CASE REPORT

Burkholderia cepacia: a rare cause of bacterial keratitisMohtar Ibrahim,¹ Jin Yi Yap^{1,2}

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SUMMARY

We describe the first clinical case of *Burkholderia cepacia* keratitis registered in Southeast Asia. A man in his mid-70s with underlying poorly controlled diabetes mellitus came with complaints of painful red left eye for 4 days. This was accompanied with photophobia and blurring of vision after being injured by a wooden particle while cutting grass. Slit-lamp examination showed a paracentral anterior corneal stromal infiltrates with overlying epithelial defect. Culture of the corneal smear isolated *B. cepacia* that was sensitive to ceftazidime, meropenem and bactrim (trimethoprim and sulfamethoxazole). Topical ceftazidime was given intensively to the patient and the infection resolved after 6 weeks of treatment.

BACKGROUND

Burkholderia cepacia infection is a rare cause of bacterial keratitis. The case we are reporting is one of the first clinical cases of corneal ulcer in South-east Asia caused by *Burkholderia* infection.

CASE PRESENTATION

A man in his mid-70s with underlying poorly controlled type 2 diabetes mellitus presented with a sudden onset of painful red left eye for a duration of 4 days and was accompanied with purulent discharge together with photophobia and blurring of vision. The symptoms started after the patient encountered a wooden particle entering his left eye while cutting grass.

Figure 1 Demonstrating paracentral infiltrates with injected conjunctiva. A streak of hypopyon was noted at the bottom of anterior chamber.

Figure 2 Demonstrating overlying epithelial defect of the keratitis.

On examination, the left eye best corrected visual acuity (BCVA) was 20/150 and 20/20 for the right eye. Slit-lamp biomicroscopy examination showed hyperaemic conjunctiva with paracentral anterior corneal stromal infiltrates; measuring 2 mm × 2.5 mm at 3 o'clock (figure 1). The margin was ill-defined and fluorescein staining test showed an overlying epithelial defect (figure 2). The surrounding cornea was oedematous due to inflammation. The anterior chamber inflammatory activity was 3+ with the presence of hypopyon and the intraocular pressure was 24 mm Hg. Posterior segment examination was normal. The right eye anterior and posterior segment examination was normal.

INVESTIGATIONS

Corneal scrapings were sent for gram's staining, giemsa staining and microbiological cultures. The corneal scraping samples were inoculated on blood agar, chocolate agar, Sabouraud dextrose agar and MacConkey agar. Gram-negative bacilli were detected on gram's staining. Cultures of the corneal smear showed prominent pure growth of shiny, colourless, gram-negative bacilli on blood agar and MacConkey culture plate. However, since there was no growth on the Sabouraud dextrose agar, thus fungal infection was ruled out. The isolate was subsequently tested using biochemical tests including triple sugar iron, indole, citrase, urase, methyl red, catalase, coagulase and colistin. The organism was then sent for final identification using VITEK 2 system. The isolated organism was confirmed to be *B. cepacia* and sensitive to ceftazidime, meropenem and bactrim (trimethoprim and

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Table 1 Reported cases of *Burkholderia cepacia* ocular infection

Author/year/article type	Age/gender/region	Predisposing factor	Disease	Visual/clinical outcome
Pathengay <i>et al</i> /2005 ⁵ /case report	53/male/India	Uncomplicated cataract surgery with postoperative endophthalmitis	Recurrent endophthalmitis	Phthisical eye No light perception
Eser <i>et al</i> /2006 ⁶ /case report	63/male/Turkey	Diabetes mellitus and uncomplicated cataract surgery	Endophthalmitis	20/63
	72/Male/Turkey	Uncomplicated cataract surgery	Endophthalmitis	20/50
Ying-Cheng <i>et al</i> /2006 ⁷ /case report	16/female/Taiwan	Underwent orthokeratology Contact lenses fitting	Keratitis	20/20
Ornek <i>et al</i> /2009 ⁸ /case report	75/female/Turkey	Complicated cataract surgery	Endophthalmitis	Loss to follow-up
Chaurasia <i>et al</i> /2011 ⁹ /case series	Not stated/India	Pterygium surgery Topical steroid eye drops	Keratitis	Corneal scar*
	Not stated/India	Chicken pox infection	Keratitis	Corneal scar*
	Not stated/India	Trauma with stone	Keratitis	Clear graft*
	Not stated/India	Postpenetrating keratoplasty with topical steroid eye drops	Keratitis	Corneal scar*
Reddy <i>et al</i> /2013 ¹⁰ /case report	27/male/India	LASIK	Keratitis	20/20

