

## Case report

***Burkholderia cepacia* complex infection complicating long-term urethral catheterisation**Olayinka Ayodele Ogundipe,<sup>1</sup> Rebecca Claire Pearson,<sup>1</sup> Amy Campbell<sup>2</sup><sup>1</sup>Department of Medicine of the Elderly, Royal Infirmary of Edinburgh, Edinburgh, UK<sup>2</sup>Department of Medicine of the Elderly, Borders General Hospital, Melrose, Scotland, UK**Correspondence to**Dr Amy Campbell;  
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**SUMMARY**

This report describes a 79-year-old Caucasian man with a history of syringomyelia, paraplegia and a long-term urethral catheter, presenting with recurrent catheter-related or catheter-associated urinary tract infections (CAUTIs) and persistent delirium. On one occasion, urine cultured bacteria from the *Burkholderia cepacia* complex (BCC). This organism is recognised as being a coloniser of fluid or aquatic settings. However, in certain circumstances (eg, immunosuppression, immunocompromise, multimorbidity), BCC has been recognised to cause infection, that is, rather than merely contamination or colonisation. In this unwell older patient, treatment of the BCC CAUTI was guided by antibiotic sensitivities and microbiology advice. The report incorporates a brief discussion of some relevant microbiological terminology, and refers to associations and commoner sites of BCC-related infection. The report concludes by exploring how three philosophical concepts (Occam's razor, Hickam's dictum and Crabtree's bludgeon) proved relevant in supporting clinical decision-making in this case.

**BACKGROUND**

The *Burkholderia cepacia* complex (BCC) is a group of Gram-negative bacilli with aerobic properties. BCC are often described as organisms of low virulence and colonisers of fluid or aquatic settings.

However, in some contexts (eg, immunosuppression, immunocompromise, extremes of age, poly morbidity and so on), BCC may cause infections. Some reported sites of human infection include lungs (eg, in patients with cystic fibrosis), endocardial tissue, skin, soft tissue, joints, bone, vertebral discs, the genitourinary tract and bacteraemia.

In scenarios where infection (rather than merely colonisation) is considered likely, treatment may be required. As the organisms can be antibiotic resistant, guidance on treatment is recommended via microbiology, infectious diseases or equivalent services.

This case report is of interest to community and hospital-based generalists, as it offers an important clinical lesson on a condition (BCC-related infection) with which non-microbiologists may not be familiar.

**CASE PRESENTATION**

A 79-year-old man initially presented to hospital with delirium, fever and signs of a catheter-associated urinary tract infection (CAUTI). He

had undergone a curative left lower lobectomy for lung cancer some 20 years prior. In the year preceding this acute admission, his notable medical history included chronically reduced mobility in the context of chronic back pain and orthostatic hypotension. He had developed constipation, urinary retention and paraplegia. These features had been collectively diagnosed earlier, with subsequent treatment for a thoracic syrinx and an associated T8 (thoracic vertebral) level epidural collection. There had been no evidence (on radiological imaging) to suggest either coexistent 'normal' pressure hydrocephalus, or a Chiari type malformation. The aetiology of the syringomyelia (syrinx) had not been established. He had required a T9 laminectomy and a period of cerebrospinal shunting. Over time, he had developed pressure ulceration to his sacral area and left heel.

In the 6 months preceding this admission, CT and MRI scans had confirmed left ischial tuberosity osteomyelitis secondary to the sacral pressure ulcer. Guided by medical microbiology and orthopaedic advice, the osteomyelitis had been successfully managed non-operatively during a previous admission. Management at that time had comprised an initial empirical 1 month course of intravenous vancomycin followed by a 2-week course of oral cotrimoxazole.

On presentation, his regular medications included amlodipine, finasteride, lisinopril, morphine sulfate modified release, omeprazole, paracetamol, pregabalin, senna and zolpidem. He took occasional over-the-counter medications (multivitamins), but did not take any complementary medicine.

