Report of an outbreak of *Clostridium difficile* infection caused by ribotype 053 in a neurosurgery unit

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Abstract

Background: We describe an outbreak of *Clostridium difficile* infection (CDI) with ribotype 053, a possible hypervirulent strain that causes outbreaks, in a neurosurgical unit.

Outbreak investigation: The outbreak was investigated by creating a timeline of all toxin positive patients with root cause analysis, supplemented with ribotyping results, hand hygiene and environmental audits. There were five cases of CDI, three caused by ribotype 053 indicating transmission.

Infection prevention measures: These included a short period of ward closure to allow enhanced cleaning, including use of vaporised hydrogen peroxide, isolation of infected patients, reinforcement of hand hygiene, education of all staff on *C. difficile*, reduction of shared bay occupancy from six to four, and addressing staffing levels.

Discussion: The patients with ribotype 053 all had long inpatient stays and had required several courses of broad-spectrum antibiotics for aspiration pneumonia. They also required enteral feeding, which can cause diarrhoea, and during long inpatient stays they had multiple toxin negative faecal samples making clinical diagnosis of CDI difficult. Hence they were not isolated promptly, leading to transmission. This is the first reported outbreak of *C. difficile* ribotype 053 in the UK and highlights the unique aspects of an outbreak in neurosurgical patients.

Keywords

Clostridium difficile, healthcare-associated infection, infection control, outbreak

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Introduction

Clostridium difficile infection (CDI) is caused by toxigenic strains of *C. difficile*, generally after the gut flora has been disturbed by antimicrobial use. Over 300 distinct PCR ribotypes have been recorded in Europe, and some specific ribotypes – notably ribotype 027 – have been associated with increased virulence and propensity to cause outbreaks (McDonald et al, 2005). We report an outbreak of CDI in a neurosurgical ward in November 2011, with *C. difficile* 053 as the predominant ribotype, which has not been reported in the U.K. or Republic of Ireland previously.

Methods

Setting

Our teaching hospital has 775 inpatient beds for most acute medical and surgical specialties. The regional neurosurgical

unit for Northern Ireland is a 23-bed ward with three six-bed bays and five side-rooms. The hospital's infection prevention and control team comprises five whole time equivalent

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Figure 1. Timeline with *Clostridium difficile* toxin test results.

(WTE) infection control nurses (ICN) and 0.4 WTE infection control doctor.

At the time of the outbreak all faecal specimens from adult intensive care patients, patients above 65 years of age, and outside these categories, on clinical request were tested for *C. difficile* toxin. The number of *C. difficile* toxin cases per 1,000 patient bed days from November 2010 to October 2011 was 0.42 and 0.47 for the hospital and neurosurgical ward respectively. From November 2011 to October 2012 it was 0.34 and 0.50 respectively. More recently from November 2012 to October 2013 it was 0.34 and 0.00 respectively.

Case definition and laboratory methods

A case of CDI was defined as a patient with diarrhoea who had tested positive for *C. difficile* toxin and had *C. difficile* isolated from conventional culture. Samples from patients with symptoms of diarrhoea were tested for *C. difficile* toxin using the Premier *C. difficile* Toxin A&B microplate enzyme immunoassay (EIA) (Meridian Bioscience Inc., Cincinnati, OH). One patient with ribotype 053 from the

cluster was transferred to another hospital, where their faeces was tested with *C. Diff* Quik Chek Complete (Techlab, Blacksburg, VA), a membrane bound immunoassay that tests for both toxin and glutamate dehydrogenase (GDH). Positive samples were cultured for *C. difficile* according to the UK's National Standard Method at the time (Health Protection Agency (HPA), 2008a). Isolates were tested for the presence of toxin genes using PCR and were ribotyped (Persson et al, 2008; Indra et al, 2008a). Isolates were identified by comparison to a panel of reference strains circulated by the European Centre for Disease Prevention and Control in November 2010.

Detection of an outbreak of CDI

The first indication of an outbreak of CDI came when four patients (patients 1, 2, 3 and 4) in two adjoining six-bed bays in the neurosurgical unit developed symptoms and tested positive for *C. difficile* toxin. Subsequently, after transfer from one of these bays to another hospital patient 5 tested positive for GDH and *C. difficile* toxin (Figure 1).

Table 1. Table of patient characteristics and laboratory results.

