Review

Chromobacterium violaceum infection in China: Three case reports and literature reviews

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Chromobacterium violaceum, Gram-negative Bacillus, is a common inhabitant of soil and stagnant water found in tropical and subtropical regions of the world. It is a rare cause of severe, often fatal, human disease. In the report, 3 cases of patients infected with C. violaceum were described in Anhui Province, China. Routine and bacteriological investigations were carried out to establish the aetiological diagnosis. Moreover, the patients were treated with appropriate antimicrobial agents and auxiliary therapy. To our knowledge, a total of 42 cases have been reported previously from Chinese mainland in the recent 20 years, with a review of the literatures.

Key words: Chromobacterium violaceum, infection, China.

INTRODUCTION

Chromobacterium violaceum commonly inhabits soil and stagnant water in tropical and sub-tropical regions which usually produces a violet pigment known a violacein, solute in ethanol and insoluble in water and chloroform. However, infections caused by nonpigmented strains are described rarely. The bacterium, motile, oxides-positive rod-shaped, facultatively anaerobic, fermentative, and Gram-negative, is classified into the opportunistic pathogen (Groves et al., 1969; Kaufman et al., 1986). It is only Chromobacterium species that are pathogenic to humans. Despite its ubiquitous distribution, humans infected with C. violaceum are rare. As the clinical manifestations of infection are not representative and the organisms are not sensitive to the antimicrobial agents, the pathogens result in systemic and severe disease with a high fatality rate. The bacteria may be responsible either singly or in combination for wound or soft tissue infection. Their main clinical features rapidly progress to sepsis with multiple organ abscesses, including the lungs, liver, and spleen.

Thus, the infection often results in severe, systemic diseases with high rate (≥60%) (Díaz Pérez et al., 2007; Groves et al., 1969). C. violaceum was firstly identified in 1881 and its pathogenic potential was first described by Woolley (1905), which was isolated from a fatal infection in buffalo in Philippines. The first human case infected with C. violaceum was found in Malaysia by Lessler in 1927 (Sneath et al., 1953). Since then, there have been more than 150 human cases reported in India, Sri Lanka, Southeast Asia, Taiwan, Hongkong, Argentina, Australia, Brazil, and the southeastern region of the United States (Chang et al., 2007; Kim et al., 2005; Miller et al., 1988; Ray et al., 2004; Wen and Chen, 2000). Three cases in Anhui Province with the pigmented strains of C. violaceum were present in the report.

CASE REPORTS

Case 1

In June 2005, a 76-year-old farmer man who lived in Chaohu, Anhui Province was admitted to the Burn Department of a local hospital, because he sustained flame burns in the upper part of his body, in a farmland.
Unfortunately, a serious wound contaminated by lake water in a rural area was detected at this time. Then, the conditions of the patient worsened quickly and he was transferred to the First Affiliated Hospital of Anhui Medical University. He denied any other disease except for hypertensive disease and chronic cardiac dysfunction. Physical examination revealed the following vital signs: temperature 38.8°C, heart rate 84 beats/min, respiratory rate 23 breaths/min, blood pressure was not examined due to noncompliance. The patient had burned more than 40% of the surface areas which were mainly located in both upper extremities and chest (I degree 12%, deep II degree 28%). Laboratory investigation upon admission showed: leukocyte count 13.0×10^9/L, with 83.3% neutrophils, erythrocyte count 5.7×10^12/L, hemoglobin 105 g/L, platelet count 169×10^9/L; total protein 39.7 g/L, albumin 21.5 g/L, A/G 1.18, total bilirubin 15.43 μmol/L, ALT 17 U/L, AST 27 U/L, urea nitrogen 5.12 mmol/L, creatinine 63 μmol/L, blood sodium 130 mmol/L, potassium 2.88 mmol/L, blood sugar 7.76 mmol/L.

