

Clostridium difficile-Associated Disease

A Clinical Investigation of *Clostridium difficile*-Associated Disease

Chung Ryul Lee, M.D., Joon Kyu Lee, M.D., Yong Suk Cho, M.D.,
Hyo Min Yoo, M.D., Won Ho Kim, M.D. and Kyong Won Lee, M.D.*

Department of Internal Medicine and Clinical Pathology*,
Yonsei University College of Medicine, Seoul, Korea

Background/Aims: *Clostridium difficile*-associated disease (CDAD) is a common cause of anti-biotics-associated diarrhea. The purpose of this study is to understand the clinical, microbiological, endoscopic and pathological features of CDAD. **Methods:** The analysis was performed for 31 patients who were diagnosed as CDAD by positive stool culture from Jan, 1988 to Dec, 1997 and subsequently underwent flexible sigmoidoscopy or colonoscopy. **Results:** Generally, CDAD occurred in elderly patients who were admitted and treated with antimicrobial agents for a long time. Major symptoms were watery diarrhea, fever, hematochezia, abdominal pain, and vomiting. On endoscopy pseudo membranous colitis (PMC) and nonspecific colitis were observed in 58.1% and in 22.6% of the patients, respectively. Normal findings were observed in 19.4% of them. Pathologic findings showed PMC in 19.4% of the patients, nonspecific colitis in 48.4%, normal finding in 22.6%. Most CDAD were cured when the use of the presumptive causative antimicrobials was quitted and vancomycin, metronidazole, or cholestyramine was used. Eight recurred cases were also cured by using vancomycin or metronidazole. **Conclusions:** CDAD is a common cause of antibiotics-associated diarrhea and shows a spectrum of endoscopic and pathologic findings from normal to PMC. CDAD is treated well by oral vancomycin or metronidazole, even in the recurred cases. (**Kor J Gastroenterol** 1999;33:338 - 347)

Key Words: *Clostridium difficile*, CDAD, Pseudomembranous colitis, Stool culture

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Clostridium difficile associated disease (CDAD)
C. difficile

