TWO CASES OF FULMINANT COLITIS DUE TO BINARY TOXIN-POSITIVE *CLOSTRIDIUM DIFFICILE*, NEITHER OF WHICH WAS PCR RIBOTYPE 027 NOR TYPE 078

Yasuaki Tagashira[1], Akira Nakamura[1], Mitsutoshi Senoh[2], Haru Kato[2]

[1] Division of Internal Medicine, Asahi General Hospital, Chiba, Japan

[2] Department of Bacteriology II,National Institute of Infectious Diseases, Tokyo, Japan

Introduction

- It has been documented that patients infected with *Clostridium difficile* producing binary toxin (CDT), such as PCR ribotype 027, are more likely to develop a severe disease.
- In Japan, while outbreaks caused by type 027 have not been documented so far, the epidemiology of *C. difficile* infection (CDI) due to CDT-positive strains is unknown.
- In this study, we present two fatal cases of CDI caused by CDT-positive *C. difficile* reported in Japan, neither of which were PCR ribotype 027 nor type 078.

Case 1:60-year-old man

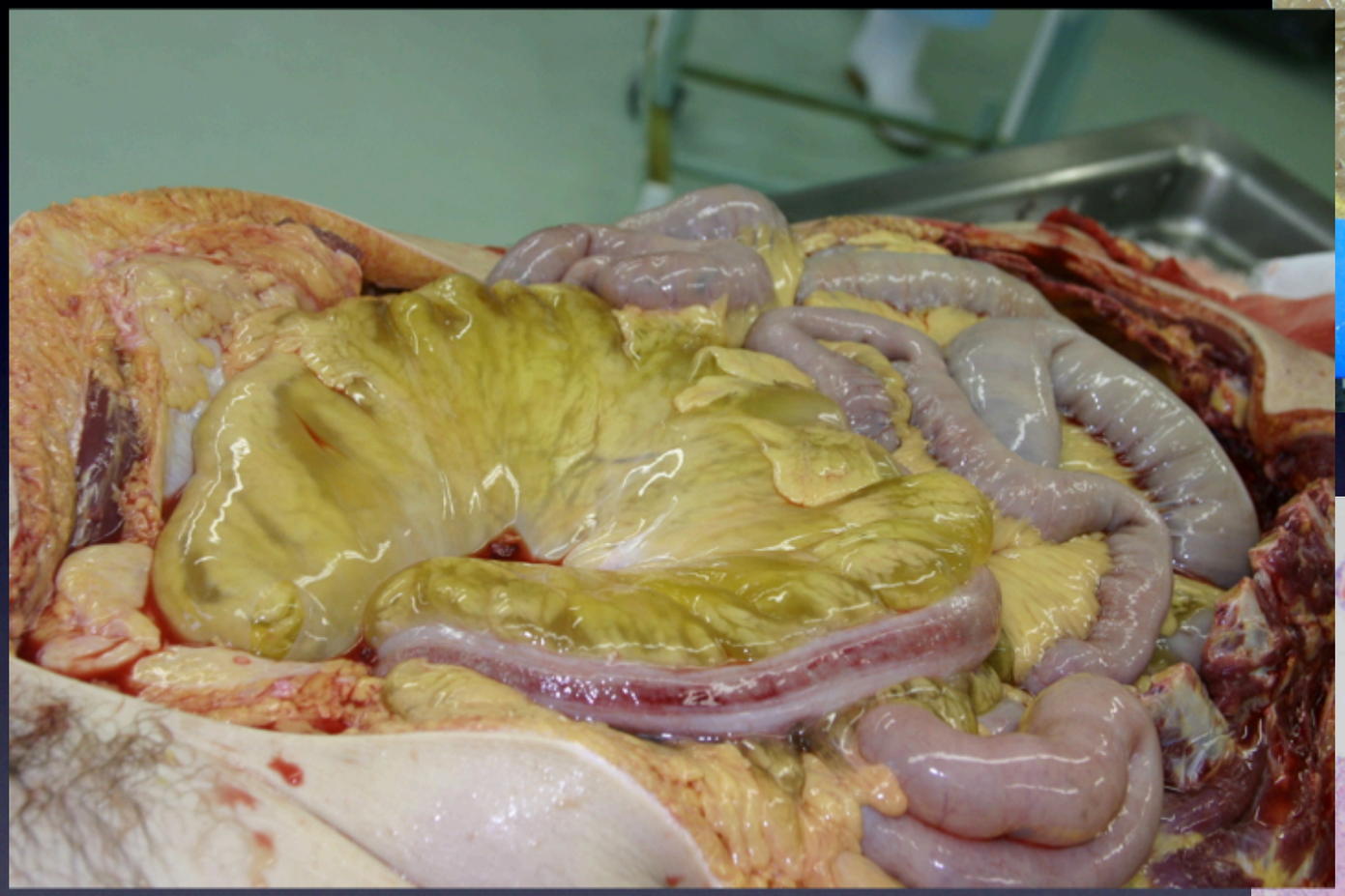
- He lived in a care home because of alcoholic liver cirrhosis and alcoholic psychosis.
- He suffered from subcortical hemorrhage and was admitted to hospital. He developed aspiration pneumonia, and ampicillin-sulbactam was administered with an anti-ulcer drug. He underwent rehab soon after admission.
- 6 days after antimicrobial therapy, he remained constipated, so a laxative was given. After a week antimicrobial therapy, he showed symptoms of severe watery diarrhea and hypovolemic shock, leading to admission to the ICU.

