**Klebsiella pneumonia** septic shock and death in a patient with community-acquired *Clostridium difficile* colitis (CA-CDI):

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**Abstract**

**Background:**

*Clostridium difficile* is the major cause of nosocomial antibiotic-associated diarrhea while secondary Gram-negative shock is rarely seen in cases of community-acquired *C. difficile* infection (CDI). Toxic megacolon and bowel perforation are also unusual clinical outcomes following community-acquired *C. difficile* infection. We present a 22-year-old female who acquired CDI in the community and subsequently progressed to toxic megacolon, septic shock and death following admission to hospital. To the best of our knowledge, this was the first case type seen in Jamaica.

**Case presentation:**

A 22-yr-old female with a 5-day history of diarrhea following clindamycin treatment for coverage of a dental abscess was admitted to the University Hospital of the West Indies, Jamaica. She progressed from diarrhea to pseudomembranous colitis, toxic megacolon, *Klebsiella pneumonia* septic shock and death despite initial treatment intervention with metronidazole. *C. difficile* ribotype 087 was isolated from stool while blood cultures grew *K. pneumoniae*. 
Conclusions:

We believe that clindamycin used for coverage of a dental abscess was an independent risk factor initiating the disruption of the bowel micro-flora resulting in overgrowth of *C. difficile* North American Pulsotype (NAP) NAP12/ribotype 087. This uncommon strain type, which is the same ribotype (087) as ATCC 43255, was apparently responsible for the increased severity of infection seen, while *K. pneumoniae* was presumably the cause of septic shock and death.

Keywords

*Clostridium difficile, Klebsiella pneumoniae*, community acquired infection, diarrhoea, clindamycin, pseudomembranous colitis, toxic megacolon.

Background

*Clostridium difficile* is the major cause of nosocomial antibiotic-associated diarrhea (1, 2) while secondary Gram-negative shock is rarely seen in cases of community-acquired *C. difficile* infection (CA-CDI). CA-CDI is defined as symptoms which occur in the community or within 48 hours of admission to a hospital, provided symptoms from onset were > 12 weeks after the last discharge from a hospital (3). CA-CDI, compared to hospital-acquired infection, occurs less frequently, is usually less severe and is more frequent among females with a median age of 50 years compared to 72 years with hospital-acquired CDI (3). The most common risk factors in CDI are broad-spectrum antibiotics including third generation cephalosporins, clindamycin, penicillins, and fluoroquinolones (2, 4). However, virtually all antibiotics are potential risk factors in CDI (5)
We report a rare and fatal case of *K. pneumonia* sepsis and shock in a 22-year-old female admitted to the UHWI. *K. pneumoniae* sepsis, a subsequent clinical outcome, occurred in hospital after a 5-day history of apparent clindamycin-induced diarrhea in community acquired *C. difficile* infection (CA-CDI).

**Case presentation**

A 22-year-old female presented to the University Hospital of the West Indies (UHWI), Jamaica, following transfer from a public hospital in Spanish Town, Jamaica where she presented with a 5-day history of diarrhea and fever. The diarrhea commenced five days after starting clindamycin therapy for a recent tooth extraction due to a dental abscess. Despite discontinuation of clindamycin therapy and the introduction of chloramphenicol and metronidazole in therapy, the fever and diarrhea continued, hence referral for further investigation and management.

Physical examination of the patient revealed a febrile female in severe cardiopulmonary distress with tachycardia, HR beats/150 min, and blood pressure 150/100 mm/Hg. Laboratory investigations showed a hemoglobin of 10.4 gm/dl, white cell count of 2.1x10^9/liter, and platelet count of 182 x 10^9/liter. Blood cultures (brain heart infusion and thioglycollate broths) collected on admission grew *Klebsiella pneumoniae* from all four bottles after 24 hours incubation at 37°C. The patient became afebrile. However, hypotension, pulmonary edema, leucopenia, and thrombocytopenia persisted despite appropriate therapy and intensive care management. Repeated blood cultures became sterile following antibiotic therapy with intravenous metronidazole, piperacillin, ceftriaxone, and gentamicin. A subsequent diarrheal stool specimen was positive for *Clostridium difficile* toxin A/B (ELISA; Alexon Inc., 1190 Borregas Ave., Sunnyvale, CA. 94089-1302) and the
corresponding organism isolated on selective culture medium cycloserine, cefoxitin, fructose agar (CCFA).

The patient died 10 days after hospital admission and an autopsy was performed. The most significant finding at autopsy was that of multiple discrete plaques of yellowish exudate on the mucosal surface of the entire large bowel, typical of pseudomembranous colitis (PMC) which was florid. Another noteworthy pathologic finding was that of markedly overweight lungs with features in keeping with adult respiratory distress syndrome.

