Chromobacterium Violaceum Infections; A Series Of Case Reports In A Malaysian Tertiary Hospital

Z Rashid, U Ali, A Sulong, R Rahman

Abstract

Chromobacterium violaceum is a saprophyte bacterium found in soil and stagnant water of tropical and subtropical regions. Although infection in human is rare, it can cause localized infections, septicemia and disseminated lesions, which may become fulminant leading to mortality. We describe 3 cases of Chromobacterium violaceum infections observed over a period of three years. Two cases were fatal; a 17-year-old chronic granulomatous disease patient with skin lesions, cellulitis, septicemia and microabscesses in the spleen and liver, and a 57-year-old intravenous drug abuser with severe necrotizing pancreatitis and intraabdominal sepsis. The third case was a successfully treated septic arthritis in a 63-year-old patient with underlying diabetes mellitus. Chromobacterium violaceum was isolated from the blood, abdominal fluid and tissue specimens respectively. In tropical regions, it should be one of the differential causes of sepsis, especially if there are skin lesions and/or multiple organ abscesses with history of soil or stagnant water exposure.

INTRODUCTION

Chromobacterium violaceum (C. violaceum) was first reported by Wooley in 1905 as the cause of fatal septicemia in water buffaloes in the Philippines (1). The first human case was described by Lesslar JE in 1927 in Malaya, and reported in 1953 (2). Human cases have been reported worldwide mainly in the South East Asia (2-7) and the United States (8,9). To date, more than 100 cases have been reported worldwide. In this report, we describe three identified cases of infections caused by C. violaceum.
aminoglycosides, ceftazidime, cefepime, piperacillin-
tazobactam, imipenem and meropenem and was resistant to
ampicillin, amoxicillin-clavulanate and cefotaxime.
Intravenous ciprofloxacin was added on to the meropenem
since his condition did not improve. However, despite active
support and treatment, he developed multi organ failure and
succumbed after 7 days of hospitalization.

CASE TWO
A 57-year-old man who was an intravenous drug abuser with
hypertension, diabetes mellitus and chronic hepatitis C virus
infection, presented with 2 days history of epigastric pain,
nausea and vomiting. There was no prior history of fever or
infective symptoms, no trauma to his abdomen or history of
recent intravenous injection. He claimed that he was not an
active drug or alcohol abuser.

At presentation, he was alert, cooperative but uncomfortable. His blood pressure was 139/98 mmHg, pulse rate of 126
beats/minute, respiratory rate of 22 breaths/minute and body
temperature of 38.9°C. His distended abdomen was tender
and guarded at the epigastrium. Initial investigations showed
raised total white cell count 15.6 x 10^9/L, serum amylase
3372 U/L and serum lactate dehydrogenase of 640 U/L. The
blood glucose was at 16.8mmol/L and C-reactive protein
(CRP) was 5.5mmol/L. Ultrasound and computed
tomography (CT) of the abdomen revealed severe
necrotizing pancreatitis with splenic vein thrombosis. He
developed metabolic acidosis and had to be intubated for
severe respiratory distress and was transferred to the ICU.
He required inotropic support and was started on IV
meropenem. Within the first week of ICU, he had two CT-
guided drainages of the intraabdominal collection, yielding
50 ml and 200 ml of pus respectively. Microbiological
culture isolated multi-drug resistant Acinetobacter spp. Thus,
tigecycline was added based on susceptibility results.

A CT abdomen a week later showed no change of the peri-
pancreatic fluid collection, worsening ascites with bilateral
pleural effusion and splenic infarction. His condition
continued to deteriorate and in his second week in ICU, he
required renal replacement therapy and developed ventilator-
associated pneumonia. He underwent two more CT-guided
drainages which drained mixture of blood and pus. These
specimens isolated C. violaceum and disk diffusion
antibiotic susceptibility testing showed susceptibility to
amoxicillin-clavulanate, ciprofloxacin, aminoglycosides,
ceftazidime, cefepime, piperacillin-tazobactam, imipenem
and meropenem. It was resistant to ampicillin, cefuroxime
and cefotaxime. IV meropenem that was at day 13 was
planned to be continued for another 2 weeks. His white cell
count persistently elevated, more than 15x10^9/L with
periodic spikes of temperature and repeated blood culture on
the fourth week isolated Klebsiella pneumoniae extended-
spectrum beta-lactamase (ESBL) and Enterobacter cloacae
ESBL. He succumbed after 39 days in ICU. His cause of
death was reported as severe acute necrotizing pancreatitis
with multiple organ failure.