Occupational history noted that he was a retired heavy goods vehicle driver, but there had been no definite association to previous trauma (as a possible cause of the syringomyelia). Social and travel histories were unremarkable. He was an ex-smoker and alcohol intake was minimal. Functionally, and on account of the paraplegia, his bed-to-chair transfers were self-accomplished manoeuvres using a banana board. He employed a self-propelling wheelchair for assisted mobility. Due to the spinal problems and chronic neurogenic urinary retention, he required long-term urethral catheterisation.

On admission, the main clinical problems were signs of a delirium; periodic left upper limb neuropathic-sounding pain, but with preserved upper limb muscle strength; dense paraplegia; presence of saddle anaesthesia; faecal incontinence; a grade 4 sacral pressure ulcer; a grade 2 left heel pressure ulcer; and a probable CAUTI. There was



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no worsening of his chronic back pain nor clinical suggestion of discitis. There were no clinical signs to suggest septic arthritis, meningitis or endocarditis. There were no vasculitic lesions nor other mucocutaneous eruptions.

### INVESTIGATIONS

#### General haematology, biochemistry and immunology

Haemoglobin of 95 g/L (reference 135–180), mean corpuscular volume 81 fL (reference 78–98). There was mild lymphopenia  $1.44 \times 10^9/L$  (reference 1.5–4), and mild eosinophilia of  $0.47 \times 10^9/L$  (reference 0.04–0.4). Other blood count parameters were normal.

Iron studies were consistent with anaemia of chronic disease. Serum B<sub>12</sub>, folate, electrolytes, urea, urate and glucose were normal. Serum C reactive peptide was 31 mg/L (reference 0–5). Liver and thyroid function tests were normal.

Serum immunoglobulins and myeloma screen noted the presence of a known and non-progressing IgG lambda paraproteinemia of <1 g/L. A screen for Bence-Jones protein was negative. Coeliac screen serology (IgA anti-tTG) was negative.

#### Radiology

##### Chest X-ray

‘Cardiac and mediastinal contours normal with clear lung fields. Visible bony skeleton and pleural spaces intact. No free air’.

##### Abdominal X-ray

‘Faecal loading of colon, with an otherwise unremarkable bowel gas pattern’.

##### MRI whole spine with gadolinium

‘Comparison is made to a previous study from one year prior. The MRI showed a normal craniocervical junction. Normal appearance of the cord from the craniocervical junction to the level of C6. At this level, there is a large (non-enhancing) syrinx, which extends to the conus. The proximal end of the syrinx was previously at T2. Previously, the syrinx extended from T2 to the conus. The central fluid component has increased, especially in the region of the thoracic spine. There is no change in the appearance of the small epidural fluid collection at T8. There are multilevel mild degenerative changes but no focal neural exit compression. Summary opinion: Compared to the previous study one year prior, the proximal extent of the syrinx has extended to the C6 level. There are no other significant changes’.

#### Microbiology

##### Catheter specimen of urine

##### Initial cultures (~1 month apart)

Grew *Klebsiella* spp and *Proteus* spp, respectively, which had individually reported microbiological sensitivities to gentamicin and amoxicillin.

##### Later cultures (~6 weeks after the second of the ‘initial cultures’)

Grew BCC >100 000 cfu/mL. Antibiotic sensitivity was listed to ceftazidime, cotrimoxazole and meropenem. A microbiology comment was added to the formal report: ‘Treatment of catheter associated bacteriuria is not recommended unless the patient is systemically unwell. If antibiotic therapy is initiated the catheter should be replaced/removed before or as soon as possible after starting therapy. Please review need for continued catheterisation and only send urine for culture in catheterised patients if there are features of systemic infection’.

#### Blood cultures (multiple sets)

Negative.

##### Sacral wound swabs

##### Initial cultures

*Staphylococcus aureus* sensitive to oral flucloxacillin.

##### Later cultures

Colonisation with *Enterococcus faecalis*, *Proteus mirabilis* and *Klebsiella pneumoniae*.