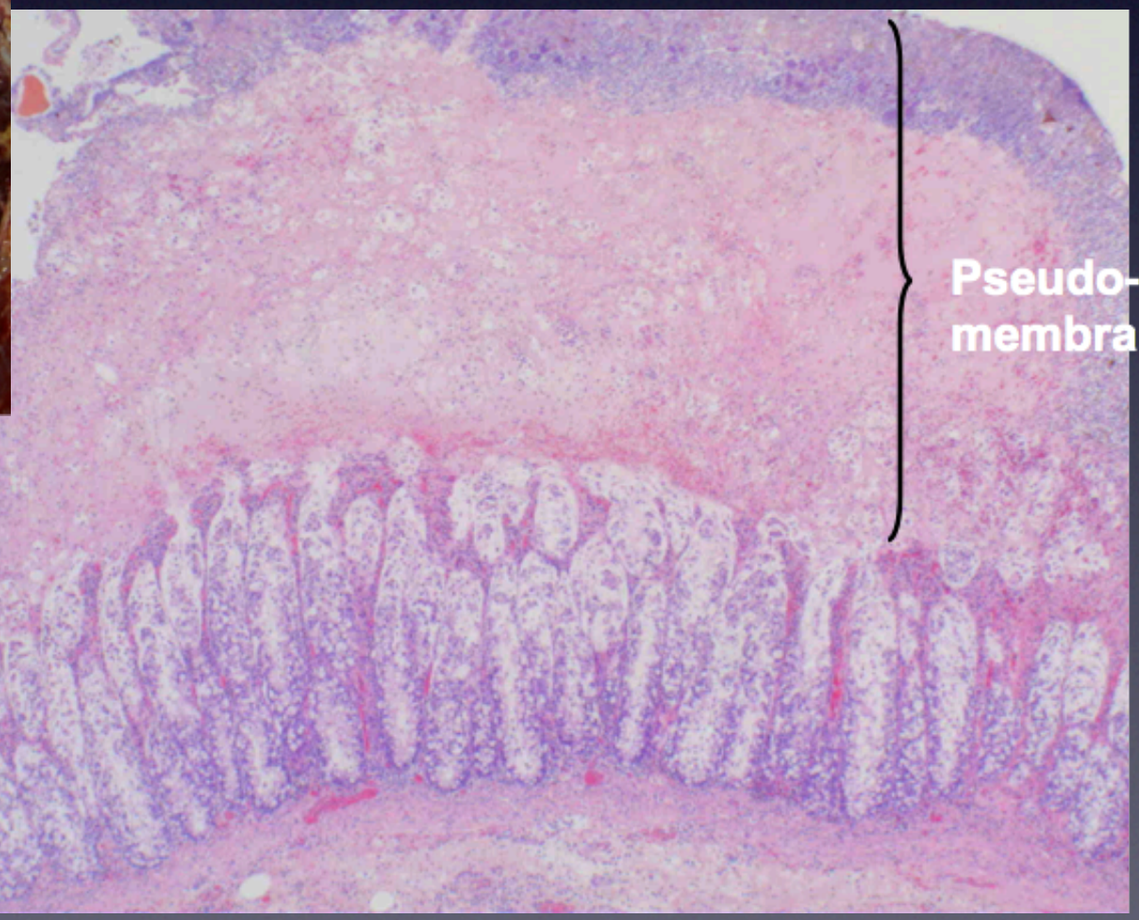
- Fecal *C. difficile* toxin was tested positive and vancomycin therapy (0.5g/day) was started. The patient was intubated but, he died 24 hours after intubation.
- Blood examination revealed a rapid increase in WBC and creatinine and a decrease in albumin.