CASE THREE
A 63-year-old retiree with diabetes mellitus for 30 years
presented to the hospital with 6 days’ history of right leg
swelling. He had a wound on his right knee, which was later
followed by formation of small pustules and progressed to
become an abscess with purulent discharge, associated with
fever, chills and rigors.

On admission his blood pressure was 113/94 mmHg, heart
rate of 140 beats/minute, respiratory rate of 22
breaths/minute and body temperature of 38.4°C. There was a
wound measuring 3x3 cm² on his right knee which was
erthematous, with superficial necrotic patch, peeling of the
surrounding skin and seropurulent discharge. He was treated
as cellulitis with an infected wound and secondary
septicemia. He was sent to the ward and started on IV
ampicillin-sulbactam 1.2 gram eight-hourly.

As the fever persisted and the cellulitis worsened, the
antibiotic was changed to IV penicillin-G and cloxacillin on
the second day of admission. An arthrotomy was performed,
which yielded 10 mls of pus. Wound debridement and
washout was done. On day 4 of admission the tissue sample
from the synovial lining, the aspirated pus and intra-articular
swab sent for culture was reported, which isolated C.
violeceum with the same antibiogram. The organism was
resistant to ampicillin, amoxicillin-clavulanate, ampicillin-
sulbactam, cefuroxime, cefotaxime, ceftazidime and
piperacillin-tazobactam. It was susceptible to ciprofloxacin,
aminoglycosides, cefepime, imipenem and meropenem. The
ampicillin-sulbactam was changed to IV ciprofloxacin 400
mg 12-hourly which was continued for ten days. He
responded to the treatment and was discharged with oral
ciprofloxacin to be continued up to 3 weeks. During follow
up visit one month later, there was complete recovery of the
wound.
DISCUSSION

Chromobacterium violaceum is a motile, facultative anaerobic gram-negative bacillus usually found as a saprophyte in soil and water in tropical and subtropical regions. Despite ubiquitous distribution, human infection with this organism is rare. It is the only species of the genus Chromobacterium that causes human disease and not considered as an inhabitant of human gastrointestinal tract (10). This mesophilic bacterium grows readily on commonly used laboratory media such as sheep blood agar, chocolate agar, MacConkey agar, Mueller Hinton agar and tryptase soy broth. Most strains produce a characteristic deep purple violacein pigment on solid media, hence its name (10). This organism is a non-lactose fermenter, gives alkaline-salt-acid-butt reaction on triple sugar iron (TSI) agar, catalase-positive, indole-negative, oxidase-positive, ability to utilise citrate and reduce nitrate.

Locally, it was the first described in 1927 (2), and several more cases have been reported (3-5,7). In our centre, after one patient was diagnosed, a search using BIOMIC® V3 Microbiology System (Giles Scientific Inc. USA) from January 2008 to December 2010 identified two other cases. The cases were summarized in Table 1. C. violaceum has been reported to cause infection in immunodeficient patients; such as CGD, severe polymorphonuclear leucocyte G-6-PD deficiency or neutrophil dysfunction (8,11-12). Macher et al. found 3 out of 12 cases in his review had underlying CGD (8). Similarly, Sirinavin et al. reported a case of invasive C. violaceum infection in a CGD patient, and reviewed 25 infections in 24 children reported in the literature worldwide. CGD was present in 9 out of the 25 cases (12). Our patient in Case One was known to have CGD which may explain his susceptibility to disseminated C. violaceum infection.

