CASE REPORT

Cepacia-like syndrome caused by
Burkholderia multivorans

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The variable severity of Burkholderia cepacia complex infections in cystic fibrosis (CF) has recently been ascribed to differences in the virulence between genotypes. Specifically, genovar III isolates have been associated with higher transmission rates and adverse outcomes compared to other B cepacia genovars, and consequently further segregation between genovar III and non-genovar III B cepacia infected patients is advocated in some centers. The important role of non-genovar III isolates is presented in the context of a clinical case whereby a patient with long-standing pulmonary infection with B multivorans developed bacteremic infection reminiscent of the fatal 'cepacia syndrome'.

Key Words: Burkholderia; Cepacia syndrome; Cystic fibrosis; Genovar

Burkholderia cepacia (previously known as Pseudomonas cepacia) complex consists of nine species that, based on molecular differences, are divided into genovars of which only some have received species names (1,2). B cepacia complex was first reported as a human pathogen in the 1960s, and until the mid-1980s case reports were sporadic and mainly limited to ill, chronically hospitalized patients (3). In 1984, the clinical impact of B cepacia complex in cystic fibrosis (CF) patients was first published (4). As well, nosocomial B cepacia complex outbreaks are being reported with increasing frequency from hemodialysis (HD) units (5). Therapy with aminoglycosides, β-lactams is ineffective and in-vitro susceptibilities often don't correlate with in-vivo activity, complicating successful treatment (6,7). These bacteria can also survive in commonly used antiseptic solutions (8).

In CF, acquisition of B cepacia complex results in increased morbidity and mortality (4,9). Consequently, segregating B cepacia complex positive and negative patients has become standard of care (9,10). CF patients with B cepacia complex are frequently categorized into one of three clinical syndromes: 1) infection/colonization without change in pulmonary status, 2) infection with accelerated pulmonary decline and 3) acute pulmonary deterioration with bacteremia, necrotizing pneumonia, leukocytosis, and death within weeks to months. The latter has been named 'cepacia syndrome' (4). A recent study suggests genovar III B cepacia is responsible for cepacia syndrome (11).

CASE PRESENTATION

A 60-year-old man was diagnosed with CF at age 48 (genotype F508/unknown) after a chronic history of cough and diabetes with associated nephropathy. Surveillance sputum cultures grew B cepacia complex five years after CF was diagnosed. His respiratory status remained stable for the next six years. Pulmonary exacerbations were infrequent (less than two per year) and responded to oral antibiotics. Past medical history was significant for allergic bronchopulmonary aspergillosis requiring steroids, gout and moderate exocrine pancreatic insufficiency.

Within the six months before expiring, he had four hospital admissions for pulmonary exacerbations that failed oral antibiotic treatment and required intravenous broad-spectrum antibiotics. Serial chest imaging demonstrated persistent bronchiectasis, fleeting infiltrates and a left upper lobe consolidation with progressive diffuse opacities developing in multiple lobes. Bronchoscopy only showed thick secretions. Sputum cultures grew Staphylococcus aureus, B cepacia complex, Acinetobacter baumannii complex, Haemophilus species and vri...
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dans streptococci. His stable renal function began to decline rapidly during this time, requiring urgent HD after an episode of uremic encephalopathy. A tunneled central venous catheter (CVC) was placed for routine HD. Shortly thereafter he experienced a severe pulmonary exacerbation associated with fever and leukocytosis. Peripheral and CVC blood cultures grew S aureus and B cepacia complex, the latter only susceptible to trimethoprim-sulfamethoxazole, which was administered along with ceftazidime, piperacillin/tazobactam and vancomycin. The S aureus bacteremia cleared promptly with antibiotic treatment. Respiratory failure and B cepacia complex bacteremia persisted despite treatment and CVC removal. He died four weeks later.

METHODS/RESULTS

B cepacia complex isolates from both blood and sputum were typed using recA primers as previously described (12). Earlier sputum isolates had been tested at the Burkholderia cepacia Research Laboratory and Repository at the University of Michigan (J LiPuma, personal communication). Every isolate was B multivorans (genomovar II).

DISCUSSION

Our patient had sputum cultures persistently growing B multivorans for five years and subsequently developed a cepacia-like syndrome after CVC placement. B multivorans bacteremia is not unheard of in the CF community. An outbreak of highly transmissible B multivorans isolates was seen in a CF centre in Glasgow and fatal "cepacia syndrome" caused by B multivorans has been observed in a patient in Manchester, England (J Govan, A Jones, personal communication).

Nevertheless, a Canadian group recently reported molecular epidemiological evidence that genomovar III isolates are more highly transmissible and are associated with increased morbidity and mortality compared with non-genomovar III isolates (11). Furthermore, they describe several patients where B multivorans was replaced with a genomovar III strain. The opposite did not occur in their population. Based on these findings, they recommend further segregation between B cepacia complex positive patients based on genomovar status. Another observation by this group was that B multivorans infection was predominantly in younger patients. In contrast, our patient was older and experienced a fatal clinical course once B multivorans bacteremia occurred. Clearly our patient suffered from other chronic comorbidities predisposing him to serious infection; however, the temporal association between CVC placement and subsequent persistent B multivorans bacteremia with progression to a cepacia-like syndrome support the important role of B multivorans in this syndrome.

Clinical studies exist whereby the relationship between CVC and B cepacia complex bacteremia has been studied. In a recent report of an outbreak of CVC-related B cepacia complex bacteremia in nine non-CF patients undergoing HD, the source was a disinfectant solution (5). Antibiotic therapy based on in vitro susceptibility testing did not result in clinical improvement or resolution of bacteremia until the CVCs were removed. Another longitudinal, retrospective analysis in non-CF patients with B cepacia complex bacteremia identified prolonged intensive care unit stay associated with CVC placement as the most common predisposing condition. All patients with CVC removal cleared the infection, but mortality was 20% if the CVC was not removed (13). Additional studies confirm that indwelling CVC was the most significant risk factor for acquisition of B cepacia complex bacteremia and for a poor prognosis if not removed (6). Unfortunately, none of these studies identified isolates by genomovar or included CF patients.

Persistent B multivorans bacteremia in our patient was surprising given that 1) CF patients with B cepacia complex bacteremia and associated respiratory failure are usually infected with genomovar III and 2) CVC-associated B cepacia complex bacteremia, even when polymicrobial, should respond favourably after CVC removal. Nevertheless B multivorans bacteremia, refractory pulmonary failure, fever and death occurred despite CVC removal.

CONCLUSION

It appears that the clinical features of cepacia syndrome are not restricted to a single genomovar, because we and others have identified CF patients with severe and fatal B multivorans infections. This is in distinct contrast to the Canadian findings that B multivorans is not highly pathogenic.

As more CF patients survive into adulthood and acquire B cepacia complex infection, clinicians will be challenged with age-related comorbidities in a population with a chronic disease that was once limited to childhood. B cepacia complex-infected CF patients, even with a strain thought to be "less virulent", can have a clinical course reminiscent of cepacia syndrome, and perhaps are at most risk after a foreign intravascular body is placed. We advocate that caregivers make every effort to avoid CVC placement or minimize duration and choose alternatives (ie, peritoneal dialysis, arterial-venous fistula) in managing renal failure, if possible, in this patient population.

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REFERENCES

of Pseudomonas cepacia by social contact in cystic fibrosis. Lancet 1993;342:15-9.