบภาวะนี้จากวิธี toxin assay หรือ จากการ ส่องกล้องทางลำไส้ใหญ่ และได้รับการตรวจด้วยวิธีเอกซเรย์คอมพิวเตอร์ ตั้งแต่มกราคม พ.ศ. 2549 ถึงมิถุนายน พ.ศ. 2552*

วัสดุและวิธีการ: *ผู้ป่วย 15 ราย จากผู้ป่วยทั้งหมด 897 ราย ผู้นิพนธ์สองคนได้ประเมินภาพเอกซเรย์คอมพิวเตอร์ ในหัวข้อ ความหนาของผนังลำไส้ wall thickening, wall enhancement, the accordion sign, pericololonic stranding, ต่อมน้ำเหลือง (lymphadenopathy), น้ำในช่องท้อง (ascites), ภาวะลำไส้อุดกั้น (gut obstruction) และภาวะร่วมอื่น ๆ เช่น small bowel involvement*

ผลการศึกษา: *พบ colonic wall thickening ประมาณ 0.5-1.6 เซนติเมตร และ mild degree of pericolonic fat stranding ในผู้ป่วยส่วนใหญ่ นอกจากนี้พบ pancolonic wall thickening ผู้ป่วย 11 ราย และผู้ป่วย 4 รายพบ segmental involvement และพบ accordion sign ในผู้ป่วย 11 ราย (73.3%) และไม่พบ small bowel involvement การประเมิน colonic wall thickness และ accordion sign จากภาพเอกซเรย์คอมพิวเตอร์ของผู้ป่วยที่ได้รับการฉีดสารทึบรังสี ให้ผลที่ดีกว่าภาพเอกซเรย์ คอมพิวเตอร์ในผู้ป่วยที่ไม่ได้รับการฉีดสารทึบรังสี แต่ไม่แตกต่างกับในผู้ป่วยที่ได้รับ rectal contrast อย่างมีประสิทธิภาพ*

สรุป: *ผู้ป่วยที่มีประวัติได้รับยาปฏิชีวนะ broad spectrum และตรวจพบ pancolonic wall thickening, mild degree of pericolonic fat stranding และ accordion sign มีแนวโน้มที่จะบ่งชี้ถึงภาวะการติดเชื้ออักเสบของลำไส้ใหญ่จากเชื้อ Clostridium difficile หรือ Clostridium difficle colitis*