Blood test

	-2day	Onset	+1day
WBC (/mm3)	5500	40300	34600
BUN (mg/dl)	14	45	27
Cre (mg/dl)	0.47	2.04	0.91
ALB (g/dl)	3.1	3.0	0.6

Autopsy





Whole colon was edematous and pseudo-membrane formation was observed.

Case2: 60-year-old woman

- Past medical history of hypertension, hyperlipidemia.
- 11 weeks after the onset of colitis in the 1st patient, she was hospitalized in the same ward, suffering from subarachnoid hemorrhage.
- After 2 weeks of hospitalization, she showed symptoms of pyelonephritis, for which piperacillin-tazobactam was administered. She had constipation for a week.
- She had severe watery diarrhea after an 18-day antimicrobial therapy. After which she was admitted to the ICU, where she was given therapy that required a much stronger dose of saline. Noradrenaline and dopamine were also given for septic shock.

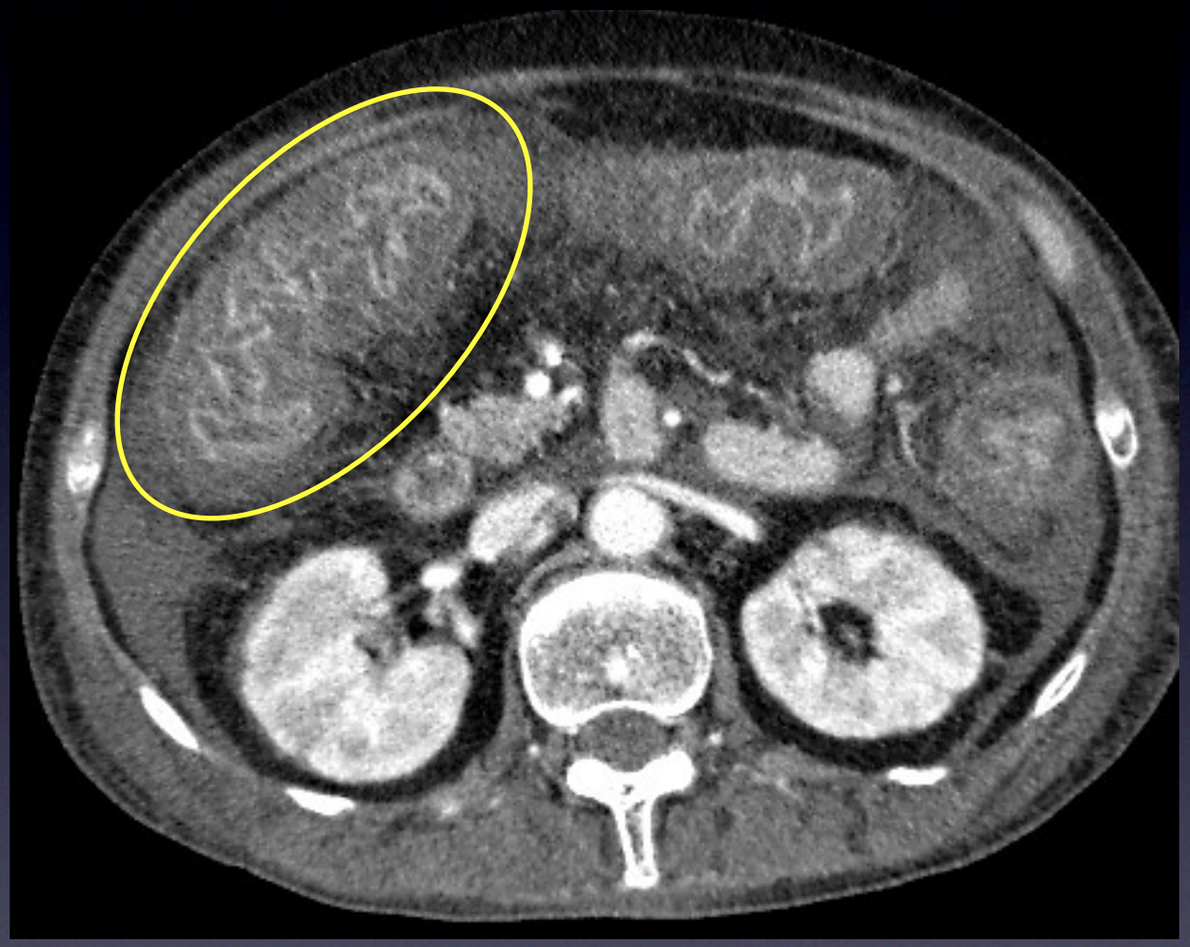
- Since fecal *C. difficile* toxin was tested positive, vancomycin (2g/day) and metronidazole(1g/day) were started. She was already intubated and treated in the ICU, but her condition worsened daily and died 4 days after the onset of colitis.