Most reported cases were associated with a prior history of skin injury exposed to soil or contaminated stagnant water. Classical manifestations are described as being a localised cellulitis at the site of trauma initially which then rapidly progress to systemic infection and fulminating sepsis, with development of multiple abscesses involving the liver, kidney and lungs (13). Melioidosis caused by Burkholderia pseudomallei has similar clinical manifestations and occurs in similar endemic regions. Interestingly, there are reports of C. violaceum-associated diarrhea (14) and infection after a scuba diving or near drowning (15). A fatal case of a young patient with appendicitis was described, who died after 48 hours of admission, where the probable route of exposure was suggested as from the ingestion of contaminated water (16). Both patients in cases One and Three had skin injury and most probably contaminated with the organisms. In Case Two, the isolation of C. violaceum after more than 2 weeks in ICU can be considered unusual or indeterminate origin. Diagnosis requires a high index of suspicion and is based on the isolation of the organism from wounds, abscess fluids, exudates and blood cultures.

C. violaceum is generally susceptible to fluoroquinolones, chloramphenicol, doxycycline, trimethoprim-sulphamethoxazole, imipenem, gentamicin, piperacillin, and mezlocillin (17). Ciprofloxacin is the an effective antimicrobial in vitro. However, there are no available breakpoints for antibiotic susceptibility interpretations. This bacterium is resistant to a relatively wide range of antibiotics such as rifampin, vancomycin, cephalosporins and review of susceptibility patterns in Southeast Asia revealed similar
findings (6). Antimicrobial susceptibility results for the three cases were summarized in Table 2.

Detailed studies of this bacterium is made possible following completion of the genomic sequencing of C. violaceum in 2003 (18). C. violaceum was found to have numerous genes associated with various mechanisms of drug resistance, including resistance against penicillin and cephalosporins, and multidrug resistance proteins (drug efflux pumps) (19). Minimum inhibitory concentration (MIC) testings is suggested to be performed in C. violaceum infections (6). Currently there is neither a recommendation on the choice of optimum antimicrobial nor the duration of treatment. Frequent relapse of the disease has been documented and postulated to be due to the presence of internal organ abscesses and hidden septic foci (12). Thus, it was suggested that antimicrobial treatment should be for at least six weeks and adequate surgical drainage of abscesses to be done where appropriate.

The patient in Case One succumbed despite an early initiation of IV meropenem and later the addition of ciprofloxacin on day 4 of hospitalization. Presentation with invasive, disseminated infection in an immunocompromised patient contributed to the poor outcome. In a review of 20 cases of C. violaceum in South East Asia, 12 patients with invasive and disseminated infections died, giving the attributed mortality of 60% (6).

In Case Two, the patient’s mortality was attributed to the severe necrotizing pancreatitis. In acute pancreatitis, systemic complications can arise, such as bacteremia due to gut flora translocation, acute respiratory distress syndrome, pleural effusions, gastrointestinal hemorrhage and renal failure. Systemic inflammatory response syndrome can also develop, leading to the development of systemic shock. It is difficult to associate the C. violaceum isolated in Case Two to his cause of death as necrotizing pancreatitis itself carries a high mortality risk.

In Case Three, the patient presented with symptoms of 6 days’ duration and received 10 days of IV ciprofloxacin after 4 days of ampicillin-sulbactam, with favourable outcome. Successful treatment in this case is most likely due to adequate surgical drainage, early recognition and appropriate antimicrobial treatment.

CONCLUSION

Human infections caused by C. violaceum are rare but when they occur, can be fulminant with high mortality rate. Its presence can be a culture contaminant, but should be regarded as clinically significant if isolated from purulent specimens. It should be included as one of the differential causes of sepsis, especially if there are skin lesions and/or multiple organ abscesses with history of exposure to soil or stagnant water. Immunodeficient patients may have higher risk of mortality. Early clinical recognition and management with the use of appropriate systemic antimicrobial therapy may prevent it from becoming fulminant, and prolonged duration of therapy is required to prevent relapse.

ACKNOWLEDGMENT

Our thanks to Aswida Arman (Medical Laboratory Technologist) for their assistance, Dr Ramliza Ramli, Head of Bacteriology Unit, and Associate Professor Dr Salasawati Hussin, Head of Department of Medical Microbiology & Immunology, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur.

References

Author Information

Zetti Zainol Rashid
Department of Medical Microbiology & Immunology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre

Umi Kalsom Ali
Department of Medical Microbiology & Immunology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre

Anita Sulong
Department of Medical Microbiology & Immunology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre

Raha Abdul Rahman
Department of Anaesthesiology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre