SEPSIS CAUSED BY CHROMOBACTERIUM VIOLACEUM AND SUGGESTIONS FOR DIAGNOSIS, TREATMENT: A CASE REPORT

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The article presented a case of bacteremia caused by Chromobacterium violaceum in a 9-year-old girl. This was a rare disease in humans, so the diagnosis and treatment were delayed. The entire prossess of disease and antibiotic therapy have been described in detail. Although life was saved, the consequences for the patient can be long-lasting.

Keywords: *Chromobacterium violaceum, opportunistic, bacteremia, sepsis, mortality.*

BACKGROUND

Emerging infectious diseases are a global public health problem. Factors that contribute to the increased risk of emerging diseases include climate change, socioeconomic development, demographic changes, including population aging and status immunity in humans[1]. In addition to viral pathogens causing pandemics such as HIV, influenza - and coronaviruses, a number of emerging microbial pathogens are also of concern to the health sector[2]. Along with melioidosis, cases of infections caused by *Chromobacterium violaceum*, continue to be reported and are associated with severe illness and high mortality[3]. *C. violaceum* is a free-living, motile, facultatively anaerobic Gram-negative bacterium, existing in the natural environment such as soil and freshwater. Human disease usually starts with a skin wound as portal of entry, followed by systemic dissemination and presenting with septicemia and skin manifestations. In the laboratory the bacterium is remarkable because of the production of a deep purple pigment called violacein, that is thought to be a virulence factor and antibiotic inhibiting substance[4].

Disease caused by *C. violaceum* in humans is relatively rare, and knowledge about this disease is limited[4]. In Vietnam, 2 cases of *C. violaceum* infection were reported in 2008 and 2013 with severe progression and death[5,6]. Limited clinical knowledge, unpredictable progression of *C. violaceum* infection and unexpected susceptibility pattern may lead to severe consequences for patients.

In this article, I present a case of sepsis caused by *C. violaceum* in a child. Although every treatment effort has been made, the consequences for the patient can be long-lasting. The features of this case may be a clinical lesson, and the antibiotic therapy indicated may be useful to clinicians in the treatment of *C. violaceum* disease.

CASE REPORT

Patient: 8 years old girl, from Thai Nguyen province. The child was previously diagnosed and treated for pulmonary tuberculosis twice (TB). TB disease was stable on presentation, and the TB drugs had been stopped for 3 months.

In this episode, the disease started with pustules on the left shoulder, with a size of 1 x 1cm, painful

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Date of submission: *November 05, 2023*

Date of reviewed completion: *November 18, 2023*

Accepted date for polication: *December 15, 2023*

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and swelling quickly. On the second day of illness, the child had a fever of 38 - 38.6^{0}C all day. On the 3rd day, the blisters broke, the fluid was cloudy, leaving a ulcers and the fever increased to 39^{0}C. The child was admitted to the district hospital for treatment for 5 days with standard injectable antibiotics, but the fever gradually increased (39 - 40^{0}C), the shoulder lesions became deep sores and she was transferred to the provincial hospital. At the provincial hospital, she was diagnosed with sepsis, and treated for 5 days with empiric cefoperazone plus tobramycin. Fever did not improve, blisters appeared all over the body, concentrated on hands and feet, with a size between 2 mm and 3 cm, progressing over 5 - 7 days. Lesions started as a maculopapular rash, then transformed into vesicles, pustules, and finally ulcerations after breaking. At the same time, the back of the right hand and the ankle joints on both sides were painfully swollen. On day 13 of illness (October 1, 2022), the patient was admitted to the National Hospital for Tropical Diseases (NHTD) in Hanoi and was diagnosed with unresponsive community acquired sepsis of unknown origin. The patient was treated with empiric Ceftazidime in combination with linezolid. After 3 days the blood culture rendered *C. violaceum* bacteria. Susceptibility testing showed they were sensitive to Ciprofloxacin and imipenem, but resistant to Ceftazidime. Therapy was then changed to Meronem plus Ciprofloxacin.

