Multiple Liver Abscesses with a Skin Pustule due to Chromobacterium violaceum

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Abstract:
A 69-year-old woman was admitted to our hospital with the chief complaints of fever and fatigue. We initially treated the patient for a tick-borne disease after noticing a pustule on her leg; however, abdominal computed tomography (CT) showed multiple low-density areas in the liver and Chromobacterium violaceum was isolated from a blood culture. We diagnosed her with multiple liver abscesses secondary to Chromobacterium violaceum bacteremia. The patient was successfully treated with ciprofloxacin.

Key words: Chromobacterium violaceum, bacteremia, liver abscess, skin pustule, wound infection

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Introduction
Chromobacterium violaceum is a Gram-negative, facultative anaerobic bacillus that is common in water and soil, especially in tropical and subtropical areas. Most strains of this organism produce a remarkable deep purple pigment called violacein. Although rare, human infection is characterized by a high mortality rate, multidrug-resistance, and frequent relapse.

Case Report
A 69-year-old woman with hypertension and osteoporosis was admitted to our hospital complaining of fever and general fatigue, which had started the previous day in August, during the Japanese summer. She lived in a rural area of Japan and worked in rice paddies as a farmer during the summer season.

On admission, a physical examination revealed the following: body temperature, 39.6°C; blood pressure, 145/85 mmHg; heart rate, 127 beats/min. She was alert and conscious. Laboratory tests revealed the following: WBC, 19,000/mm³ with 87.4% neutrophils and 5.4% lymphocytes; RBC, 3.99 million/mm³; hemoglobin, 12.9 g/dL; hematocrit, 37.7%; platelet, 215,000/mm³; aspartate aminotransferase (AST), 61 IU; alanine aminotransferase (ALT), 44 IU; alkaline phosphatase (ALP), 276 IU; lactate dehydrogenase (LDH), 328 IU; blood urea nitrogen (BUN), 7.1 mg/dL; creatinine (Cr), 0.54 mg/dL; albumin (Alb), 3.5 g/dL; C-reactive protein (CRP), 22.07 mg/dL; prothrombin time-international normalized ratio (PT-INR), 1.02; activated partial thromboplastin time (APTT), 47.1 seconds; fibrinogen, 784 mg/dL; and fibrinogen degradation product (FDP), 7.3 mcg/mL. On physical examination, we found a small pustule on her right lower leg (Fig. 1) without any other skin...
Although she was uncertain about the cause of the skin lesion, we suspected a tick-borne disease, such as Japanese spotted fever, and administered minocycline (200 mg/day, intravenous). The following day, abdominal CT revealed multiple intrahepatic low-density areas (Fig. 2, arrowheads) and Gram-negative bacillus was isolated from both 2 sets of blood cultures (both aerobic and anaerobic bottles) taken on the day of admission. We then tentatively diagnosed her with multiple liver abscesses and replaced minocycline with sulbactam/ampicillin (9 g/day). On the 3rd day after admission, purple-colored colonies were found on a Sabouraud agar plate (Fig. 3). Based on the characteristic appearance of the colonies and the clinical manifestations of the patient, we suspected *Chromobacterium violaceum* bacteremia and changed sulbactam/ampicillin to ciprofloxacin (600 mg/day, intravenous).

The isolated organism was identified as *Chromobacterium violaceum* using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) (VITEK MS, bioMérieux, Craponne, France). Based on the sensitivity profile, the organism was considered to be resistant to all beta-lactam antibiotics and sensitive to levofloxacin, gentamycin, minocycline, and sulfamethoxazole/trimethoprim (Table). Two days after changing the antibiotic to ciprofloxacin, the patient became afebrile, and blood cultures taken on the same day were negative. The patient’s WBC and CRP levels decreased to 11,000/mm³ and 11.5 mg/dL, and to 6,300/mm³ and 0.29 mg/dL on the 5th day and 18th day after admission, respectively. Further imaging studies indicated the absence of metastatic lesions in the brain, lung, and spleen. Since the liver abscesses decreased gradually, intravenous ciprofloxacin was continued until the day of discharge, 25 days after admission, with oral ciprofloxacin subsequently prescribed as maintenance therapy. Antibiotic treatment was discontinued 74 days after admission when an abdominal CT scan revealed no evidence of liver abscesses. She was asymptomatic and doing well at a four-month follow-up examination.

