

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

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## 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*.

## CASE REPORTS

### CASE ONE

A 17-year-old boy presented with 3 days' history of persistent fever with chills, rigors and abdominal pain which have been treated with anti-pyretic and oral cloxacillin by a general practitioner. Prior to his symptoms, he had sustained multiple abrasions during a camping trip. As his condition worsened he was brought to the emergency department. He had chronic granulomatous disease (CGD) diagnosed since childhood, but was without any follow up and antibiotic cover for the last five years.

On presentation, he was restless and dehydrated. His blood pressure was 90/56 mmHg with pulse rate of 135 beats/minute, respiratory rate of 22 breaths/minute and body

temperature of 40°C. There were multiple abrasions that were erythematous with serous discharge over his face, left arm and thigh. The abdomen was guarded with generalized tenderness but there was no organomegaly. Crepitations were noted on auscultation of the left lower zone of the lung. Other systemic examinations were unremarkable. Laboratory investigations showed leukocytosis with predominant neutrophils. Arterial blood gases showed metabolic acidosis. Serum creatinine was 166 U/L and urea was 9.6 mmol/L, which were slightly elevated and his coagulation profile were deranged (prothrombin time 79.2 seconds, INR 9.85 and APTT of 166.7 seconds). The chest radiograph showed pneumonic patches over left lower zone. He was intubated and transferred to the intensive care unit (ICU). He was further resuscitated, with inotropic support and started on intravenous (IV) meropenem 500 mg eight-hourly with cloxacillin 2 g six-hourly. The surgical team decided on an emergency laparotomy which found multiple micro-abscesses on the spleen and liver.

Specimens were sent for bacteriologic culture and sensitivity testing, which was reported on day 3 of admission. *C. violaceum* was isolated from the blood and wound swab specimens but nothing from the abdominal wash. Antibiotic susceptibility testing using disk diffusion method showed the presence of zones of inhibition with ciprofloxacin,

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  $15.6 \times 10^9/L$ , 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  $15 \times 10^9/L$  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  $3 \times 3 \text{ cm}^2$  on his right knee which was erythematous, 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. violaceum* 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.

**Figure 1**

Table 1: Summary of *Chromobacterium violaceum* infections in UKMMC from January 2008 to December 2010

Case no.	Age	Sex	Clinical presentation	Specimen	Treatment	Outcome
One	17	Male	CGD, infected wound, skin lesions, cellulitis, septicemia, microabscesses in spleen and liver	Blood, wound swabs, abdominal washings	Meropenem, Cloxacillin, Ciprofloxacin	Died
Two	57	Male	Ex-IVDU, diabetes mellitus, chronic Hepatitis C, necrotizing pancreatitis	Abdominal fluids	Meropenem, Tigecycline	Died
Three	63	Male	Diabetes mellitus, infected wound, cellulitis, septic arthritis	Synovial tissue, knee aspirate, intra-articular swab	Ampicillin-sulbactam, then ciprofloxacin (total >4 weeks ciprofloxacin)	Recovered

CGD= chronic granulomatous disease

IVDU= intravenous drug user

**Figure 2**

Table 2: Antibiotic susceptibility results by disk diffusion method for *Chromobacterium violaceum* isolates in UKMMC from January 2008 to December 2010

Antibiotics	Case One	Case Two	Case Three
Ampicillin	R	R	R
Amoxycillin-clavulanate	R	S	R
Ampicillin-sulbactam	NA	NA	R
Ciprofloxacin	S	S	S
Gentamicin	S	S	S
Amikacin	S	S	S
Cefuroxime	R	R	R
Cefotaxime	R	R	R
Ceftazidime	S	S	R
Cefepime	S	S	S
Piperacillin-tazobactam	S	S	R
Imipenem	S	S	S
Meropenem	S	S	S

S= Acceptable zone of inhibition, susceptible

R=Resistant

NA= Not available

## 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 trypticase 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-slant-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). Meliodosis 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.