A Gram-negative bacillus formed smooth and violaceous colonies on sheep blood agar and Mueller-Hinton agar was cultured from purulent discharge of putrid skin on admission (Figure 1). No growth of organisms had been detected from blood culture. No evidence of abnormality was found in chest X-ray. The bacillus was identified as *C. violaceum* by API 20 NE and Vitek system. The clinical strain was susceptible to imipenem, levofloxacin and ciprofloxacin, intermediate to amikacin, gentamicin and tobramycin, but resistant to aztreonam, cefepime, cefotaxim, ceftazidime, ceftriaxone, piperacillin, and trimethoprim-sulfamethoxazole. During hospitalization, the patient was suspected to infection with Gram-negative organism and empirically treated with intravenous penicillin (2 g, every 4 h) for 3 days. When identification and susceptibility reports were available on the fourth day, the therapeutic schedule was changed into intravenous levofloxacin (0.4 g, one time per day). The wound was debrided twice per day. On eighth day after hospitalization, the patient’s symptoms disappeared. There was no fever, wound gradually healed, and liver function recovered. Serial blood culture was again obtained, but no growth of organisms had been detected.

Case 2

A 42-year-old male patient who lived in Anqin, Anhui Province had multiple traumas on exposed parts of his body due to a tractor accident while plowing on December 6, 2007. He was first admitted to ICU of the local hospital for management of shock and then transferred to ICU, the First Affiliated Hospital of Anhui Medical University. He had hemopneumothorax and respiratory failure, rib and pelvis fracture, pancreas hematoma and back contusion. On admission, physical examination revealed the following vital signs: temperature 38.6°C, respiratory rate 26 breaths/min, HR 138 beats/min, BP 130/80 mmHg, and oxygen saturation 94%. The laboratory investigation showed: hemogram (leukocyte count 19.89×10^9/L, with 78.6% neutrophils, erythrocyte count 2.6×10^12/L, hemoglobin 17 g/L, albumin 21.5 g/L, A/G 1.18, total bilirubin 15.43 μmol/L, ALT 17 U/L, AST 27 U/L, urea nitrogen 5.12 mmol/L, creatinine 63 μmol/L, blood sodium 130 mmol/L, potassium 2.88 mmol/L, blood sugar 7.76 mmol/L).

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rib. Ultrasonography of abdomen confirmed seroperitoneum. The ascites cell count showed: WBC 3000×10^6/L (monocaryon 75%, polyvalent 25%), RBC 200×10^6/L; however, biochemical data were within normal limits.

The patient empirically treated with intravenous cefoperazone (1 g, every 8 h) and ciprofloxacin (0.75 g, one time per day) in addition to symptomatic treatment. On the fourth day, ascetic culture was inoculated and identified as C. violaceum, with antibiograms showing sensitivity to imipenem, amikacin, gentamicin, and tobramycin, resistance to aztreonam, cefepime, cefotaxim, ceftazidime, cefatrizine, piperacillin, ticarcillin, ciprofloxacin, and trimethoprim-sulfamethoxazole. The successful treatment with antimicrobial regimen initiated intravenous imipenem (1.0 g, every 8 h) for 7 days according to the isolated organisms. Seven days after admission, the patient’s symptoms disappeared. There was no fever, cough and expectoration relieved, liver function parameters were normalized, renal function recovered, routine urinalysis was normal, and he accepted oral food well. Ultrasound examinations showed disappearance of ascites. Chest X-ray showed disappearance of chest pleural effusion. Abscesses in liver and kidney were not showed by the computed tomographic scan of the abdomen. Serial blood cultures were again obtained, however, no growth of organisms had occurred. The patient recovered 2 months later, and then was discharged.