Disease progression, laboratory results and antibiotic therapy performed during treatment were presented in Table 1. Other tests were also performed, including: HIV test, influenza A, B, COVID-19, nasopharyngeal culture, and blister fluid culture. All results were negative. The intra-abdominal and cardiac findings were unremarkable. Cerebrospinal fluid examination and cranial CT scan results were normal. CD4 test: 346 cells (December 1, 2022). Treatment monitoring tests: Urine test: 1st (Oct 1, 2022) protein 0.3g/L, red cells 200, 2rd (Oct 6, 2022) protein 1.0g/L, red cells 80, 3rd (Oct 12, 2022) normal results. Chest x-ray: 3 times (October 3; 7 and 11, 2022) all shown pneumonia, chest CT scan (October 17, 2022) showed pneumonia and TB stable. Blood cultures were repeated twice (October 12 and November 4, 2022) and culture of left knee pus (November 4, 2022) were negative. MRI scan: inflammatory reaction of the right hand and wrist bones (October 19, 2022), osteomyelitis - bone marrow in the upper third of the left tibia (December 1, 2022).

During treatment progress, on October 6, 2022, the disease progressed to severe, respiratory failure (breathing 50 times/minute; SpO2 85%, pulse 150 times/minute, blood pressure 100/50), blood lactate 4.37 mmol /L, blood gas PH: 7.57, pCO2 34.6, pO2 61.5, P/F 1.54, HCO3^7 31.1.

After 4 weeks of treatment, the disease stabilized, but left osteomyelitis consequences.

Table 1. Disease progression, laboratory results and antibiotic therapy performed during treatment

	Oct 1, 2022	Oct 4, 2022	Oct 6, 2022	Oct 14.2022	Nov 4. 2022
Clinical					
Temperature	39 - 40^0 C	39 - 40^0 C	39^{0}C	38^{0}C	38.2^{0}C
Glasgow Come Scale	15	15	15	15	15
Pulse (times/min)	100	110	150	130	-
Blood pressure (mmHg)	90/60	90/60	100/50	-	-
Breathing (times/ min)	20	-	50	35	25
Rale in the lungs	[7]	(+)	(+)	(+)	[7]
SpO_2	98%	-	85 %	98%	98%
Skin	Blister rash, scattered	Cloudy blisters, whole body	Cloudy blisters, whole body	Blisters scab	Blisters scab

	Oct 1, 2022	Oct 4, 2022	Oct 6, 2022	Oct 14.2022	Nov 4. 2022
Other issues	Left shoulder ulcer 1cm, yellow discharge Swelling of the right hand and ankle joints on both sides	Left shoulder ulcer 1cm, yellow discharge Swelling of the right hand and ankle joints on both sides	Right hand swelling Bleeding at the site of infusion Severe edematous extremities. Abdominal distended	Swelling of right forearm and back of hand	Leaky hand tissue inflammation, many small abscesses of knees and elbows
Liver, spleen (below costal margin)	Spleen 2cm	Spleen 2cm	Enlarged liver and spleen	[7]	[7]
Laboratory					
Red blood cells (T/L)	4.63	4.36	3.67	3.39	3.92
Hb (g/L)	113	106	92	87	98
Hct	0,34	0.33	0.28	0.27	0.30
White blood cells (G/L)	19.8	3.9	5.7	5,9	11.5
Neutrophil (%)	83.6	77.6	75.5	68.1	75.9
Platelet (G/L)	232	41	12	167	534
CRP (mg/L)	228.3	-	208.4	121.6	79
AST/ALT (U/L)	114/259	1345/653	106/193	184/170	30/9
Albumin/protein	-	-	25/56	29	
Creatinine(mmol/L)	38	108	37	23	27
Natri/Kali (mmo/L)	132/3.4	124/3.6	135/3.0	131/3.8	139/3.6
PT%			75 %	76%	73%
APTT (s)			35	31.4	
Fibrinogen (g/L)			5.15	4.98	
D-Dimer (ng/ml)			16015	16739	5241
Treatment	Ceftazidime (Oct 2-4) plus Linezolid (Oct 1 - 11)	Meronem (Oct 4 - Nov 4) plus Ciprofloxacin (Oct 4 - 28) High-flow nasal cannula oxygen therapy Platelet transfusion: 150ml (Oct 6) and 250ml (Oct 7) Transfusion of human Abumin: 20g (Oct 5 and 6 and 7) Transfusion of red blood cells 250ml (Oct 5 and 12 and 17)			

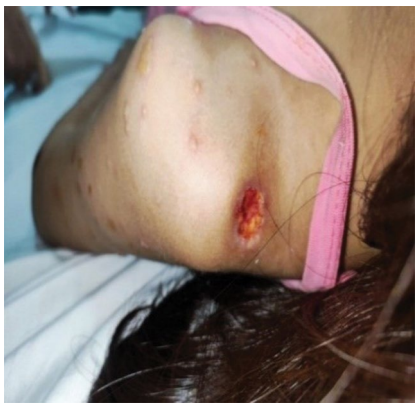

Figure 1a. primary ulcerative lesion

Figure 1b. The rash spreads all over the body

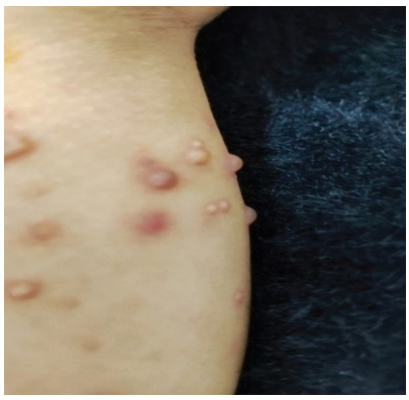

Figure 1c. Progression of rash

Figure 1. Development of a rash caused by C. violaceum (patient: L. L. Ph.Tr)

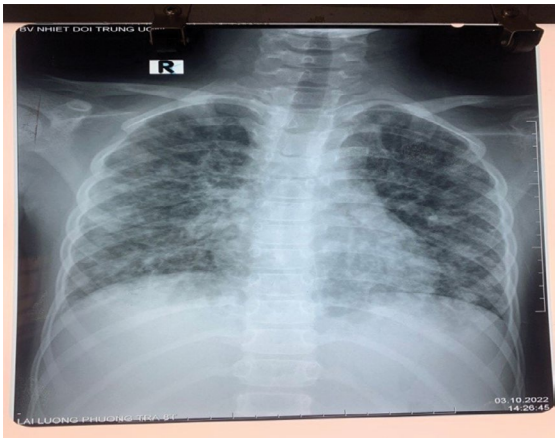

Figure 2a. X-ray of the lungs (Oct 3.2022)

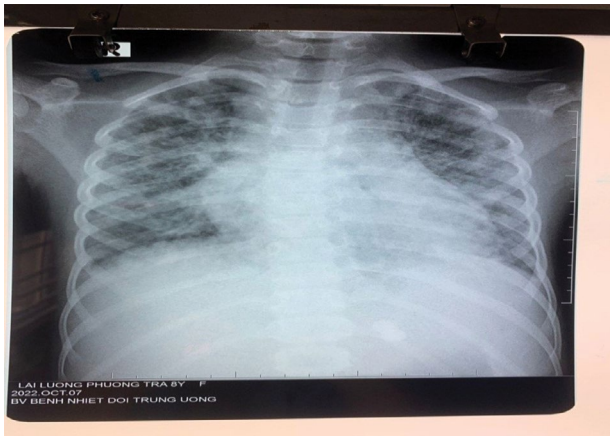

Figure 2b. X-ray of the lungs (Oct 7.2022)

Other treatments: Right hand pus drainage (Nov 1, 2022. Dredge the osteomyelitis of the hand (Nov 12, 2022). The child was treated for 73 days at the NHTD and continued to be monitored as an outpatient. Children were assigned to dredge the right heel bone twice (January 12, 2023 and February 2, 2023). The patient continued to be monitored as an outpatient and periodically examined the progression of osteomyelitis.

DISCUSSION

Infections by *C. violaceum* were still rare in humans. In the period between 1953 and 2020, globally only 132 cases of *C. violaceum* disease in humans were reported[3]. The disease is reported in both tropical countries and subtropical regions, in both high, and low- and middle-income countries[3,6,8-12].

One issue of concern is that clinical knowledge and awareness of this infection is limited. The entry route of *C. violaceum* was also unknown, possibly through the skin[3,4]. Reported cases have described disease caused by *C. violaceum*, such as sepsis and septic shock, organ damage such as pneumonia and severe respiratory distress syndrome, osteomyelitis, meningitis, endocarditis, peritonitis, liver abscess, postpartum infection, gastrointestinal infection, urinary tract infection[3,4]. Although the biological characteristics of the bacteria were known, case reports suggest that these were difficult entities to manage due to lack of clinical experience and treatment guidelines. This lead to a high mortality rate of the disease[2,3,13].