Tel: (02) 361-5435, Fax: (02) 393-6884

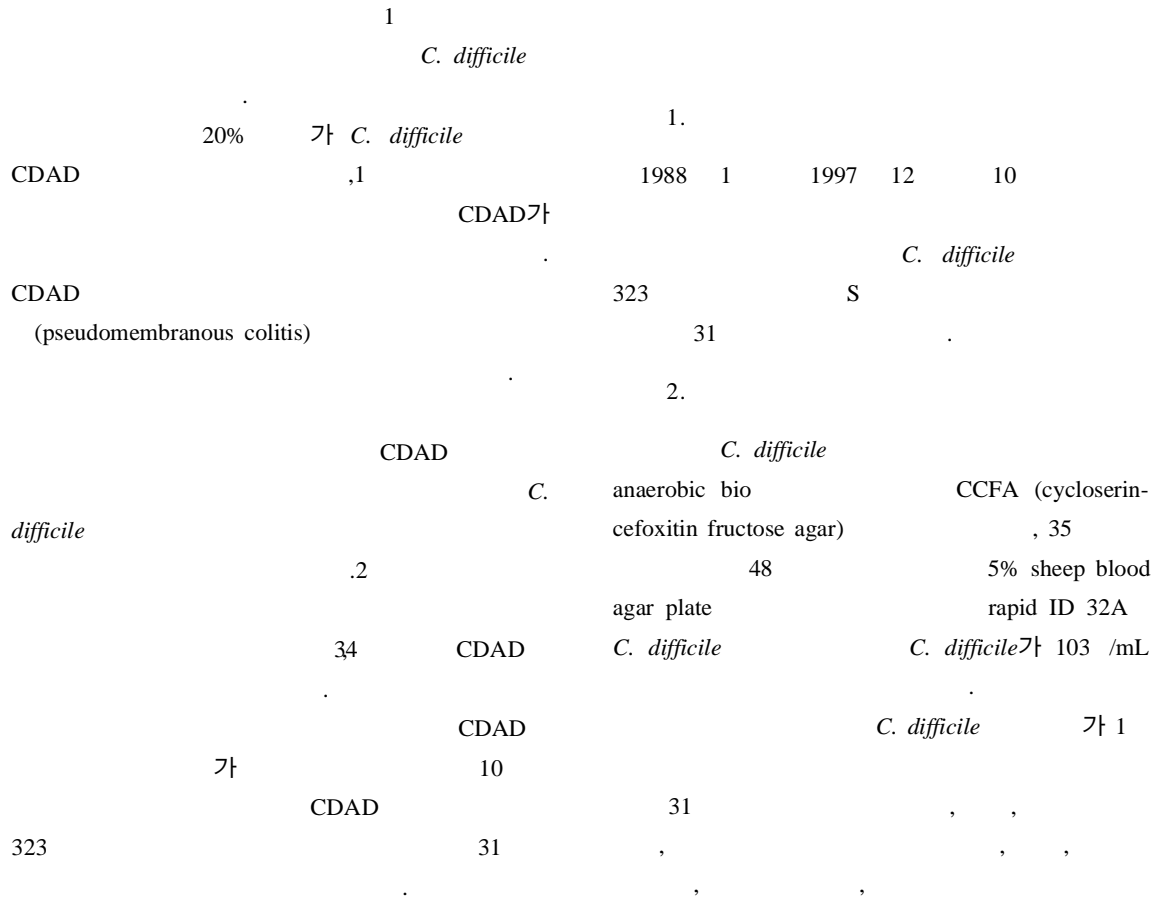


Fig. 1. Age and sex distribution of CDAD. Among the 31 CDAD patients, 22 cases (71%) were older than 50 years old.

10 , 8 , 7 ,
 2 , 2 ,
 1. (CAPD peritonitis) 1 ,
 31 가 19 , 가 12 1 (Table 1).
 56 (23-77) 20 2 , 30 4 , 40
 3 , 50 10 , 60 6 , 70 6 50 3.
 가 71% (Fig. 1). (Table 2).
 2. 3 ,
 31 가 1 27
 27 12 , 6 , 가 21
 2 , 3 , , 가 6 .
 , 1
 4 . , cephalos-

Table 1. Underlying Conditions of Patients and Causes of Antibiotic Use

Underlying diseases	No. of patients	Causes of antibiotic use	No. of patients
Cerebrovascular accident	12	Operation*	7
		Pneumonia	3
		Fever	2
Malignancy (excluding hematologic malignancy)	6	Fever	3
		UTI †	2
		Pneumonia	1
Hematologic malignancy	2	Pneumonia	1
		Fever	1
End stage renal disease	3	Operation ‡	1
		CAPD peritonitis	1
		Fever	1
Diabetes mellitus	1	Fever	1
Pulmonary tuberculosis	1	Tuberculosis	1
Tuberculous meningitis	1	Tuberculosis	1
Acute renal failure	1	Pneumonia	1
No underlying disease	4	Acute pyelonephritis	1
		Operation §	1
		Spontaneous abortion	1
		Pneumonia	1
Total	31		31

*, prophylactic antibiotics use after neurosurgical operation; †, Urinary tract infection; ‡, Prophylactic antibiotics use after ophthalmologic operation due to cataract; §, Prophylactic antibiotics use after vocal polyp removal; , Prophylactic antibiotics use after spontaneous abortion.

Table 2. Antimicrobials Presumed to be Causes of CDAD

Antibiotics	Administration route	No. of patients
Cephalosporin	IV	22
	PO	2
Aminoglycoside	IV	17
Quinolone	IV	3
Fluconazole	PO	2
Antituberculosis drugs	PO	2
Clindamycin	IV	1
Metronidazole	IV	1
Vancomycin	IV	1
Teicoplanin	IV	1
Ampicillin	PO	1
Unknown antibiotics		3
No antibiotics		1

Table 3. Clinical Manifestations of CDAD Patients

	No. of patients (%)
Diarrhea	31/31 (100)
Abdominal pain	9/17 (52.9)*
Fever (>37.5)	13/31 (41.9)
Hematochezia	10/31 (32.3)
Vomiting	1/31 (3.2)

*, 14 patients were unable to communicate.

Table 4. Onset of Diarrhea according to the Hospital Day

Onset (days)	No. of patients (n=31)
Before admission	3 (9.7%)
1-10	9 (29.0%)
11-20	3 (9.7%)
21-30	5 (16.1%)
31-40	2 (6.5%)
41-50	4 (12.9%)
51-	5 (16.1%)

porin 24 (88.9%), aminoglycoside 17 (63.0%), quinolone 3, fluconazole 2, (isoniazid + rifampicin + ethambutal + pyrazinamide)가 2, clindamycin, me-

Fig. 2. The duration of antibiotics use before the development of CDAD was from 1 day to 30 days. The mean duration of antibiotics use was 8 days.

tronidazole, vancomycin, teicoplanin, ampicillin
 1
 4.
 가 31, 17 9 (52.9%), 37.5 가 13 (41.9%), 10 (32.3%), 가 1 (3.2%) (Table 3).
 가 93, 29 가

Table 5. Endoscopic and Pathologic Findings

Endoscopic findings	Pathologic findings				Total (%)
	PMC (%)	Colitis (%)	Normal (%)	Others (%)	
PMC	6	8	2	2*, †	18 (58.1)
Colitis		5	1	1 [‡]	7 (22.6)
Normal		2	4		6 (19.4)
Total	6 (19.4)	15 (48.4)	7 (22.6)	3 (9.7)	31

*, Biopsy tissue was too small to be examined; †, Biopsy was not performed due to associated rectal ulcer with bleeding; ‡, Biopsy revealed intestinal tuberculosis with granuloma.