**Case 3**

An 81-year-old man who lived in Hefei, Anhui Province was admitted to the department of nephrology on October 20, 2008, presenting with a history of hypertension, coronary heart disease, installation of pacemaker, and chronic renal failure for over 2 years. Through examination, patients were found with hypodynamia, oedynuria, and edema for a month. The patient slipped and fell on land near a pond when he went for a walk in the park 5 days ago. Physical examination revealed the following vital signs: temperature 39.2°C, respiratory rate 19 breaths/min, heart rate 93 beats/min, BP 110/80 mmHg. Blood analysis on admission showed an abnormal hemogram (leucocyte count 14.52×10^9/L, with 81.3% neutrophils, erythrocyte count 4.2×10^12/L, hemoglobin 96 g/L, platelet count 57×10^9/L) and an aggravating renal impairment (urea nitrogen 44.27 mmol/L, creatinine 1037 μmol/L, occult blood 3+, protein 2+). Blood sodium, potassium, calcium levels were within normal limits. The parameters of liver function revealed total protein 51.7 g/L, albumin 31.5 g/L, total bilirubin 21.7 μmol/L, ALT 21 U/L, AST 27 U/L. The patient’s empirical treatment with antimicrobial agents received intravenous cefotaxime (2 g, every 8 h). On the fifth day, bacillus was inoculated from the midstream urine and subsequently identified as C. violaceum. Blood cultures did not grow C. violaceum. The strain was resistant to aztreonam, cefotaxime, piperacillin, or ticarcillin, intermediate to cefotazidime, and susceptible to amikacin, tobramycin, ceftazidime, imipenem, or trimethoprim-sulfamethoxazole. Hemodialysis was given to the patient lasting for 3 days and antimicrobial agents was switched to intravenous imipenem (0.5 g, every 8 h) in the light of results of susceptibility tests. On the tenth day after hospitalization, the patient’s symptoms disappeared. There was no fever, routine urinalysis and liver function recovered. Another blood and midstream urine culture were again obtained, but no growth of organisms had occurred. The patient felt better then and was discharged from the hospital.

**DISCUSSION**

More than 150 cases of patients infected with C. violaceum have been reported worldwide (de Siqueira et al., 2005; Wen and Chen, 2000). Since the first case of human infection was described in 1987 in Zhejiang Province of China, 45 cases have been found in Chinese mainland in the recent 20 years. Among literatures, 30 cases with partly clinic materials were documented in different periods (Chen and Dong, 1990; Gu et al., 1987; Wu et al., 1988; Xu et al., 1993; Zhang et al., 1990; Zhou and Yang, 2006; Zhu et al., 1991) (Table 1). Of 42 patients of previous reports and 3 at present, most cases infected with C. violaceum occurred in the Southern coastal areas of the Chinese mainland (Figure 2). Moreover, C. violaceum is frequently confined to tropic and southern subtropic zones and the central subtropical zone (Figure 2). 3 cases of human infection with C. violaceum have been reported in Hong Kong (1 discharged and 2 died) (Teoh et al., 2006). In 1968, a 5-year-old child who died of sepsis was the first case infected with C. violaceum in Taiwan (Wu et al., 1986). According to 7 cases reported from Taiwan, 3 successfully recovered and 4 unfortunately died (Wu et al., 1986).

From the age characteristics, the young people had high incidence compared with the teenagers and middle-aged people. Only 9 cases infected with C. violaceum ranging from 16 to 45 years have been reported in the literature, while 11 cases were teenagers (from 0 to 15 years) and 10 middle-aged people (older than 45 years). The youngest patient was a 13-day-old infant with respiratory infection associated with left eye infected with C. violaceum. The oldest patient, who was an 81-year-old man with the history of kidney failure appeared urinary tract infection by C. violaceum and was discharged without adopting any antimicrobial therapy. C. violaceum is an opportunistic pathogen. Nevertheless, the incidence of exposure to infection in teenagers and the elderly is...
Table 1. Clinical manifestation of 30 cases caused by *C. violaceum* in Chinese mainland.