Patient details	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Sex	F	F	F	M	M
Age (years)	31	67	59	63	30
Diagnosis	Post-surgical meningitis	Meningioma resection	Brain haemorrhage	Subdural haematoma	SAH Fracture fixation
Source of admission	Direct transfer from another hospital's A&E	Transfer from another hospital	Direct transfer from another hospital's A&E	Home	Home
Antibiotics pre-CDI	Ceftriaxone & metronidazole	Tazocin	Tazocin Meropenem	Tazocin Meropenem	Levofloxacin Tazocin Meropenem
Anti-ulcer medication	PPI	PPI	PPI	PPI	Ranitidine
Enteral feeding	None	NG	PEG	PEG	PEG
Outcome	Discharged	Died	Discharged	Died	Transferred to another hospital
Premier toxin test	Positive	Positive	Positive	Positive	GDH & toxin positive ¹
<i>C. difficile</i> ribotyping	002	014	053	053	053

SAH=subarachnoid haemorrhage; A&E=accident and emergency; CDI=*Clostridium difficile* infection; PPI=proton-pump inhibitor; NG=nasogastric feeding; PEG=percutaneous endoscopic gastrostomy; GDH=glutamate dehydrogenase.

¹GDH and toxin positive by Techlab C.diff Quik Chek Complete.

Results

Patients' characteristics and laboratory results

In the cluster there were in total five cases of CDI, of which three patients had *C. difficile* ribotype 053, indicating transmission. This met the definition of an outbreak, i.e. two or more cases caused by the same strain related in time and place over a defined period that is based on the date of onset of the first case (HPA, 2008b). Of the other two cases, one had ribotype 014 and the other had ribotype 002. All patients were treated according to hospital treatment guidelines for CDI. Details and laboratory results of the patients are summarised in Table 1.

Infection control measures

An outbreak control team consisting of infection prevention and control nurses, doctors, managers, neurosurgeons, nurses, domestic staff and public relations personnel was convened. The outbreak was investigated by creating a timeline of all toxin positive patients with a root cause analysis of each case, supplemented with ribotyping. The root causes were felt to be: not isolating patients with potentially infectious diarrhoea, low hand hygiene compliance and environmental contamination. To resolve these issues, *C. difficile* toxin positive patients were isolated in

side-rooms, hand hygiene educational sessions and audits were carried out, and enhanced environmental cleaning measures were implemented.

Ward reconfiguration, closure, cleaning and environmental disinfection

The neurosurgical ward was closed to admissions for five days to facilitate de-cluttering, reusable equipment cleaning and environmental disinfection. The frequency of cleaning of the ward by domestic staff was increased from twice a day to four times a day. Environmental cleaning and decontamination of reusable equipment was carried out with a hypochlorite based product Actichlor Plus® (Ecolab Ltd, Leeds, England) 1,000 parts per million available chlorine. This cleaning was followed by vaporised hydrogen peroxide (VHP) cleaning of each bay and side-room during the ward closure. Due to staff reporting adverse upper respiratory effects and for ease of use, Actichlor Plus® (Ecolab Ltd, Leeds, England) was replaced with a chlorine dioxide disinfectant DIFFICIL-S® (Clinimax Ltd, Suffolk, England). Bed screen curtains from bay areas were all changed. Cleaning compliance was audited by the infection and prevention control nurses using standardised audit tools.

The ward changed from six-bed bays to mostly four-bed bays to increase space between beds and to have one hand

wash basin for four patients. Unfortunately because of bed pressures it was only possible to sustain this for a few months. More nursing staff were recruited.

Infection prevention and control input

Patients with suspected CDI were isolated in side-rooms with dedicated en-suite toilets. Health care staff utilised contact precautions, which included the use of personal protective equipment such as gloves and disposable plastic aprons for patient care while in the room of a patient with CDI. Hand washing using soap and water instead of alcohol gel, was mandatory and checked for in hand hygiene audits. There was no cohorting of patients and no one-to-one nursing.

Refresher educational sessions on *C. difficile*, including demonstration of correct hand hygiene techniques, aseptic non-touch technique, and use of personal protective equipment, were held by the ICNs for neurosurgical nursing and medical staff. Hand hygiene audits in November 2011 carried out by the ICNs and in January 2012 by ward staff, showed a sustained improvement from 50% to 100% compliance.

Antibiotic management

Weekly antimicrobial stewardship ward rounds with a medical microbiology consultant, antimicrobial pharmacist and a senior neurosurgical doctor were initiated. These rounds did not find many instances of inappropriate antimicrobial use. No changes were made to the antimicrobial prophylaxis for neurosurgical procedures or to antimicrobial guidance for the ward.

Discussion

In an Austrian hospital experiencing a cluster of severe cases of CDI, 10 out of 22 cases were caused by ribotype 053 (Indra et al, 2008b). The same group reported patient care-associated CDI due to ribotype 053 in a 24-year-old nurse caring for patients with symptomatic CDI (Hell et al, 2009). Because of these features ribotype 053 was felt to be highly transmissible, hypervirulent and a cause of CDI outbreaks.

Some neurosurgical patients have complex dependency needs which require intensive manual handling and nursing care, making it difficult to consistently maintain good infection control precautions, particularly when staffing levels were 60% of the quota required for the ward at the time of the outbreak. They are also at risk of aspiration, leading to aspiration pneumonia, requiring broad-spectrum antimicrobial treatment, which is a risk factor for CDI. To reduce this risk of aspiration these patients receive enteral feeding. A proportion of patients on enteral feeds will develop diarrhoea due to their feeds and it is difficult to

distinguish from diarrhoea secondary to CDI (Whelan and Schneider, 2011). Enteral feeding has been associated with increased risk of CDI (Bliss et al, 1998). The three cases of CDI with ribotype 053 had percutaneous endoscopic gastrostomy (PEG) tubes in-situ. Endoscopy unit practices were excluded from review because cases were closely associated with the neurosurgical unit. During their long inpatient stays they had multiple faeces samples (14 in total) which tested *C. difficile* toxin negative and two had gastroenterology consultations. However CDI had been felt to be less likely due to these *C. difficile* toxin negative results. The difficulty of diagnosing CDI because of these factors may have led to a delay in isolation of these patients causing contamination of the environment leading to transmission contributing to the outbreak.

To prevent this there has been the introduction of a hospital-wide policy, that if a patient is suspected of infectious diarrhoea, they must be isolated in a side-room, which should reduce transmission to other patients. Coincidentally the laboratory has introduced testing for GDH as well as *C. difficile* toxin as per national guidelines (Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI), 2012).

Additional typing using multilocus variable-number tandem repeat analysis may be required to confirm that cases involving common ribotypes are likely to be related, to avoid incorrect associations (Fawley et al, 2011). Northern Ireland is unique in that all *C. difficile* toxin-positive specimens within the region are cultured, and all cultured isolates are ribotyped. The three ribotype 053 isolates reported here were the only 053 strains isolated in Northern Ireland between April 2009 and December 2011, out of ~2,600 ribotyped isolates. Given the rarity of this ribotype and the clear epidemiological links between the cases, ribotyping data was felt to be sufficient to confirm that these three cases were part of an outbreak.

In conclusion this report describes an outbreak of ribotype 053 on a neurosurgical ward. The first two cases of CDI, with non-053 ribotypes, highlighted a problem with CDI on the ward which led to isolation of patients and ward closure with environmental cleaning, which brought this outbreak under control.

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Declaration of conflicting interests

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References

- Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (2012) *Updated Guidance on the Diagnosis and Reporting of Clostridium difficile*. London: ARHAI, Department of Health.
- Bliss DZ, Johnson S, Savik K, Clabots CR, Willard K and Gerding DN (1998) Acquisition of *Clostridium difficile* and *Clostridium difficile*-associated diarrhea in hospitalized patients receiving tube feeding. *Annals of Internal Medicine* 129(12): 1012–1019.
- Fawley WN and Wilcox MH; *Clostridium difficile* Ribotyping Network for Enland and Northern Ireland (2011) An enhanced DNA fingerprinting service to investigate potential *Clostridium difficile* infection case clusters sharing the same PCR ribotype. *Journal of Clinical Microbiology* 49(12): 4333–4337.
- Health Protection Agency (2008a) *Processing of faeces for Clostridium difficile*. National standard method BSOP 10. London, UK: Health Protection Agency.
- Health Protection Agency (2008b) *Clostridium difficile Infection: How to Deal with the Problem*. London, UK: Health Protection Agency.
- Hell M, Indra A, Huhulescu S and Allerberger F (2009) *Clostridium difficile* infection in a health care worker. *Clinical Infectious Diseases* 48(9):1329.
- Indra A, Huhulescu S, Schneeweis M, Hasenberger P, Kernbichler S, Fiedler A, Wewalka G, Allerberger F and Kuijper EJ (2008a) Characterization of *Clostridium difficile* isolates using capillary gel electrophoresis-based PCR ribotyping. *Journal of Medical Microbiology* 57(pt 11): 1377–1382.
- Indra A, Schmid D, Huhulescu S, Hell M, Gattringer R, Hasenberger P, Fiedler A, Wewalka G and Allerberger F. (2008b) Characterization of clinical *Clostridium difficile* isolates by PCR ribotyping and detection of toxin genes in Austria, 2006–2007. *Journal of Medical Microbiology* 57(pt 6): 702–708.
- McDonald LC, Killgore GE, Thompson A, Owens RC Jr, Kazakova SV, Sambol SP, Johnson S and Gerding DN (2005) An epidemic, toxin gene-variant strain of *Clostridium difficile*. *New England Journal of Medicine* 353(23): 2433–2441.
- Persson S, Torpdahl M and Olsen KEP (2008) New multiplex PCR method for the detection of *Clostridium difficile* toxin A (tcdA) and toxin B (tcdB) and the binary toxin (cdtA/cdtB) genes applied to a Danish strain collection. *Clinical Microbiology Infection* 14(11): 1057–1064.
- Whelan K and Schneider SM (2011) Mechanisms, prevention, and management of diarrhea in enteral nutrition. *Current Opinion in Gastroenterology* 27(2): 152–159.