Burkholderia cenocepacia ET12 transmission in adults with cystic fibrosis

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ABSTRACT

This report describes transmission of a *Burkholderia cenocepacia* ET12 strain (ET12-Bc) at the Toronto Adult Cystic Fibrosis (CF) Centre occurring from 2008 to 2017. Epidemiological and genomic data from 11 patients with CF were evaluated. Isolates were analysed using whole genome sequencing (WGS). Epidemiological investigation and WGS analysis suggested nosocomial transmission, despite enhanced infection control precautions. This was associated with subsequent deaths in 10 patients. ET12-Bc positive patients are no longer cared for on the same unit as ET12-Bc negative patients.

BACKGROUND

Infection with *Burkholderia cenocepacia*, particularly the ET12 epidemic strain (ET12-Bc), has been associated with patient-to-patient transmission,[1] accelerated lung function decline and earlier mortality in persons with cystic fibrosis (CF).[2] Current infection prevention and control (IPAC) guidelines recommend gowns and gloves use for healthcare workers caring for CF patients; segregation of patients according to *Burkholderia cepacia* complex (Bcc) infection status is not currently recommended.[3] We evaluated the epidemiology of ET12-Bc acquisitions and their clinical outcomes in an adult CF clinic in relation to IPAC practices.

METHODS

We identified all adults with CF who were diagnosed with their initial infection with ET12-Bc at the Toronto Adult CF Centre between 2008 and 2017. Whole genome sequencing (WGS) was performed (see online supplementary material) on isolates from these patients as well as on isolates from patients previously infected with ET12-Bc who had overlapping hospital admissions with the newly infected patients.

RESULTS

In total, 37 patients had new-onset of Bcc infection between 2008 and 2017 and 11 of these infections were due to ET12-Bc. By comparison, 23 patients became infected with Bcc between 1998 and 2007, with five of these being due to ET12-Bc (see online supplementary material). Ten of the 11 patients newly infected with ET12-Bc had a hospital admission within the 60 days prior to their first ET12-Bc positive sputum culture, and all 11 patients were admitted to the CF unit at the same time as patients known to be previously infected with ET12-Bc (figure 1). Patient characteristics are summarised in table 1. Ten of the 11 patients died within 3 years of infection. The surviving patient received 245 days of intravenous antibiotics in the 12 months after acquisition. The relatedness between strains is shown in a phylogenetic tree (figure 2). WGS analysis supported the epidemiological investigation, together suggesting transmission between the five patients with ET12-Bc acquisition in 2008 and the cohospitalised patient known to be ET12-Bc infected (known positive patient A). Findings also supported transmission between patient 9 and known positive patient F, as well as patient 10 and patient 11 and known positive patient G.

DISCUSSION

Epidemiological data were consistent with nosocomial transmission of ET12-Bc in all 11 new acquisition cases between 2008 and 2017. WGS was suggestive of nosocomial transmission of ET12-Bc in at least eight newly positive patients. New onset ET12-Bc acquisition led to early mortality in the majority of patients and significant morbidity in the one surviving patient.

IPAC measures used at the Toronto CF Adult Center are described in online supplementary material. Of note, universal hand hygiene was already in place since the early 1990s. In 1992, segregated outpatient clinics (occurring on a separate day for ET12-Bc positive patients) were established. However, all patients continued to be admitted on the same inpatient CF ward, consisting of 12 rooms. Patients are encouraged to remain in their rooms, with closed doors. If they step out of the room, they must be at least 2 m apart from other CF patients and wear a medical mask. Most patient rooms are not under negative pressure but all rooms have six air exchanges per hour. The rooms and equipment cleaning methods did not change during the study period. The occurrence of 5-new ET12-Bc positive in 2008 triggered a change in IPAC policies (prior to the publication of the new CF IPAC guidelines[3]) including universal gowning and gloving by healthcare workers, in addition to stringent recommendations that patients completely avoid social contact in common areas. Despite these measures, there have been six additional acquisitions of ET12-Bc from 2009 onward.

