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# Fatal septicaemia from *Chromobacterium violaceum*: case reports and review of the literature

## 因紫色色桿菌引致致命敗血病：病例研究和文獻回顧

*Chromobacterium violaceum* rarely causes infection in humans and its mechanism of pathogenicity is not well understood. Human infection carries a high mortality rate with a fulminating clinical progression. A high index of suspicion is required for diagnosis, and is based on recovering the organisms from blood cultures or other appropriate specimens. We present three cases of human infection managed in a tertiary referral hospital in Hong Kong with a review of the literature.

紫色色桿菌極少感染人類，而真正的致病機制仍不清楚。若被感染，臨床病情會迅速惡化，致命率亦極高。要診斷此症需要高度警覺性，並且要在血液培養或其他樣本中確認此病菌。本文報告三宗於第三層轉介醫院處理的人類感染個案，並進行文獻回顧。

### Introduction

In Hong Kong, the recent fatal infection with *Chromobacterium violaceum* in a fit and healthy man generated widespread media attention and public interest in this rare human pathogen. Wooley<sup>1</sup> first described the pathogenic potential of this organism in 1905. Since then, more than 150 cases of human infection have been reported, with the majority being rapidly fatal.<sup>2</sup> We present the first report of three cases in Hong Kong with a positive culture of *C. violaceum*.

### Case reports

#### Case 1

In May 2005, a 40-year-old man was admitted to the orthopaedics ward for management of a 1-cm right forearm abscess which developed after trivial trauma to the arm while camping near a pond in Tuen Mun 4 days earlier. There was no history of insect bites. The abscess was incised and drained and the patient was prescribed intravenous ampicillin and cloxacillin. Blood analysis on admission showed a normal white cell count and unexplained renal impairment (urea, 10.1 mmol/L; creatinine, 163 µmol/L). The next morning the patient complained of sudden-onset severe epigastric pain. He was afebrile with a blood pressure of 110/70 mm Hg. Physical examination revealed epigastric tenderness without peritonism. Within 30 minutes, his vital signs began to deteriorate with his blood pressure dropping to 70/40 mm Hg. Repeated blood analysis showed a pancytopenia and renal impairment (Table). Arterial blood gas analysis showed severe metabolic acidosis of pH 7.18 with base excess of -15 mmol/L. He was transferred to the intensive care unit for further management. Computed tomography demonstrated multiple hypodensities ranging from a few mm to 1.5 cm in both lobes of the liver. There was no free gas or fluid within the abdominal cavity (Fig 1).

Reassessment of the initial right forearm wound revealed a more severe proximal spreading cellulitis involving the right arm, associated with right axillary lymphadenopathy. A gram stain of the blood cultures identified gram-negative bacilli. Intravenous antibiotics (ampicillin and cloxacillin) were switched to ciprofloxacin, metronidazole, and cefotaxime. His condition continued to deteriorate despite fluid resuscitation and escalating inotropic support. He

#### Key words:

Bacteremia;  
vioC protein;  
*Chromobacterium violaceum*;  
Liver abscess

#### 關鍵詞：

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紫色色桿菌；  
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**Table. Results of blood tests for case 1**

Blood test	Results	Reference range/level
Haemoglobin (g/L)	118	134-172
Platelet count ( $\times 10^9$ /L)	49	152-358
White cell count ( $\times 10^9$ /L)	0.7	3.9-10.7
Urea (mmol/L)	16	3.4-8.9
Creatinine ( $\mu$ mol/L)	324	44-80
Bilirubin (IU/L)	31	<15
Alkaline phosphatase (IU/L)	28	30-80
Alanine transferase (IU/L)	263	<58

succumbed to multi-organ failure secondary to uncontrolled sepsis less than 24 hours after admission. *Chromobacterium violaceum* was subsequently isolated from cultures taken from the right forearm abscess, from blood cultures taken on the day of admission and from autopsy spleen cultures. The same organism was also cultured from water samples taken from a pond at the campsite.