Laboratory data

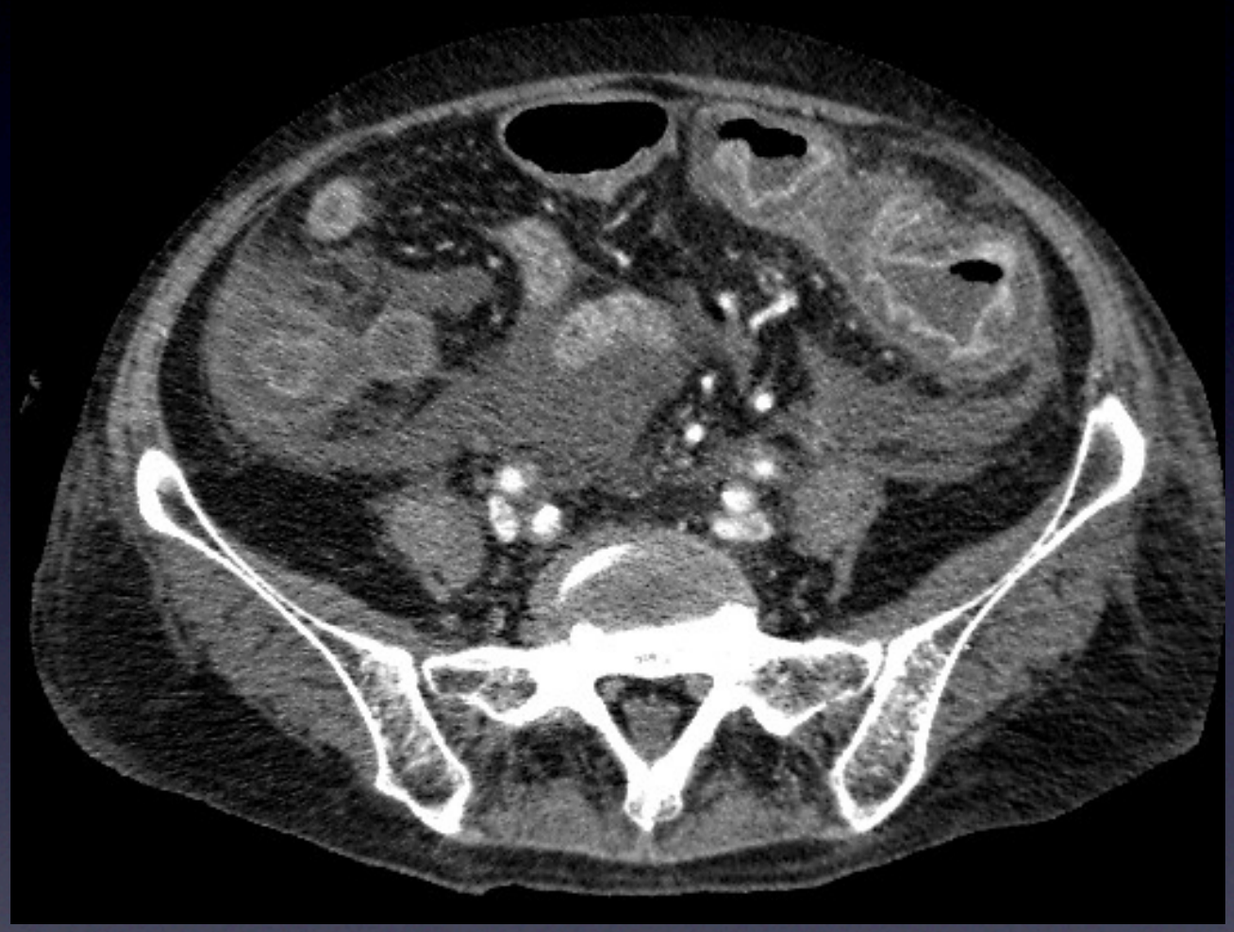
	-3day	-1day	Onset	+1day
WBC (/mm3)	6200	13600	18600	29400
BUN (mg/dl)	15	32	42	52
Cre (mg/dl)	0.35	0.76	1.10	1.80
ALB (g/dl)	3.6	2.0	1.5	1.5

In the laboratory test, both WBC and creatinine increased and albumin decreased in the same way as case 1.