### DIFFERENTIAL DIAGNOSIS

The diagnostic workup included:

1. Delirium—of probable multifactorial aetiology.
  - The notable risk factors were a tendency to recurrent infections, blockage of the urethral catheter, constipation, intermittent neuropathic pain/dysaesthesia to the left upper limb and polypharmacy.
2. Multilevel syringomyelia and an associated (non-infective) epidural collection.
  - This had been further complicated by problems of chronic reduced mobility, dense paraplegia, saddle anaesthesia, double incontinence (faecal incontinence + chronic neurogenic urinary retention with overflow incontinence) and pressure-related ulceration of the sacrum and left heel.
  - The presence of new and intermittent left upper limb hyperaesthesia and dysaesthesia was noted. Based on clinical and radiological features, this was attributed to the expanding thoracic syrinx, with spinothalamic tract symptoms. This in turn impacted adversely on his ability to self-transfer, for example, from a bed into wheelchair.
  - There were no clinical or imaging features to suggest the presence of meningitis; formation of an abscess in the spine (or an alternative site); or recurrent malignancy (eg, there was minimal gadolinium enhancement on the MRI). The risk of undertaking a lumbar puncture and cerebrospinal fluid analysis was judged to be too high in the context of his frailty and comorbidities. There was particular concern about the potential infection risk arising from the faecal incontinence and the proximate location of the sacral pressure ulcer.
3. Chronic normocytic anaemia.
  - The abnormal iron studies were supportive of anaemia of chronic disease.
  - Serum B<sub>12</sub>, folate and thyroid function tests were normal.
  - Myeloma screening was unremarkable apart from the known and stable light-chain paraproteinaemia.
  - Serological coeliac screening was normal.
  - There was no suggestion of haemolysis. He was deemed too frail for more invasive tests, for example, bone marrow biopsies or trephine studies.
4. Infected sacral pressure ulcer.
  - During the course of the prolonged admission, he also developed a sacral ulcer infection with *S. aureus*.
  - The presence of infection was marked by pain, redness/erythema and the presence of a purulent exudate.
5. Recurrent CAUTIs.
  - In the early part of the admission, he had become unwell with fever and delirium. Two separate catheter samples grew *Klebsiella* spp and *Proteus* spp, respectively. These initial urine samples were taken ~1 month apart, and

represented separate clinical episodes of symptomatic CAUTIs.

- Thereafter, he developed another distinct episode of acute illness. This was ~6 weeks after the last CAUTI described above. This latter episode was characterised by suprapubic tenderness, haematuria, blockage of the urethral catheter and a further more persistent episode of delirium. At this time, a further urethral catheter specimen of urine grew BCC. Further to microbiological results and consultation with clinical microbiology, and the evolving clinical picture of a persistent delirium the focus was narrowed down to the possibility that this was an active CAUTI due to BCC, rather than merely colonisation.
- The features considered as being against the likelihood of a BCC infection were: the absence of a leucocytosis and/or neutrophilia; and the previously described medical literature status of BCC being more often a colonising organism. A urine dipstick was not undertaken as this is often falsely positive with long-term catheters, and also does not reliably distinguish between the presence of 'colonisation' versus 'infection'.
- In comparison, the features considered as being supportive of a BCC infection were: his clinically unwell status with suprapubic pain, haematuria and the presence of systemic symptoms and signs including persistent delirium; lymphopenia (although possibly non-specific); recent multiple courses of antibiotics (with the possibility of immune modulation); presence of a known light-chain paraproteinemia; and presence of a foreign body (an indwelling urethral catheter which also showed evidence of debris-related blockage).