### Case 2

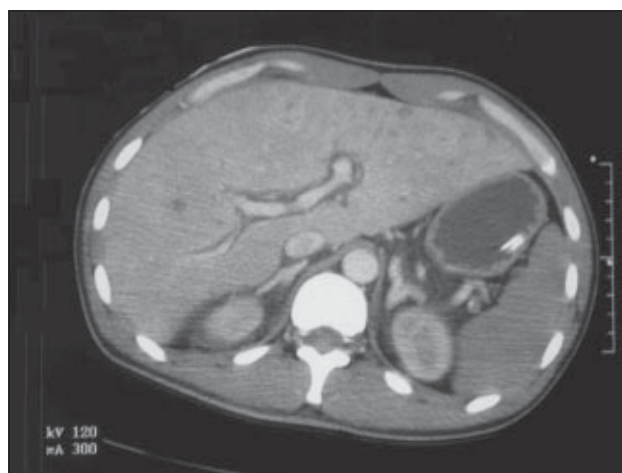
A 64-year-old man was admitted in June 1997 with a 10-day history of progressive limb weakness. Magnetic resonance imaging of the cervical spine showed severe stenosis of the C3/4 and 6/7 regions with evidence of cord compression. Cervical laminoplasty was performed from C3 to C7. His postoperative course was complicated by pneumonia and respiratory failure necessitating intubation and admission to the intensive care unit. Tracheal aspirates for culture yielded a positive growth of methicillin-resistant *Staphylococcus aureus* (MRSA), *Acinetobacter* species, and *Pseudomonas aeruginosa*. The initial antibiotic regimen included intravenous ceftazidime, netilmicin, imipenem, and vancomycin for 2 weeks, according to the sensitivity of the isolated organisms.

Despite this, the patient continued to have persistent sepsis. All antibiotics were stopped and the sepsis workup repeated. The femoral line was also removed and sent for culture. A chest X-ray showed improving consolidation of the lungs and computed tomography of the neck revealed no evidence of postoperative infection. Blood and femoral line tip cultures grew *C. violaceum* and *Acinetobacter* species. All lines were changed and intravenous ceftazidime and amikacin were commenced.

Unfortunately, sepsis persisted and necessitated further septic workups and antibiotic changes. Strains of *C. violaceum* continued to be isolated from blood cultures taken 1 month after the initial culture. Antibiotics given according to bacterial sensitivities during that period included ciprofloxacin, sulfamethoxazole-trimethoprim, imipenem, and vancomycin. The patient continued to deteriorate and finally succumbed to multi-organ failure secondary to uncontrolled sepsis 3 months following cervical laminoplasty.

### Case 3

In September 2002, a 23-year-old man was admitted to the



**Fig 1. Computed tomographic scan of abdomen showing multiple hypodense foci ranging from a few mm to 1.5 cm in both lobes of the liver**

surgical department for management of multiple trauma following a fall from 30 m. In view of unstable vital signs and a massive haemothorax, emergency operative exploration was performed. On median sternotomy, an 8-cm lower lobe rupture was identified in the right lung. Intra-abdominally, there was an expanding zone-one haematoma that required exploration and haemostasis, and a zone-three haematoma that was treated conservatively. He also sustained other injuries including fractures of the petrous temporal bone, skull base, pelvis, and T10 to L2 spinous processes. Postoperatively he was managed in the intensive care unit for 21 days and during this time he developed persistent sepsis. Blood cultures were positive for MRSA. Tracheal aspirates yielded a heavy growth of *C. violaceum* and *S. aureus*. Sepsis was controlled with a course of vancomycin and piperacillin/tazobactam (Tazocin; Wyeth, Carolina, US). He was discharged to a convalescent hospital for further rehabilitation after 1 month's hospitalisation.