In our case, the patient was diagnosed with *C. violaceum* sepsis based on clinical evidence and blood culture results[14]. The portal of entry of bacteria *C. violaceum* was assumed to be the left shoulder ulcera. After the child scratched the affected skin, painful swelling pustules appeared. The infection progressed rapidly, with continuous fever on the 2nd day and on the 3rd day the pustules burst, leaving ulcers (see Figure 1a). From day 8 of infection, a blistering rash develops over the whole body (see Figure 1b), initially characterized by a vesicular rash, followed by pustular and ruptured pustules, progressing in 5-7 days (see Figure 1c). From day 16 of infection (June 4, 2022) the disease worsened, such as high fever, systemic pustules, pneumonia (see Figures 2a and 2b and rales in the lungs), peripheral blood leukocyte count reduced from 19.8 G/L to 3.9 G/L (see Table 1).

Notably, this patient used to have recurrent tuberculosis, possibly in this patient there was a state of cellular immunodeficiency. Moreover, after 2 months (December 1, 2022), when the disease was stable, the CD4 test showed 346 cells. Thus, it was possible that *C. violaceum* was the bacteria causing opportunistic infections in immunocompromised individuals[3,4].

About treatment: Although the child was treated with injectable antibiotics for 10 days, from the 3rd day of illness (in the provincial hospital, the combination of cefoperazone + tobramycin was treated), but the disease still progressed seriously.

At the time of admission to NHTD, the patient

was diagnosed with suspected sepsis based on the symptoms[14]: Presence of fever (39 - 40^{0}C), skin cellulitis (left shoulder), warmth, swelling of an extremity and joint (right hand and ankle on both sides) and pustules on the skin (see Figure 1c). However, the cause of hospital-acquired infection has not been ruled out because the patient's condition was very serious, moreover, the child has been treated at district and provincial hospitals for 10 days. Therefore, the initial indication for antibiotics was Ceftazidime combined with linezolid. After blood culture results confirmed *C. violaceum*, antibiotic therapy was changed according to the antibiogram (Meronem plus Ciprofloxacin). After 3 days of changing antibiotic therapy (October 6, 2022) and being treated according to the sepsis guideline[14], the patient's condition still deteriorated rapidly: pulse 150 beats/min, acute respiratory distress syndrome, infusion site bleeding, severe edema, abdominal distention, enlarged liver and spleen, severely reduced platelet count (12 G/L) and disorders of coagulation factors. The disease only tended to be in remission after 10 days of Meronem combined with Ciprofloxacin (October 14, 2022) and stabilizes after 4 weeks. However, the patient still needs to be continued to deal with the consequences, such as osteomyelitis of the right hand and the left tibia. This was a 9-year-old child, so the consequences were not only costly for subsequent treatment interventions, but also affected their ability to work and live later. In our opinion, these consequences were related to too late appropriate antibiotic therapy (day 16 of illness). If the child was given the right antibiotics early, it was certain that the disease stabilized faster, the time needed to prescribe antibiotics can be shorter and with less consequences. Although immune status may still affected the duration of treatment.

Therefore, an opinion needs to be proposed, in the context of the HIV pandemic and on acquired immunodeficiencies such as old age, underlying disease (not to mention primary immunodeficiency), if one In patients with rapidly progressive scalded skin lesions and systemic disease, *C. violaceum* should be considered. To reduce the risk of mortality and consequences events, these patients may require first-line antibiotics Meronem or Ciprofloxacin pending culture results, although *C. violaceum* was rare[3].

CONCLUSIONS

This was a case of *C. violaceum* bacteremia in a child. The child has a history of recurrent pulmonary tuberculosis and low CD4 cells. The entry route of bacteria was the site of scratching the skin. The disease progressed rapidly with features of a blistering rash, purulent progression, and high fever. Treatment with Meronem in combination with Ciprofloxacin was successful. Early diagnosis and treatment can limit the consequences of the disease.

Declaration of Figures Authenticity

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