**Table.** The Results of Antibiotic Susceptibility Testing.

| Antibiotics                      | MIC (μg/mL) |
|----------------------------------|-------------|
| Ampicillin                       | >16         |
| Piperacillin                     | >64         |
| Piperacillin/tazobactam          | >64/4       |
| Ceftazidime                      | >8          |
| Cefotaxime                       | >2          |
| Ceftriaxone                      | >2          |
| Cefepime                         | >16         |
| Cefmetazole                      | >32         |
| Meropenem                        | >2          |
| Aztreonam                        | >8          |
| Gentamycin                       | <2          |
| Minocycline                      | <2          |
| Levofloxacin                     | <0.5        |
| Sulfamethoxazole/Trimethoprim    | <2          |

MIC: minimum inhibitory concentration

Antimicrobial susceptibility testing was performed using a Microscan Walkaway system (SIEMENS; Tokyo, Japan).
Discussion

Since it was first reported in Malaysia in 1927 (1), fewer than 200 human infections with *Chromobacterium violaceum* have been reported. The majority of these cases have been reported from the USA, the East Western Pacific, and Southeast Asia (2). To our knowledge, only 4 cases have been reported from Japan (3-5), and we could find only 6 more cases in the Japanese proceedings. Despite its rarity, the number of reported cases has been increasing in the last few decades and the difficulties associated with successfully treating this infection are becoming clear (2). The typical manifestations of the infection include rapid progression to sepsis with localized or metastatic abscess (liver, lung, or spleen) and skin lesions (2). To date, nosocomial pneumonia (3), lymphadenitis (6), urinary tract infection (7), orbital cellulitis (8), and brain abscesses (9) have also been reported. Skin lesions, including pustules (9), abscesses (10), or cellulitis (11) are a predominant manifestation. Some reports have suggested that the organism enters the bloodstream via an open wound (12-15). In our case, the patient had a pustule on her right lower leg and she explained that she had noticed a skin eruption in the same place (at least one week prior to her admission) while working in rice paddies filled with muddy water. Episodes of trauma and exposure to natural water or soil are important predisposing factors that are associated with this disease (2). Some reports indicate that patients with underlying chronic granulomatous disease (CGD) seem to be susceptible to infection by this organism (11).

These organisms usually produce violacein, the origin of the species’ name, which is a striking purple pigment that is insoluble in water but soluble in alcohol. The observation violacein on solid media led us to highly suspect this organism. However, since a few cases caused by non-pigmented strains have been reported (3, 16), the absence of violet pigmentation should not exclude a diagnosis of *Chromobacterium violaceum* genomes. The observation violacein on solid media led us to highly suspect this organism. However, since a few cases caused by non-pigmented strains have been reported (3, 16), the absence of violet pigmentation should not exclude a diagnosis of *Chromobacterium violaceum* (17). Yang et al. reported that comorbidity in patients with underlying chronic granulomatous disease (CGD) seem to be susceptible to infection by this organism (11).

Due to the rarity of human infection, the optimal antibiotic therapy for *Chromobacterium violaceum* infection is not well established. Although it is known to be generally resistant to penicillins and cephalosporins (9, 18), the strains isolated from clinical specimens are usually susceptible to fluoroquinolones, carbapenem, tetracycline, chloramphenicol, and trimethoprim/sulfamethoxazole (2). In *vitro* studies have suggested that ciprofloxacin seems to be the most active antibiotic (19). Interestingly, our case was considered to be resistant to all beta-lactam antibiotics, including meropenem. Although chromosomally mediated AmpC-type beta-lactamase has been described in *Chromobacterium violaceum* (20), the mechanisms of carbapenem resistance are not well established. According to a genomic analysis, *Chromobacterium violaceum* seems to have various mechanisms of drug resistance (21). Due to frequent relapse, prolonged antibiotic therapy for a period of several weeks to a few months is recommended (2, 12).

In conclusion, *Chromobacterium violaceum* infections in humans are rare but often fatal. Physicians should maintain a high degree of clinical suspicion when treating septic patients, especially those with sepsis associated with wound infection, skin lesions, multiple organ abscesses, or with a history of exposure to water or mud in tropical or subtropical areas.

The authors state that they have no Conflict of Interest (COI).

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