Enhanced CT Scan(2 days after the onset of colitis)



Accordion sign



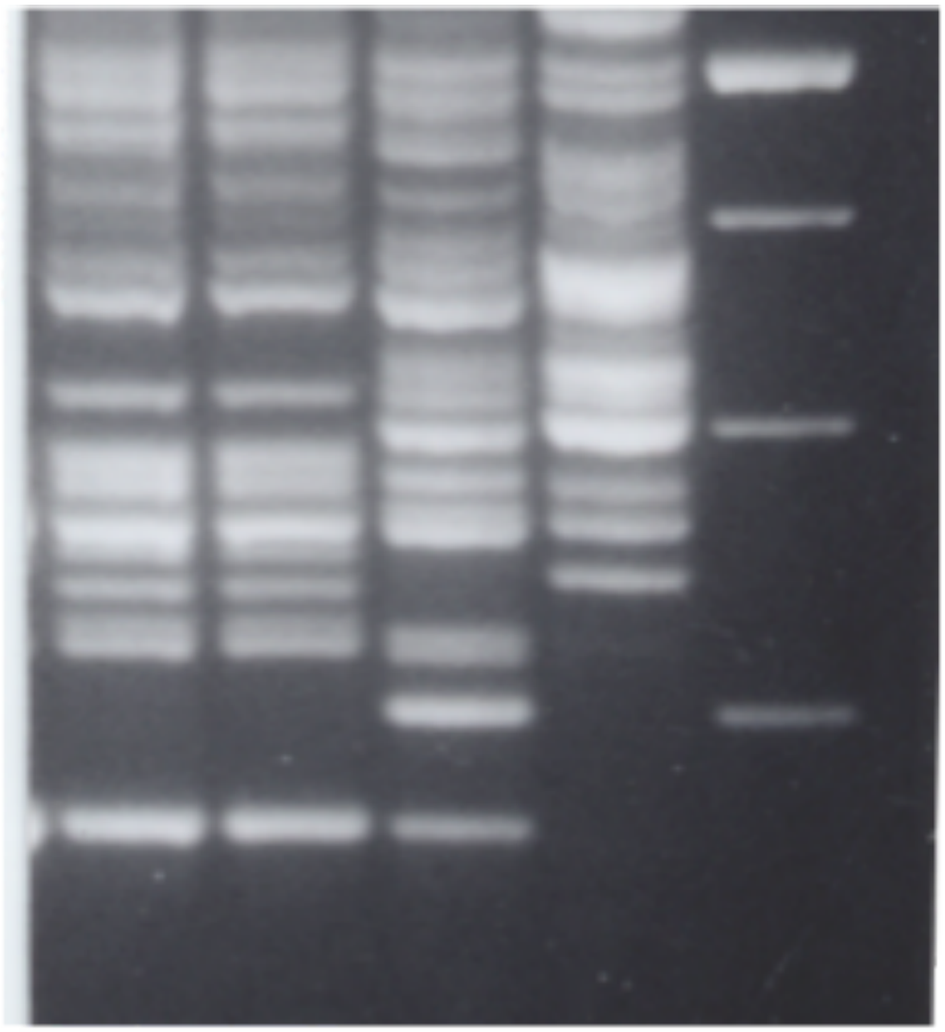
Pancolitis and Acites

Analysis of *C. difficile* isolates recovered from both patients

- The isolates from both patients were toxin A-positive, toxin B-positive, binary toxin-positive.
- Sequence analysis of *tcdC* showed that the sequences of the isolates differed from those of *C. difficile* 027, but a single-base pair deletion at position 117 as well as a 18-bp deletion, which were identical to the sequence results in that of the reference strain of 027 were found.
- Sequence analysis of *slpA* showed that the sequences of the isolates differed from those of *C. difficile* 027.

PCR ribotype patterns of *C. difficile* isolates recovered from the patients

- Both isolates were identical by PCR ribotyping and the banding patterns of the isolates differed from that of PCR ribotype 027 as well as that of PCR ribotype 078.



Lane 1, JND11-001;Case1
Lane 2, JND11-064;Case2
Lane 3, PCR ribotype 027;
Lane 4, PCR ribotype 078;
Lane M, 100bp ladder.c

Conclusion

- **Fulminant colitis due to *C. difficile* positive for CDT, which was neither PCR ribotype 027 nor type 078 occurred in two cases within 11 weeks.**
- ***C. difficile* recovered from the patients may be a new hypervirulent strain.**
- **Further studies for virulence factors and epidemiology of this strain are required.**