### Discussion

*Chromobacterium violaceum* is a motile, facultative anaerobic, gram-negative bacillus. It is now believed to be the only species in the genus. The organism inhabits soil and water, especially in tropical and subtropical areas. It grows readily on commonly used laboratory media such as sheep blood agar, MacConkey agar, and nutrient agar. Most strains produce a characteristic deep purple pigment, violacein, hence its name (Fig 2). Non-pigmented strains showing similar virulence and pathogenicity have been identified in the past. Hence, Sivendra and Tan<sup>3</sup> have stressed the importance of not using violet pigmentation as the sole criterion for separating *C. violaceum* from other gram-negative bacteria, in particular *Aeromonas* spp and *Vibrio* spp, to avoid misdiagnosis and confusion. *Chromobacterium violaceum* also produces catalase, nitrate reductase, and arginine dihydrolase.<sup>4,5</sup> Separation from *Pseudomonas* spp and *Aeromonas* spp can be done using a



**Fig 2. *Chromobacterium violaceum* colonies on sheep blood agar**

number of biochemical tests and flagellar morphology as illustrated by Sivendra and Tan.<sup>3</sup> The complete genomic sequence of this bacterium has recently been revealed and has provided a basis for detailed studies of its antiviral and bactericidal activities, cytotoxicity, and drug resistance mechanisms. This may also explain why *C violaceum* is pathogenic in mammals and sometimes fatal in cases of human infection.<sup>6-10</sup>

Reported human infections have generally occurred in subtropical and tropical areas: more than 150 cases have been reported from Vietnam, Taiwan, Japan, United States, Brazil, Argentina, Australia, Senegal, and Sri Lanka.<sup>3</sup> A search of our hospital microbiological database showed our cases are the only three documented cases in Hong Kong from 1993 to 2005. Cases 1 and 2 represented true infection by the organism, whereas case 3 was likely to represent colonisation rather than true infection by the bacteria.

Infections commonly occur in summer months and most reported cases are associated with a prior history of injury to skin and exposure to soil and stagnant water. Unusual routes of exposure include infection after scuba diving or near drowning,<sup>11-13</sup> after breast surgery<sup>14</sup>, and appendicectomy.<sup>15</sup> The presumed reservoir of the organism in case 1 was likely to be the surrounding campsite water, from which positive cultures of the organism were isolated. In case 3, the patient could have had contact with the organism during or after his fall. The mechanism by which the organism caused line sepsis in case 2 was not clear. Surgery was carried out under aseptic conditions and the probability of contamination from the intensive care unit was low.

Classical manifestation begins with a localised cellulitis at the site of trauma, then rapid progression to fulminating sepsis with multiple abscesses involving the liver, kidney, and lung. Presentation as an acute abdomen (as in case 1) with multiple liver abscesses is possible but

rarely reported.<sup>16</sup> Other presentations include conjunctivitis, pneumonia, diarrhoea, urinary tract infection, and meningitis.<sup>2,15,17,18</sup>

Human infections are rare but usually fatal. An indolent clinical course such as that of case 2 is rarely reported. The exact mechanism of infection is unknown and the reason why infection does not occur in all case of exposure is uncertain, as illustrated in case 3. Children with chronic granulomatous disease appear to be more vulnerable.<sup>17</sup> Nonetheless, there is currently no evidence to support an immunocompromised state as a risk factor for infection.

Diagnosis requires a high index of suspicion and is made on the basis of isolation of the organism from wounds and blood cultures. Ciprofloxacin is the most effective antimicrobial in vitro although other fluoroquinolones such as norfloxacin and pefloxacin are also very effective. The organism is also susceptible to imipenem, piperacillin, and mezlocillin. Most strains are resistant to other penicillins and cephalosporins.<sup>16</sup> The multi-drug resistant nature of the organism (as in case 1) has been highlighted.<sup>19</sup> Prompt treatment with antibiotics is vital as patients with bacteraemic sepsis carry the worst prognosis.<sup>17</sup> Fatalities similar to cases 1 and 2 have been repeatedly reported despite the use of appropriate antibiotics. Prolonged antimicrobial treatment for 6 weeks is recommended, as relapse of the disease has been documented and postulated to be due to the presence of internal organ abscesses.<sup>17</sup> In the absence of treatment, the prognosis is grave. Rapid deterioration is expected with mortality rates as high as 50% to 60% reported.<sup>9,13,17</sup>

In conclusion, human infections caused by *C violaceum* are rare but when they occur, are usually fatal. A high index of suspicion is required for diagnosis, especially in the presence of a history of outdoor activities. Appropriate systemic antimicrobial therapy to halt progression of infection is mandatory, even when the infection appears to be localised.

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