Singapore Med J 1997; Vol 38(3):263-265

Case Report and Review of Chromobacterium Sepsis – A Gram-Negative Sepsis Mimicking Melioidosis

C Y Chong, M S Lam

Abstract

Chromobacterium violaceum **has recently been recognised as a pathogen which can cause life-threatening disease. It is the only *Chromobacterium* species which is pathogenic to humans. Due to its unfamiliarity, clinicians often do not appreciate its importance when it is isolated in sterile cultures and may dismiss it as a "contaminant". It is therefore important for us to be aware of this infection and its clinical spectrum since it is a disease of the tropics. We report a paediatric case of documented *Chromobacterium* sepsis in Singapore who presented like septicaemic melioidosis associated with diminished T-cell numbers. A review of both fatal and non-fatal *Chromobacterium*, infections is also included.**

Keywords: chromobacteria, sepsis, infection, paediatric, tropics

INTRODUCTION

Chromobacterium violaceum is a soil and water inhabitant that has only recently been identified as a human pathogen. It can cause severe life-threatening sepsis with metastatic abscesses similar to melioidosis. There are fewer than 50 cases reported in the world, the youngest being a 2-year-old boy. In this article, we report the third documented case of *Chromobacterium violaceum* sepsis in Singapore.

CASE REPORT

NBH was an 11-year-old girl admitted to the Paediatric ward in Tan Tock Seng Hospital on 31 August 1995. She presented with fever associated with rigors for a week and colicky abdominal pain for 3 days before admission. She was previously well with no major illnesses and had completed the routine childhood immunisations without adverse effects. Her elder sister had died from asthma at the age of 16 years. There was no history of exposure to soil or water via swimming or fishing. The only positive history was a prior jogging trip to the East Coast Park, a seaside esplanade.

On admission, she was febrile at 39°C, toxic-looking, tachypnoeic with a respiratory rate of 30 breaths/min and tachycardic with a pulse rate of 130 beats/min. She had nasal flaring and bilateral crepitations on auscultation of the lungs. Her abdomen was unremarkable and she had no cardiac murmurs. She was however alert and rational. There were a few papules noted over the abdomen and pubic area. Her blood counts showed Hb of 10.5 g/dL, total white cell count of 14,100/mm^3 polys 89%, platelet count of 155 X 10^9/L. Her chest X-ray on admission revealed bilateral patchy opacities consistent with bronchopneumonia. A provisional diagnosis of bronchopneumonia was made and she was started on ceftriaxone 100 mg/kg/day.

Fifteen hours after admission, she developed more severe respiratory distress with subcostal retractions. She had markedly decreased air entry bilaterally with end-expiratory rhonchi. Her oxygen saturation was 77% on room air and she was transferred to the intensive care unit. She was given oxygen and beta-agonist nebulisation. One hour later, she became hypotensive and was started on dopamine and colloid infusions. She was intubated and put on positive - pressure ventilation. She also developed bleeding from the upper gastrointestinal tract and disseminated intravascular coagulation. Pustules were noted over the lower abdomen and thighs, however there were no peripheral embolic signs. The diagnosis was changed provisionally to Gram-negative pneumonia, with possible melioidosis. The antibiotics were changed to ceftazidime and cloxacillin. (to cover possible *Staphylococcus aureus sepsis*). A differential diagnosis of chickenpox was raised; however the skin lesions were not typical. Empiric intravenous acyclovir was started while awaiting the results of the varicella zoster immunofluorescence (VZ-IF) from the pustules. The VZ-IF results were negative and intravenous cotrimoxazole was added for better coverage of presumptive melioidosis.

Thirty hours from the time of admission, she developed tenderness over the right iliac fossa and intravenous metronidazole was added to her antibiotic regimen. The paediatric surgeon who was called in did not think she had a surgical abdomen. The abdominal X-rays showed prominent bowel shadows; however, no thickening of the bowel walls nor free air was seen. The abdomen became increasingly distended and the bowel sounds were sluggish. A likely diagnosis was paralytic ileus secondary to severe sepsis. Her serum creatinine had climbed to 131 μmol/L. Fifty-two hours from admission, she developed new pustules around both arms and was in coma 3.

On the fifth day of admission, the blood cultures were reported as purple colonies due to Chromobacterium which was sensitive to gentamicin,

Department of Paediatrics
Tan Tock Seng Hospital
Moulmein Road
Singapore 308433

C Y Chong, MBBS, M Med (Paed), MRCP (UK)
Registrar

Department of Infectious Diseases and Department of Clinical Epidemiology
Communicable Disease Centre
Moulmein Road
Singapore 308433

M S Lam, M Med (Int Med), MRCP (UK), FAMS
Consultant

Correspondence to:
Dr C Y Chong

chloramphenicol, aztreonam, and ciprofloxacin. She was started on gentamicin. She did not respond to the antibiotics and piperacillin, gentamicin and cloxacillin were used instead. She went into renal failure with hyperkalemia and oliguria on the seventh day of admission. The final blood culture came back as *Chromobacterium violaceum* sensitive to piperacillin, gentamicin, chloramphenicol, ciprofloxacin, cotrimoxazole and aztreonam and resistant to the rest of the antibiotics. Aztreonam was added and gentamicin was taken off. Her condition improved somewhat by the next day; however her liver had enlarged to 3 cm. By then, she was too ill to go for further imaging studies. On the tenth day of admission, she became hypotensive again and went into heart failure. She died on the tenth day of hospitalisation.