*Visual outcome of the case series was not mentioned in the study.

LASIK, laser-assisted in situ keratomileusis.

sulfamethoxazole) and resistant to chloramphenicol, colistin and gentamicin.

DIFFERENTIAL DIAGNOSIS

Bacterial keratitis is commonly caused by gram-positive bacteria. A clinical review showed that out of 306 cases of bacterial keratitis, 65.2% were caused by gram-positive cocci. There were only about 16.4% of cases were due to gram-negative bacilli.¹ Among all the gram-negative bacilli, *Pseudomonas aeruginosa* top the list of the causative agents.¹ Clinically, it would be difficult to differentiate the causative agent of the bacterial keratitis as both gram-negative and gram-positive organisms can have rapid onset, predominance of central (23%) and inferior (nasal 24% and temporal 22%) infiltrates, presence of anterior chamber inflammation and the visual acuity can widely vary.¹ All these features were seen in the case we presented.

Our initial diagnosis was *P. aeruginosa* bacterial keratitis based on the immediate gram staining result which showed gram-negative bacilli. However, the corneal scraping culture, biochemical tests and VITEK 2 organism identification system confirmed the organism as *B. cepacia*. The treatment changes were made based on the sensitivity result.

TREATMENT

The patient was initially started on topical ceftazidime 5% and topical moxifloxacin 0.5% half hourly instillation. Topical ceftazidime 5% was prescribed initially to empirically cover for *P. aeruginosa*, the the most common organism that causes bacterial keratitis at our centre.² Topical moxifloxacin, a broad-spectrum antibiotic, was used to cover other gram-positive organism. Topical homatropine 2% and preservative free artificial tears drops were initiated as well for pain relief and to prevent formation of synechiae. On receiving the cultures and sensitivity results, the patient was subsequently treated intensively with topical ceftazidime and his symptoms improved dramatically within 1 week. The stromal infiltrates reduced greatly in size. There was regression of conjunctival hyperaemia and anterior chamber inflammatory activity with signs of corneal re-epithelisation. The diameter of stromal infiltrates also reduced.

OUTCOME AND FOLLOW-UP

During subsequent follow-up, the epithelial defect fully re-epithelised with resolution of the corneal oedema and corneal infiltrates, leaving behind a faint nebulous scar. Topical antibiotics were tapered down with clinical resolution of his keratitis. Topical dexamethasone 0.1% four times a day was added later to assist in reduction of scars formation. Unfortunately, after 6 weeks of treatment, his visual acuity improved to only 20/70 as there was a residual corneal scar near the visual axis. The reduced best corrected vision was contributed by the presence of dense corneal scar. Alternatively, further treatment with optical penetrating keratoplasty for a better visual outcome was offered but was declined by the patient.