## TREATMENT

### General treatment modalities

1. He had a period of comprehensive geriatric assessment and concurrent inpatient rehabilitation facilitated by a multidisciplinary team.
2. Nursing, medical and dietetics teams monitored his nutritional assessments.
3. A tissue viability nurse (TVN) specialist coordinated the pressure area management.
4. The chronic constipation was managed with regular oral laxatives, and employing a combination of stool softeners and bowel stimulants. Personal and bowel hygiene was nursing and carer assisted.
5. Targeted oral analgesia reviews and dose modifications were undertaken to optimise the control of mixed-type pain: using paracetamol, regular modified release morphine sulfate, morphine solution (latter for 'as required use' for breakthrough pain) and pregabalin (as a neuropathic agent).
6. The neuropathic pains to his left arm had also been noted to worsen during periods of straining to defaecate. This was attributed to possible association with episodic increases in pressure within the expanding thoracic syrinx, and thereby linked to transmitted pressure along the spinal nerves. The introduction of an oral laxative with additional stool softening properties (macrogol 3350) that is, in addition to his existing use of a prokinetic/stimulant agent (senna) aided the overall pain relief strategy. This non-conventional approach was deemed clinically relevant in this frail patient's context, specifically to allow for use of the lowest possible doses of other medications (morphine and pregabalin) as these could predispose to future episodes of delirium.

### Specific treatment modalities

1. The initial urinary tract infections (UTIs) were treated ~1 month apart, with separate courses of intravenous gentamicin (for the *Klebsiella* spp) and oral amoxicillin (for the *Proteus* spp), based on their individual microbiological sensitivities.
2. A sacral wound infection (*S. aureus*) was treated with a 7-day course of oral flucloxacillin.
3. The BCC-related UTI was treated with a 7-day course of oral cotrimoxazole. A decision to treat followed consultation with medical microbiology to determine the best course of action. The clinical rationale for treatment in this case is as presented in the Differential diagnosis section.
4. The urethral catheter was changed soon after starting treatment. Care was provided within a side-room for temporary isolation and other standard infection control precautions were applied (eg, hand hygiene precautions; barrier and clinical waste disposal precautions and so on).
5. An updated neurosurgery assessment and opinion concluded that the risks of further neurosurgical intervention (for the worsening syringomyelia) were too high in the context of his frailty and poly morbidity. This decision was also informed by the previously noted presence of significant adhesions between the dura and arachnoid spinal layers (at the previous laminectomy), which had required extensive and challenging surgical dissection.

### OUTCOME AND FOLLOW-UP

He responded well to sensitivity-guided antibiotic therapy for the BCC-related CAUTI, the constipation responded to laxatives and the delirium resolved.

The left upper limb dysaesthesia impacted on his ability to continue to self-transfer using a banana board. Consequently, physiotherapy and occupational therapy assessments recommended provision of a Sara Steady transfer aid. The latter device allowed him to continue with use of a self-propelling wheelchair for assisted mobility.

After the prolonged period of inpatient rehabilitation, he was discharged home with supportive services comprising of two carers attending four times a day. Assisted bowel and long-term urethral catheter care was coordinated jointly via the carers and a district nursing team. Ongoing community-based care for the healing pressure ulcers was also supported by the district nursing team, guided by detailed transitional advice provided by the specialist TVN.

## DISCUSSION

### Basic epidemiology, definitions and terminology

UTIs occur commonly both in the community and in hospital inpatients, with *Escherichia coli* being one of the most frequent pathogens.<sup>1</sup> UTIs are the most common hospital-acquired infection, with long-term urethral catheters being a significant risk factor.<sup>2</sup>

A long-term urethral catheter is defined as a catheter remaining in situ for over 28 days. Scottish Intercollegiate Guidelines Network guidelines identifies that all patients with a long-term indwelling urinary catheter will be bacteriuric, meaning that their urine will contain bacteria. It is recognised that the greater the duration of the indwelling catheter, the higher the risk of infection.<sup>2</sup> Zeeshan *et al* state that '*Burkholderia cepacia* is not a common genito-urinary tract infection causing pathogen and is usually introduced after some urological procedures or catheterisation'.<sup>3</sup>

**Table 1** Definitions of colonisation versus infection adapted from Patel<sup>5</sup>

Summary of definitions of terminology used	
Term	Definition
Contamination	The presence of bacteria on the surface of a wound, before multiplication takes place.
Colonisation	The presence of multiplying bacteria in a wound, but with no patient immune response. <sup>16</sup> There is no active disease or ill-health, therefore no signs or symptoms.
Critical colonisation	The point where the patient's immune system is no longer able to control the colonising bacteria in a wound.
Infection	The presence of multiplying bacteria that overwhelms the patient's immune system and results in spreading cellulitis. <sup>17</sup> Active signs and symptoms of disease present.