Polymerase chain reaction (PCR) was used to confirm the presence of *C. difficile* triphosphate isomerase (*tpi*), toxins *tcdA* and *tcdB* genes, the lack of binary toxin *cdtB* gene, and no deletion in *tcdC* gene (6). PCR ribotyping on the isolate revealed a ribotype of 087 and the pulsed-field gel electrophoresis (PFGE) macrorestriction pattern identified a fingerprint type 0515, which has not been seen previously using this method in a Canadian national collection of over 700 unique fingerprint types from more than 7,100 CDI isolates (Figure 1). However, the fingerprint pattern was closely related (one band difference) to the North American Pulsotype (NAP) NAP12 strain (Figure 1). The minimal inhibitory concentrations (MIC) as determined by Etest were as follows: susceptible to metronidazole 0.094 ug/ml; vancomycin 1 ug/ml; moxifloxacin 1 ug/ml; rifampicin < 0.002 ug/ml; tigecycline 0.125 ug/ml; and resistant to clindamycin 256 ug/ml. *K. pneumoniae* was isolated from 2 sets of blood cultures following overnight incubation at 37°C.

The present case of *C. difficile* associated PMC and the subsequent progression to toxic megacolon, bowel perforation, and *K. pneumonia* septic shock are uncommon clinical presentations in community-acquired infections (3). In addition to these clinical presentations were associated hypotension and admission for intensive care
classifying this patient as a severe complicated case of CDI (7). Haematogenous dissemination of *C. difficile* is rare and toxemia was more likely to have been due to the toxicity of the *C. difficile* toxins and the induction of proinflammatory cytokines by the toxins (8), hence the septic presentation was entirely due to disseminated *K. pneumoniae*. The source of *K. pneumoniae* sepsis in our patient was presumably the gastrointestinal tract as there were no symptoms or signs to suggest other systems involvement. The unresponsiveness and progression to toxic megacolon and bowel perforation despite treatment with metronidazole were probably due to failure in administering appropriate and adequate clinical and surgical interventions. While oral metronidazole is the preferred first line drug for treatment, vancomycin is usually reserved for severely ill patients and recurrence of *C. difficile* colitis (9). Interestingly however, these interventions including vancomycin treatment with recommended total colectomy were not indicated in the management of the present case. It is important to note that the confirmation of PMC was made at autopsy and the failure to apply the optimal required clinical and surgical interventions, were probably due to the rapid progression to these clinical outcomes.

Besides the toxins A and B produced by this isolate, there was no deletion observed in the negative regulator *tcdC* gene suggesting normal toxin expression. However, ATCC 43255, which also has a wild type *tcdC*, has been shown to have increased toxin expression (10). Interestingly, ATCC 43255 has the same ribotype (087) as the clinical isolate and only a single band difference in the DNA fingerprints was observed between the two isolates (Figure 1). Based on the similarity of ribotypes and fingerprint patterns between the two isolates, one could speculate that the rapid progression to PMC in this patient may be due to increased toxin expression.
Ribotype 087 is the predominant strain in Hungary but is uncommon internationally (11).

It is to be noted that no previous history of hospitalization or health care-associated risk factors to CDI was indicated in this patient. On the contrary, this young adult was actively pursuing a university education, which was disrupted by the occurrence of CDI consistent with that of a community-acquired infection (3). The progression to toxic megacolon in our patient was not a predicted clinical outcome even after hospitalization. The presence of a perforated colon was a clear indication for surgical intervention, especially if there were unresponsiveness to other treatments and if clinical improvement was not noted within 2 to 3 days of patient management (12).

**Conclusions**

The present case was fraught with many challenges to diagnosis and clinical management. It is, however, important to note that the clinical manifestations of community-acquired infections in the present case rapidly progressed to serious complications and should be given equal importance as hospital-acquired CDIs. In conclusion, we believe that clindamycin used for coverage of a dental abscess was an independent risk factor initiating the disruption of the bowel micro-flora resulting in overgrowth of NAP12/ribotype 087, which apparently was responsible for the increased severity of CDI seen. We also believe that total colectomy was required for management of bowel perforation and that Gram-negative shock syndrome may have been prevented with early and appropriate treatment implementation.

**Consent**

Not applicable due to patient’s demise.

**Competing interests**

All authors declare that they have no competing interest.
Authors’ contributions

All authors read and approved the final manuscript. OH wrote the manuscript and conducted the initial laboratory diagnosis of the present case. KR wrote the case report along with KC who wrote the pathological findings. MM contributed to the molecular analysis and writing of manuscript as well as conducted the genotyping of the clinical isolate.

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Figure 1. Dendrogram depicting the Smol C. difficile fingerprint patterns from isolates used in this study; N10-01734 (clinical isolate); 09ACD005 (typical NAP12 isolate); ATCC4325S (hypervirulent reference strain).