DISCUSSION

B. cepacia, previously known as *Pseudomonas cepacia*, is one out of 17 species of the *B. cepacia* complex. The species was first discovered in the 1950s by Walter Hagemeyer Burkholder, an American plant pathologist, who observed that the organism had caused the soft rot of onion skin. Only in the early 1990s, the taxonomic reappraisal regrouped the RNA group II pseudomonads to a new genus, *Burkholderia*, and *B. cepacia* as one of these species.³ It is a gram-negative, non-spore forming, non-fermentative, motile, aerobic bacillus, and it is catalase and oxidative positive. The optimal temperature for the *B. cepacia* to grow is at 30°C–35°C. It is commonly found in plants, animals, water, soils and also as human pathogens.^{3,4}

The organism was labelled as non-pathogen until early 1980s as it emerged as one of the opportunistic pathogen.³ Initially it was only found to be due to contact with contaminated disinfectant and anaesthetic solution. However, later on it became an emerging nosocomial infection in the USA.³ *B. cepacia* infection is mainly found in patients with cystic fibrosis, a genetic disease that causes persistent lung infections. Fatal cases reported in early 1990s were due to severe *B. cepacia* pneumonia and septicaemia. Other than that, *B. cepacia* can also be implicated in urinary tract infection and endocarditis.

B. cepacia is an opportunistic pathogen that may implicate a wide array of diseases. The systemic *Burkholderia* infection can

Table 2 Antibiotic sensitivity pattern

No	Cephalosporins	Chloramphenicol	Quinolones	Aminoglycosides
1	S	R	S	R
2	S	—	S	R
3	S	—	S	R
4	S	—	S	R
5	S	—	S	R
6	S	S	S	S
7	S	R	S	S
8	S	R	R	R
9	S	R	R	R
10	R	—	R	R
11	S	R	—	R

Number of patient arranged chronologically as in the sequences of [table 1](#).

R denotes resistance and S denotes sensitive.

No 11 is the antibiotic sensitivity pattern for the case that we are reporting.

be severe or even fatal. In terms of *Burkholderia spp*-related ocular infection, the incidence rate is relatively lesser. [Table 1](#) lists the five case reports and one case series that has been reported for the *Burkholderia spp*-related ocular infection.^{5–10} From the table we can observe that there were six reported cases from India, two cases from Turkey and one from Taiwan. This will be the first reported case in the region of Southeast Asia. There were no gender predilection or specific age group for the disease as well.

There are various virulence factors that can assist the organism in the infection of host cells. These include the presence of specific glycolipid and glycoprotein receptors on the organism surface, ability of the intracellular invasion and in vivo survival, secretion of lipases, proteinase, metalloproteinases and also exotoxin.¹¹ Similar to the cases reported, the presence of underlying factor, breaking the integrity of the eye, such as trauma and intraocular surgery, would have resulted in higher risk of *Burkholderia* ocular infection. Another noticeable predisposing factor is the host immunity status which is seen in our patient who had underlying poorly controlled diabetes mellitus that may have weakened his immune system and thus, predisposed him to the infection.

[Table 2](#) showing the antibiotic sensitivity of all the cases reported. From the table we found that *Burkholderia spp* was resistant to most of the common antibiotics we use in daily clinical practice. It is due to the following mechanism: presence of various efflux pumps that remove the antibiotics from the bacteria, presence of biofilm and changes in the cell envelope that will reduce the membrane permeability to antibiotics. These protective mechanisms of the organism cause multiple-drug resistance including aminoglycosides, quinolones, polymyxins and β -lactams.⁴ Our patient was fortunate as the organism was still sensitive to ceftazidime, the third-generation cephalosporins, and he responded well to the treatment.

Learning points

- Recognising the clinical features of *Burkholderia* ocular infection which can mimic the features of other common organism that causes bacterial keratitis.
- Understanding about the characteristics and virulence factors of this rare organism.
- Taking note on the high antibiotic resistance of this organism as inappropriate antibiotics use can result in treatment failure.

Contributors MI: was the main physician in charged of the patient we reported; planned and designed the write up of this case report; provided important intellectual content for the discussion of the write up; and finalized the case report before the submission. JYY: was in charged of the write up of the case presentation and data collection including the consent taking and obtaining the images; involved in the literature review of the case report as well; and designed the tables for the literature review.

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