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>Year</th>
<th>Province</th>
<th>Clinical presentation</th>
<th>Specimen</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>2.5</td>
<td>1992</td>
<td>Anhui</td>
<td>Septicemia</td>
<td>Blood</td>
<td>Died</td>
<td>Xu and Xu (1996)</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>20</td>
<td>1992</td>
<td>Zhejiang</td>
<td>Skin wound</td>
<td>Wound pus</td>
<td>Recovered</td>
<td>Lei et al. (1994)</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>49</td>
<td>1995</td>
<td>Zhejiang</td>
<td>Skin ulcer</td>
<td>pus</td>
<td>Recovered</td>
<td>Wu et al. (1998)</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>30</td>
<td>1997</td>
<td>Inner Mongolia</td>
<td>Finger injury</td>
<td>Wound pus</td>
<td>Unknown</td>
<td>Li (1997)</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>4</td>
<td>1999</td>
<td>Shandong</td>
<td>Left ear suppuration</td>
<td>Ear secretions</td>
<td>Recovered</td>
<td>Wang and Mi (1999)</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>24</td>
<td>2000</td>
<td>Chongqing</td>
<td>Puerperal infection</td>
<td>Vaginal secretions</td>
<td>Recovered</td>
<td>Xie et al. (2001)</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>26 days</td>
<td>2000</td>
<td>Shandong</td>
<td>Sepsis of newborn</td>
<td>Blood</td>
<td>Recovered</td>
<td>Wei et al. (2001)</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>7</td>
<td>2001</td>
<td>Guangdong</td>
<td>Septicemia</td>
<td>Pus, blood</td>
<td>Recovered</td>
<td>Fu et al. (2002)</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>76</td>
<td>2001</td>
<td>Anhui</td>
<td>Extensive burn</td>
<td>Wound pus</td>
<td>Died</td>
<td>Present study</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>50</td>
<td>2003</td>
<td>Jiangsu</td>
<td>Septicemia, MODS</td>
<td>Blood</td>
<td>Died</td>
<td>Yang et al. (2005)</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>65</td>
<td>2005</td>
<td>Sichuan</td>
<td>Septicemia</td>
<td>Blood</td>
<td>Recovered</td>
<td>Xia et al. (2007)</td>
</tr>
<tr>
<td>20</td>
<td>F</td>
<td>1</td>
<td>2006</td>
<td>Zhejiang</td>
<td>Pneumonia, septicemia, MODS</td>
<td>Sputum, Blood</td>
<td>Died</td>
<td>Hua et al. (2006)</td>
</tr>
<tr>
<td>21</td>
<td>F</td>
<td>13 days</td>
<td>2006</td>
<td>Fujian</td>
<td>Left eye conjunctivitis, neonatal respiratory infection</td>
<td>Ocular secretion</td>
<td>Recovered</td>
<td>Hu et al. (2009)</td>
</tr>
<tr>
<td>22</td>
<td>F</td>
<td>9</td>
<td>2006</td>
<td>Zhejiang</td>
<td>Left ear suppuration, hepatapostema, septicemia</td>
<td>Pus, blood</td>
<td>Recovered</td>
<td>Tong et al. (2007)</td>
</tr>
<tr>
<td>23</td>
<td>M</td>
<td>42</td>
<td>2007</td>
<td>Anhui</td>
<td>Multiple trauma</td>
<td>Peritoneal drainage fluid</td>
<td>Recovered</td>
<td>Present study</td>
</tr>
<tr>
<td>24</td>
<td>M</td>
<td>81</td>
<td>2008</td>
<td>Anhui</td>
<td>Renal insufficiency</td>
<td>Midstream urine</td>
<td>Unknown</td>
<td>Present study</td>
</tr>
<tr>
<td>25</td>
<td>M</td>
<td>5</td>
<td>unknown</td>
<td>Guangdong</td>
<td>Multiple abscesses</td>
<td>Pus</td>
<td>Recovered</td>
<td>Ge (1995)</td>
</tr>
<tr>
<td>26</td>
<td>M</td>
<td>49</td>
<td>unknown</td>
<td>Zhejiang</td>
<td>Skin and soft tissue infections</td>
<td>Pus, blood</td>
<td>Recovered</td>
<td>Zhu and Zhu (1996)</td>
</tr>
<tr>
<td>27</td>
<td>M</td>
<td>59</td>
<td>unknown</td>
<td>Zhejiang</td>
<td>Multiple liver abscess</td>
<td>Blood</td>
<td>Died</td>
<td>Huang et al. 2006</td>
</tr>
<tr>
<td>28</td>
<td>M</td>
<td>26</td>
<td>unknown</td>
<td>Zhejiang</td>
<td>Suppurative lung infection, septicemia</td>
<td>Blood</td>
<td>Died</td>
<td>Huang et al., 2006</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>38</td>
<td>unknown</td>
<td>Zhejiang</td>
<td>Right arm abscess, infectious shock</td>
<td>Pus, blood</td>
<td>Unknown</td>
<td>Huang et al., 2006</td>
</tr>
<tr>
<td>30</td>
<td>M</td>
<td>45</td>
<td>unknown</td>
<td>Guangxi</td>
<td>Cholangitis, septicemia</td>
<td>Blood</td>
<td>Died</td>
<td>Wei, 2007</td>
</tr>
</tbody>
</table>