Transmission may have occurred through improperly disinfected equipment and/or environmental contamination on the ward, healthcare worker non-adherence with hand hygiene or lack

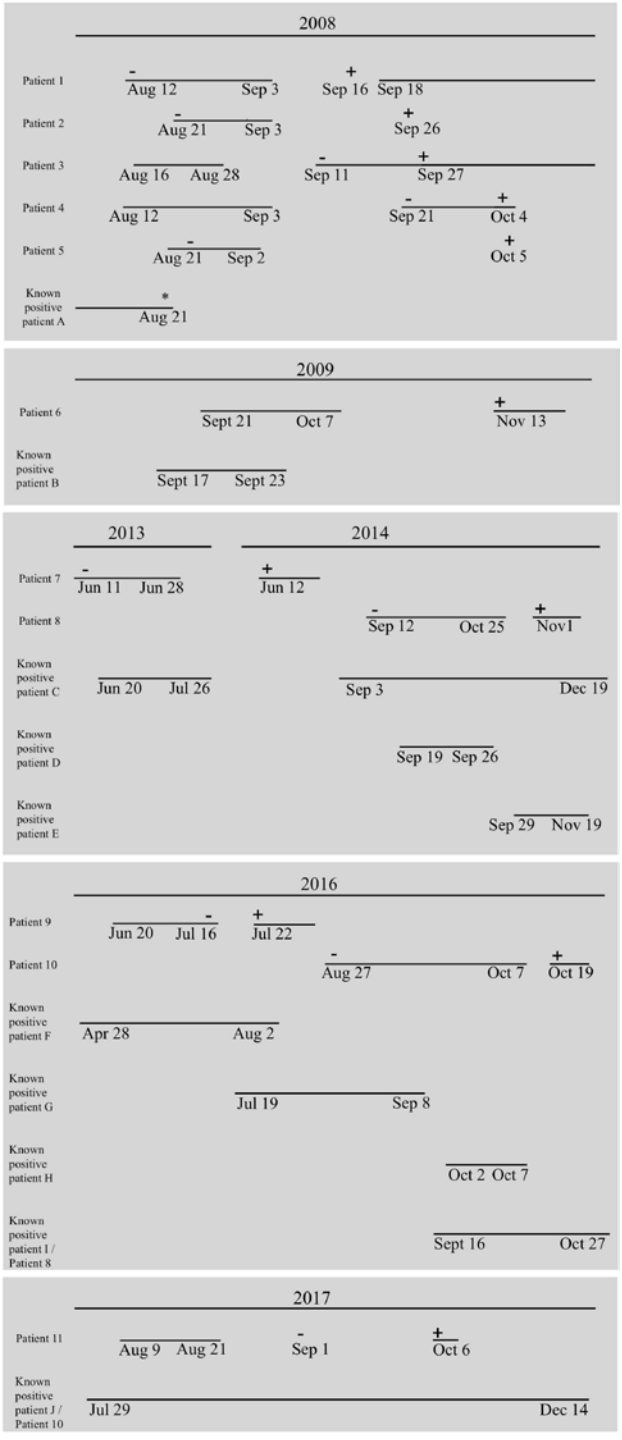

Figure 1 Overlapping inpatient stays for suspected hospital-acquired ET12-Bc cases (2008–2017). –Last negative culture. +First positive culture. *Resuscitation event on Ward. -----Admission to hospital. *The 2008 cluster had the largest number of patients with new acquisition of ET12-Bc co-admitted at the same time. During that summer, a known positive patient A had a clinical event requiring resuscitation on the ward, five new ET12-Bc acquisitions occurred 5–8 weeks later. Newly positive patient four shared a nurse with the known positive patient and all of the five patients with new acquisition shared nursing assignments at some point during their admission. Note: Newly positive patient 8 (2014) and new-patient 10 (2016) had overlapping hospital admissions with three known positive patients. Both these new patients subsequently became contacts of other new acquisition cases (known positive patients I and J) in 2016 and 2017.