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## **References**

1. Wooley PG: *Bacillus violaceus manilae* (a pathogenic organism). *Bull Johns Hopkins Hosp*; 1905; 16:89.
2. Sneath PH, Whelan JP, Bhagwan SR, Edwards D: Fatal infection by *Chromobacterium violaceum*. *Lancet*; 1953; 265:276-7.
3. Hassan H, Suntharalingam S, Dhillon KS: Fatal *Chromobacterium violaceum* septicemia. *Singapore Med J*; 1993; 34: 456-8.
4. Sagin DD, Tan PT, Dolkadir J: *Chromobacterium violaceum* septicemia in Malaysia [Letter to the editor]. *Singapore Med J*; 1994; 35: 426.
5. Ang YM: A very rare and rapidly fatal case of *Chromobacterium violaceum* septicemia. *Med J Malaysia*; 2004; 59 (4): 535-7.
6. Jitmuang A: Human *Chromobacterium violaceum* infection in Southeast Asia: case reports and literature review. *Southeast Asian J Trop Med Public Health*; 2008; 39:452-60.
7. Cheong BMK: A Fatal Case of Pulmonary *Chromobacterium violaceum* Infection in an Adult. *Med J Malaysia*; 2010; 65 (2): 148-9.
8. Macher AM, Casale TB, Fauci AS: Chronic granulomatous disease of childhood and *Chromobacterium violaceum* infections in the South-eastern United States. *Ann Intern Med*; 1982; 97:51-5.
9. Ponte R, Jenkins SG: Fatal *Chromobacterium violaceum* infections associated with exposure to stagnant waters. *Pediatr Infect Dis J*; 1992; 11: 583-6.
10. Steinberg JP, Burd E: Other gram-negative and gram-variable bacilli. In: Mandell GL, Bennett JE, Dolin R, Eds. *Principles and practice of infectious diseases*. 7th ed. Philadelphia: Churchill Livingstone; 2010. pp. 3019-20.
11. Mamlok RJ, Mamlok V, Mills GC, Daeschner CW, Schmalstieg FC, Anderson DC: Glucose-6-phosphate dehydrogenase deficiency, neutrophil dysfunction and *Chromobacterium violaceum* sepsis. *J Pediatr*; 1987; 111: 852-4.
12. Sirinavin S, Techasaensiri C, Benjaponpitak S, Pornkul R, Vorachit M: Invasive *Chromobacterium violaceum* infection in children: case report and review. *Pediatr Infect Dis J*; 2005; 24:559-61.

13. Teoh AYW, Hui M, Ngo KY, Wong J, Lee KF, Lai PBS: Fatal septicemia from *Chromobacterium violaceum*: Case reports and review of the literature. *Hong Kong Med J*; 2006; 12: 228-31.
14. Dromigny JA, Fall AL, Diouf S, Perrier-Gros-Claude JD: *Chromobacterium violaceum*: a case of diarrhea in Senegal. *Pediatr Infect Dis J*; 2002; 21 (6): 573-4.
15. Starr AJ, Cribbett LS, Poklepovic J, Friedman H, Ruffolo EH: *Chromobacterium violaceum* presenting as a surgical emergency. *South Med J*; 1981;74:1137-9.
16. Chen CH, Lin LC, Liu CE, Young TG: *Chromobacterium violaceum* bacteremia: a case report. *J Microbiol Immunol Infect*; 2003;36:141-4.
17. Aldridge KE, Valainis GT, Sanders CV: Comparison of the in vitro activity of ciprofloxacin and 24 other antimicrobial agents against clinical strains of *Chromobacterium violaceum*. *Diagn Microbiol Dis*; 1988; 10: 31-9.
18. Brazilian National Genome Project Consortium: The complete genome sequence of *Chromobacterium violaceum* reveals remarkable and exploitable bacterial adaptability. *Proc Natl Acad Sci USA*; 2003;100: 11660-5.
19. Fantinatti-Garboggini F, de Almeida R, Portillo VAD, Barbosa TAP, Trevilato PB, Ramalho CE et al: Drug resistance in *Chromobacterium violaceum*. *Genet Mol Res*; 2004; 3:134-47.

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