Clinical manifestations of the other 15 cases did not show integrity, so they were not described.

higher than in young people which may be due to immunocompromise, leading to the dissemination of infection. Thus, one of the important factors was immunocompromised, caused by many underlying diseases, old age and serious injuries, which could involve the pathogenesis of case 2 and case 3, respectively. From the point of view of gender difference, the majority of patients infected with *C. violaceum* were male (21 cases),
Figure 2. The geographic distribution of 12 provinces and 1 municipality in Chinese mainland (A), the map of Chinese mainland shows 12 provinces and 1 municipality, in which *Chromobacterium violaceum* isolates were reported (©From 1998 to 2009, Zhejiang (17 cases), Guangdong (9 cases), Anhui (4 cases), Shandong (3 cases), Hunan (3 cases), Guangxi (2 cases), Sichuan (1 case), Chongqing (1 case), Jiangsu (1 case), Jiangxi (1 case), Liaoning (1 case), Inner mongolia (1 case), Fujian (1 case) were reported in Chinese mainland; (©Liaoning, Shandong, Jiangsu, Zhejiang, Fujian, Guangdong, Guangxi are adjacent to the oceans in Chinese mainland). (B), the map shows the 17 cities in Anhui Province (Anhui Province locates in eastern China with the population of 66.757 million and covers the area of 139,600 square kilometers, the Yangtse River and Huaihe River traverse the province boundary; with Huaihe River as...
which accounted for 70.0%. C. immunocompromise, leading to the dissemination of infection. Thus, one of the important factors was immunocompromised, caused by many underlying diseases, old age and serious injuries, which could involve the pathogenesis of case 2 and case 3, respectively. From the point of view of gender difference, the majority of patients infected with *C. violaceum* were male (21 cases), which accounted for 70.0%. *C. violaceum* is often found in the soil and environmental water.

Moreover, men usually took up the impaired occupation (cultivating and fishing) and easily injured or contaminated skin lesions, which increased the incidence of exposure to pathogen. In the report, 3 patients infected with *C. violaceum* were male; moreover, the history of exposure to soil and stagnant water on account of cutaneous injury caused by various factors was described in 3 cases. Most infection caused by *C. violaceum* occurred in summer, especially from July to September.

In Chinese mainland, the definite time of *C. violaceum* infection was detected in 20 cases as following (1 case in January, 2 cases in June, 2 cases in July, 7 cases in August, 3 cases in September, 2 cases in October, 2 cases in November, 1 case in December). The reason of increasing incidence might attribute to the suitable temperature for the growth of *C. violaceum* which was more than 30°C. The patients usually wear thin clothes when the weather got hot. *C. violaceum* usually made incursions into the bodies via broken skin.