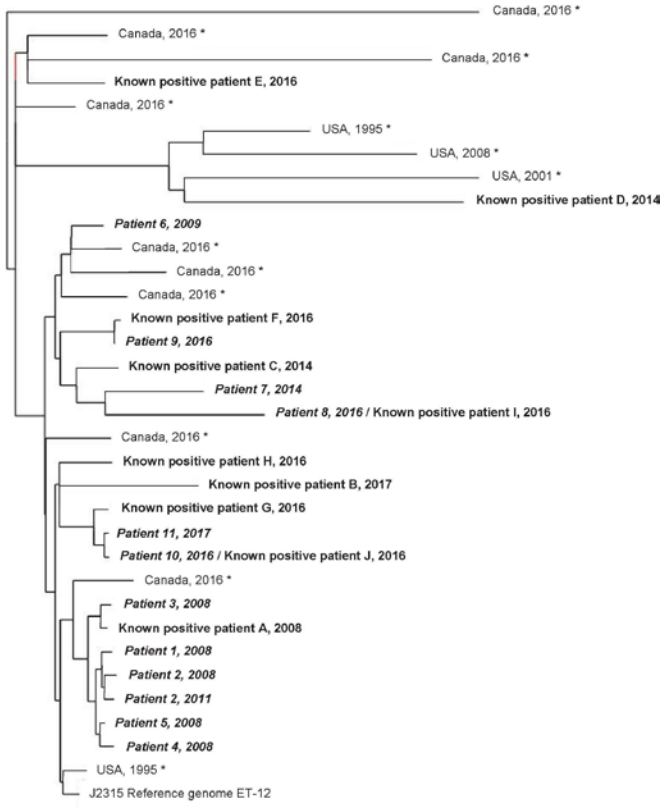

Figure 2 Phylogenetic tree based on whole genome sequences of ET12-Bc isolates: each branch is labelled with the source and the year the sequenced isolate was recovered in culture.

of patient adherence to social distancing recommendations. Of note, pulmonary function testing is done in the patient's room using a portable machine and equipment is cleaned after each test using hydrogen peroxide wipes. Previous studies have documented the presence of several virulence factors contributing to transmissibility and persistence of *B. cenocepacia* in the environment.[4 5] Cleaning techniques are not assessed systematically on the ward and Bcc can survive for prolonged periods of time on surfaces and resist to disinfectants.[6] In addition, respiratory pathogens in patients with CF can be aerosolised by coughing up to 4 m of distance and remain viable for up to 45 min, suggesting possible airborne transmission.[7 8] Infection may also have been transmitted directly via healthcare workers. Of note, in 2008, the five new-onset acquisitions occurred after known positive patient A had a resuscitation event requiring acute nursing and medical response. At the Toronto Adult CF Center, hand hygiene adherence has been routinely audited by direct observation since 2010. Adherence rates before and after patient contact were: 83% and 88% in 2014; 75% and 89% in 2016; as well as 92% and 97% in 2017. Since 2015, nursing assignments have not been shared between Bcc-positive and Bcc-negative patients.

Given the recognition of ongoing nosocomial transmission of ET12-Bc despite adherence to recommended infection control practices for a CF unit, we began segregating ET12-Bc positive and ET12-Bc negative patients as of May 2018. Currently, all Bcc negative and Bcc positive but ET12-Bc negative patients receive inpatient care on a dedicated CF unit. ET12-Bc positive patients are cared for on a different non-CF ward. Since the implementation of this policy, no new cases of potential nosocomial ET12-Bc have been identified.

Table 1 Patient characteristics and clinical outcomes

Patient	Year of acquisition	Age at first+culture	Sex	Pancreatic insufficiency	CF- related diabetes	FEV_1 % pred at first positive culture	Days from first+culture to death	Outcome
1	2008	32	M	Yes	Yes	28	55	Death
2	2008	21	F	Yes	No	21	1154	Death
3	2008	76	F	No	No	36	37	Death
4	2008	21	M	Yes	Yes	21	90	Death
5	2008	26	F	Yes	No	60	104	Death
6	2009	33	F	Yes	Yes	61	676	Death
7	2014	29	F	Yes	No	28	711	Death
8	2014	39	F	Yes	No	36	1364	Death
9	2016	32	M	Yes	No	38	–	Alive
10	2016	18	F	Yes	No	37	654	Death
11	2017	18	F	Yes	No	39	93	Death
Median		29 (range: 18–73)				36 (range: 21–61)	379.5 (range: 36–1137)	

1st+culture: first positive respiratory tract culture.
FEV_1 % pred: forced expiratory volume in 1 second % predicted.
CF, cystic fibrosis.

This study had some limitations including the facts that a limited number of isolates was analysed for each patient and that isolates were not always collected at the time of suspected transmission. In addition, contact between patients outside the hospital setting was not known.

In conclusion, this study shows significant clinical impacts of ET12-Bc infection and highlights ET12-Bc transmission in hospital despite adherence to current CF IPAC guidelines.

Contributors ET, VJW and ACB planned the study. ACB performed a chart review to collect clinical data and obtained information regarding the epidemiological investigation from LT and MM. TS and JJL who had performed whole genome sequencing analyses, provided scientific interpretations of the results. ACB wrote the manuscript. LT, MT, MM, TS, JJL, VJW and ET reviewed the manuscript and provided feedback. ACB and ET are the guarantors of the overall content of this study.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Approved by the St Michael's Research Ethics Board (REB#18-100).

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