The presence of *Burkholderia cepacia* in the urine of catheterised patients is often regarded as colonisation.<sup>4</sup> Table 1, taken from Patel,<sup>5</sup> offers definitions of the terms colonisation, infection and important related terminology. Although table 1 illustrates the various definitions with reference to an article referring to wound care, the general terminology and definitions used are broadly relevant to this case. Explanation of the terminology specifically promotes a clearer understanding of how the various terms would apply to other conditions, body sites and samples (eg, urine). *B. cepacia* will generally only be pathogenic to those who are immunocompromised, in addition to hospitalised patients who have received broad-spectrum antibiotics.<sup>1</sup> Antibiotic administration can also alter one's immune defences and therefore potentially have harmful effects.<sup>6</sup>

### History of the pathogen

Initial descriptions of BCC as a pathogen were in the 1960s.<sup>7</sup> It was previously known as *Pseudomonas cepacia*, and was first recognised from the rot of onion bulbs.<sup>8</sup> *B. cepacia* is an aerobic, Gram-negative bacillus, often found in water and soil.<sup>9</sup> The organism is well recognised to cause infection in those with cystic fibrosis and chronic granulomatous lung disease, as well as those with immunocompromise.<sup>8</sup> It has been less well documented as to how these organisms act in those with a normal immune response.<sup>10</sup> However, there have been reports linking BCC to cases of septic arthritis, UTI, spondylodiscitis and osteomyelitis in the immunocompetent.<sup>1-8-10</sup>

### Treatment considerations

Guidelines state that we should not routinely treat those with bacteriuria if they are asymptomatic.<sup>2</sup> In catheterised patients, diagnosing a symptomatic UTI can be more difficult as patients may not present with typical symptoms such as dysuria and frequency. In older patients, they may present non-specifically with symptoms such as new onset confusion (delirium) or fever. Ideally, and where complete removal is not a practical option (eg, dependent on clinical indication), patients should have their long-term catheter changed prior to or soon after commencing antibiotics.<sup>2</sup>

*B. cepacia* can be difficult to treat due to high resistance to antimicrobials. That said it is often sensitive to trimethoprim-sulfamethoxazole combination (cotrimoxazole). However, resistance to these agents is a growing cause for concern.<sup>1</sup> Alternative antimicrobial agents may include meropenem, ceftazidime and some penicillin-based agents (eg, piperacillin, piperacillin-tazobactam and ticarcillin-clavulanate).<sup>4 11 12</sup> Cephalosporins may be a less ideal option as they may increase the risks of *Clostridium difficile* infection in frailer older patients.

### Rationale for treating the index case

As mentioned previously, BCC is normally only considered to be pathogenic in those with immunocompromise, immunosuppression and/or other accompanying risk factors. The risk factors in this case were: multiple medical comorbidities; prolonged hospitalisation; the presence of an indwelling 'foreign body' (a long-term urethral catheter); having received multiple courses of broad-spectrum antibiotics for recurrent UTIs and an infected sacral ulcer (potential immune modulation); and a low level although non-evolving light-chain paraproteinaemia without overt signs of immunosuppression.

The patient had had treatment of UTIs linked to different organisms prior to growth of BCC from a catheter specimen. Although rare, there are previous case reports of BCC-related CAUTI.<sup>12</sup> In the context of persistent delirium and recent haematuria with suprapubic pain and debris-related catheter blockage, a clinical decision was taken to treat the patient for a BCC-associated CAUTI. He received and responded well to a 7-day course of oral cotrimoxazole.