However, it was cold in December, which was not suitable for bacterial growth. In the report, the patient in case 2 probably was low immunity owing to sever injuries. Thus, opportunistic infection was caused by *C. violaceum* from contaminated wound. The main clinical symptoms included fever (22 cases), the increase of leukocyte (15 cases), the increase of neutrophils (14 cases), focal or multiple abscesses (5 cases), and regional lymphadenectasis (4 cases), etc. If patients were showing hypoinnunity with some predisposing factors, a localized infection would be rapidly developed into the systemic infection, which could lead to the progression to sepsis and multiple organ failure involving the liver, kidney, and spleen (Díaz Pérez et al., 2007; Jin et al., 2003).

13 cases were related to skin ulceration caused by trauma or insect bite and had the contact history of soil and water; however, some infection routes were still unclear. Systemic infection was even possibly due to the intrusion of swallowing sewerage including pathogens (Kim et al., 2005; Miller et al., 1988; Xu and Li, 2004). Thus, we suspected that ingestion of seafood which was freeze-drying processed and stored, might have been the source of infection in some cases because of more and more convenience to transportation. Some patients denied ever going into the sea or other direct exposure to estuarine water or seawater; but they often bought seafood from the local supermarket to eat.

A few patients, only 13 cases, recovered after hospitalization. 9 patients were dead of septicemia caused by *C. violaceum* (Table 1). Thus, poor prognosis and high mortality were described in patients infected with *C. violaceum*, if the disease was quickly developed into a fatal systemic infection (Sneath et al., 1953). However, symptoms were not obvious and typical, when the initial stage of infection although the human infectivity of *C. violaceum* is low. According to some related literatures, the mortality rate of local infection with *C. violaceum* was more than 65%, and of septicemia was higher than 80% (Chang et al., 2007; Miller et al., 1988; Jin et al., 2003). As effective antimicrobial treatment in time, 3 cases described in the report did not progress to severe bacteremia and sepsis, which was important to the treatment of *C. violaceum* infection.

Diagnosis requires a high index of suspicion and is made on the basis of isolation of the organism from specimen cultures. The organism is usually sensitive to carbapenems and fluoroquinolones, but resistant to penicillins, aminoglycosides, and cephalosporins. Thus, the rational use of carbapenems and fluoroquinolones plays an important role in the pathogenic treatment. However, it should be mentioned that there were discrepancy of sensitivity and efficiency to aminoglycosides and cephalosporins in different regions.

In the meantime, it is the importance of early diagnosis and empirical treatment, timely with antimicrobial agents in order to avoid progression to sepsis and multiple organ failure. The patient should receive not only antimicrobial treatment but also symptomatic and supportive treatment in time for the benefit of infection control, which could evidently improve the prognosis (Rahal et al., 1998). In the report, Cases 1, 2, and 3 have been rapid recovery with accurate identification and susceptibility test of the pathogen in time, as well as effectively supportive care, apart from appropriate antimicrobial therapy.

In sum, the most severe complication of infection with *C. violaceum* was sepsis, infectious shock, and multiple organ failure. Distinctive features of infection were low morbidity and high mortality. Clinical manifestations of *C. violaceum* infection often initially show minor localized abscess. Then, local lesions rapidly developed into sepsis, multiple organ failure, even death owing to their immunocompromise or irrational use of antimicrobial agents.

As the opportunistic pathogen, it was rare that human infections were caused by *C. violaceum*. However, microbiological researchers and physicians should pay more attention to the increasing incidence in recent years (Ge, 1995). The history of exposure to stagnant water and soil could not be ignored, which was important to early diagnosis of infection. Empirical use of antimicrobial agents in time, the adjustment of therapeutic schedule
timely on the basis of susceptibility tests, and intensive nursing also played important role in disease control and improving the prognosis (Ray et al., 2004).  


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