Table 6. Management of *Clostridium Difficile*-Associated Colitis and Effect

	Cure		Not cured	Others	Total
	No recur.	Recur.			
Vancomycin	12	5	1	3*	21
Metronidazole	3	1	0	0	4
Vancomycin + Metronidazole	3	0	0	0	3
No use	1	2	0	0	3
Total	19	8	1	3	31

Recur, recurrence; *, 3 patients were expired due to underlying diseases.

Table 7. Time Interval from Clinical Onset to Decrease of Diarrhea

Diarrhea	Effect		
	No. of patients	Decrease (days)	Disappearance (days)
Cure	19	6.9	10.1
Recurrence	8	5.8	11.2
Not improved	4*	13	-
Mean	31	6.8	10.8

*, 3 patients were expired due to underlying diseases and 1 patient discharged without improvement o symptoms.

(Table 4). 가 7 (22.6%), 6 (19.4%)
 1 30 , 8 6
 가 (Fig. 2). 3 (19.4%), 15 (48.4%), 7
 33 10 (22.6%)
 . 1 , 가 1
 5. , 가
 18 (58.1%), 1 (Table 5).

6. 가 3 (9.7%) (Table 6).
 vancomycin 21 (67.7%),
 metronidazole 4 (12.9%),
 metronidazole 3 (9.7%)
 가 28 ,
 가 1 27 (96.3%)
 가 27 6.5 가
 , 10.8 가
 27 8 (29.6%)
 가
 가 (Table 7),
 vancomycin metronidazole
 CDAD
 ficile ,
 8
 CDAD
 Clostridium (spore)
 100
 . C. difficile
 1935 5 3%
 50% 가
 cephalosporin
 가 10-50%
 90-100% .67
 CDAD
 가 C. difficile CDAD
 .8-10
 ,
 가
 3 (colonization inhibition) C.
 difficile II C. difficile
 A B CDAD
 .12 C. difficile
 가 A , B
 , .1 A
 가 B , , B
 2-3 , B
 A 가 .13
 B 가 A
 CDAD가 .14
 CDAD
 clindamycin 가 가
 15 가 가 cep-
 halosporin penicillin CDAD
 erythromycin, ampicil-
 lin, amoxicillin CDAD ,15-17
 tetracycline, chloramphenicol, rifampin, metronida-
 zole, CDAD
 .17,18
 , , ,
 CDAD가 , CDAD가
 CDAD
 .21920 31
 가 21
 , CDAD
 cephalosporin 24
 CDAD

21 가

2-3 가 ,

가 , , 4-6 .9

가 , 4-6 , 가

.22 , , 가

CDAD 50%

가

10%

.23 S

CDAD가

*C. difficile*가

.8

. C. difficile

1979 CCFA (cycloserin-cefoxitin fructose agar) cycloserin

Enterococci *Staphylococci* 14% , 30%

cefoxitin 가 .8

가 .24 31 18 58.1% ,

7 (22.6%), 6 (19.4%)

(rectal swab)

가 . *C. difficile* CDAD

(cell culture cytotoxic assay), (immunoenzyme assay), 가 CDAD

latex (latex test) 25-28

70-100% 가

.26 *C. difficile*

.29 CDAD

가 van

*C. difficile*가 A B comycin metronidazole vancomycin 1-2

A B 가 125 mg 4 , metronidazole

가 5-7% . 1-2 250 mg 3 95%

가 가 ,30 가

.30 Vancomycin

CDAD metronidazole 가

vancomycin-resistant enterococci

metronidazole

50% .810 .31

2-5 mm 3 가 7

가 .323 , 22.6%

vancomycin, metronidazole

CDAD 27 CDAD 8 (30%)가

5-50% 34 , vancomycin, metronidazole

vancomycin metronidazole : CDAD anti-

50-92% .29 , , ,

cholestyramine , bacitracin, rifampicin , vancomycin,

, *Saccharomyces boulardii*, metronidazole .

Lactobacillus .30

Cholestyramine vancomycin ,

.34

가 ,35

.29

: *Clostridium difficile*-associated disease (C-

DAD)

CDAD ,

: 1988 1 1997 12

10 *C. difficile* 31

, , ,

: CDAD

가 . 31

, ,

58.1% , 22.6%

, 19.4%

19.4% , 48.4%

van-

comycin, metronidazole

CDAD 8 (30%)가

vancomycin, metronidazole

: CDAD anti-

biotics-associated diarrhea ,

, , ,

vancomycin,

metronidazole .

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