However, we recognise that the clinical response could arguably be due to possibilities other than a sole response to antibiotic therapy for the presence of BCC in the urine. Despite our consensus clinical position to treat the index case for a possible BCC infection (rather than colonisation), we nevertheless recognise the existence of plausible alternative clinical arguments. For example, he may have had a (persisting) staphylococcal infection to the healing pressure ulcer site; or a partially treated pelvic osteomyelitis—both of which may have shown temporary improvement to further antibiotic treatment with cotrimoxazole. However, it is perhaps noteworthy that following the patient's eventual discharge from hospital, and up to the 9-month follow-up period of our writing this report, he had not represented to hospital for symptoms or signs that would indicate either a recurrence of the pelvic osteomyelitis, or reinfection to the site of the previous sacral pressure ulcer. Alternatively, given the often multifactorial nature of delirium, it is equally plausible that he responded to the direct resolution of a non-infective cause. This might be the case if changing the blocked urethral catheter and relieving any associated distress caused improvement in the persistent delirium, rather than the antibiotic treatment for a possible BCC CAUTI.

Consequently, we do not advocate for routine treatment by clinicians for merely identifying the presence of BCC in urinary samples. Rather, our report endeavours to promote the adoption of a more critical approach to making treatment decisions in such complex cases. In the index case, we (medicine of the elderly physicians) placed value on a decision to treat that was informed by liaison with other relevant specialties including clinical microbiologists, radiologist, orthopaedic surgeons and TVN specialists.



### Some philosophical concepts relevant to the clinical decision-making in this case

In arriving at a decision to treat this patient for a BCC-related infection, we consider the potential influence (and limitations) of applying the previously described heuristic principle of Occam's (or Ockham's) razor.<sup>13</sup> Considering this principle (from a medical perspective) would potentially see a clinician seeking to make a single (unifying) diagnosis, rather than making two or more unrelated diagnoses.<sup>13</sup> The index patient had multiple symptoms and signs, and these necessitated consideration of more than one justifiable diagnosis.

Hickam's dictum has previously been put forward as a counterweighting concept to Occam's razor.<sup>13 14</sup> Analysis of this dictum (from the perspective of medical application) would translate into a general principle that multiple symptoms and signs may in fact be due to more than one disease. Applying Hickam's dictum to this patient's case translated into contemplating the range of multimorbidity acquired with advancing age. Accordingly, there was a need to establish whether or not alternative hypotheses could be put forward for the patient's clinical presentation.<sup>14</sup>

If we examine a third and previously described philosophical concept referred to as Crabtree's bludgeon (from a medical context), it would caution one against seeking over-elaborate explanations for a given presentation.<sup>13 15</sup> This principle promotes the important lesson that on finding a plausible unifying diagnosis, clinicians should still endeavour to test the validity thereof. Put differently, clinicians need to be careful to avoid the potential trap of accepting an over-elaborate explanation merely because it could explain all the symptoms or signs. The latter scenario could arise, for example, when a clinician is

faced with a theoretical argument, but the overall probability of such an occurrence is actually quite low.

Taking on board the three aforementioned principles, the informed clinical decision was made to treat this patient for a possible BCC-related CAUTI. The patient improved with the specified treatments, with accompanying resolution of the features of the UTI and the associated delirium.

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### Learning points

- ▶ This report serves as a reminder of an important clinical lesson that, subject to the context, organisms that are more commonly identified as being colonisers (eg, *Burkholderia cepacia* complex (BCC)) may occasionally also cause symptomatic opportunistic infections.
- ▶ In clinical situations where probable BCC infection is considered (eg, in patients with relevant predisposing risk factors), further individualised clinical assessments and treatment may be required.
- ▶ Treatment strategies and options in complex cases of BCC-related infection are best guided by microbiology, infectious diseases or comparable services.

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