Her serum immunoglobulins were normal with a high IgA (4.85 g/L Reference: 0.2-2.85) and IgE (153 IU/L Reference: 5-100), normal IgG (12.5 g/L Reference: 5.02 -18.1) and IgM (1.03 g/L, Reference: 0.37-1.52) and mycoplasma serology was negative. Her B cell markers showed raised percentage of B cells: CD19: 50.1% (Reference: 5.4%-26%), but normal absolute numbers: 306/uL (Reference: 100-480/uL), CD 20: 62.9% (Reference: 3.3-25.5%), but normal absolute numbers: 384/uL (Reference: 100-480/uL). T-cell markers showed a decreased CD4: absolute values 84/uL (Reference: 342-929), 13.6% (Reference: 26.6-37) and decreased CD8: absolute numbers 52/uL (Reference: 103-717), 8.5% (Reference 16.3-28.1%) with a CD 4/CD 8 ratio of 1.6 and the presence of NK cells (NK CD 16+ CD 56=0.5 %). We were unable to do further immunological tests as she had already died when these results returned. We do not know the reason for the low T-cell CD4 number, whether it was associated with sepsis, or whether she had an underlying T-cell defect which was undiagnosed previously.

This patient may have had liver abscesses as a result of hematogenous seeding although this could not be confirmed.

DISCUSSION

Chromobacterium violaceum is the only Chromobacterium species pathogenic to humans. It is a long Gram-negative bacillus and a facultative anaerobe that requires special media for isolation . Diagnosis is made by culture of blood, abscess fluid, or skin exudate; serological tests are not available. Most strains produce violacein which imparts a violet/black colour to the colonies on solid media, hence its name.

Fewer than 50 cases of *Chromobacterium violaceum* sepsis have been reported worldwide. In South-East Asia, four cases have been reported from Malaysia; a 19-year-old Malay male who succumbed 11 days after the onset of illness and 3 paediatric patients, 10 months, 9 years and 4 years old[1-3]. The first paediatric patient was a 10-month-old patient who had furuncles over the buttocks and gangrene of the toes, fingers and nose and later eye sepsis with corneal ulceration and septic arthritis of the elbow despite appropriate antibiotics. The last 2 paediatric patients presented with septic shock and died. Two cases had previously been reported from Singapore[4] from the National University of Singapore. A 3-year-old patient survived because she presented early in the course of the disease with a localised skin abscess and was given appropriate antibiotics. The second patient, a 24-year-old Englishman who had travelled to Australia and Indonesia, presented late and died of fulminant sepsis with abscesses in multiple organs. In Taiwan, a 2-year-old boy died one month later despite chloramphenicol and gentamicin[5]. Cases have been reported following near-drowning or in patients with chronic granulomatous disease[6]. An association with glucose-6 phosphate dehydrogenase (G6PD) deficiency and leukocyte dysfunction[7] was also reported in a 3 year-old child who died from Chromobacterium sepsis.

Chromobacterium sepsis tends to occur in the tropics and subtropics[8]. Of the 22 cases reported in United States, 15 had been from Florida[9]. Infection follows exposure of non-intact skin to contaminated water (often stagnant) or soil.

Most of the patients had presumed intact host defenses, however the majority of them died before the immune function tests were completed. Here, we report the first case with documented decreased T-cell number in association with Chromobacterium sepsis, either as a cause or effect of the sepsis.

Local cellulitis or lymphadenitis commonly precede systemic invasion[10]. Symptoms include pain at the site of infection, vomiting, fever, abdominal pain and diarrhoea. Septic shock develops rapidly and metastatic involvement of the lungs, liver and spleen are not uncommon.

Cases reported have included prosthetic valve endocarditis[11], periorbital cellulitis[12], conjunctivitis[13], skin abscesses[14], lymphadenitis[6], liver abscesses[15], meningitis[16], osteomyelitis and urinary tract infection. One patient experienced reinfection from insect bites received while fishing in the river, 18 months after the first infection[17]. Chromobacterium sepsis has a high mortality rate. A series in the United States[18] reported a mortality rate of 64%.

It is unfortunate that the *Chromobacterium violaceum* could not be detected earlier to enable prompt institution of appropriate antibiotics. On hindsight, this condition resembled septicaemic melioidosis. *Chromobacterium violaceum* should in future be suspected if the clinical picture resembles *Burkolderia pseudomallei* infection (melioidosis) and the patient does not respond to ceftazidime or cotrimoxazole. The laboratory may need to be alerted to the possibility of the infection since Chromobacterium may be viewed as a 'contaminant' of sterile fluid cultures.

The optimum antibiotic therapy for this condition is unknown due to the rarity of the condition. Some of the cases who survived were treated with chloramphenicol or aminoglycosides. Among the antibiotics that have been tested, ciprofloxacin was the most active in-vitro. However this antibiotic is relatively contraindicated in the paediatric population. The organism is susceptible to piperacillin, imipenem,

chloramphenicol, doxycycline, trimethoprim-sulfamethoxazole, and aztreonam. Gentamicin was more active than amikacin and tobramycin[19]. *Chromobacterium violaceum* strains are highly resistant to rifampicin, vancomycin and erythromycin. Resistance to cephalosporins is also common. Ciprofloxacin may be the most active antibiotic in-vitro but there has been insufficient clinical experience with this drug in this condition.

CONCLUSION

The importance of recognising this bacteria as a pathogen rather than as a 'contaminant' in sterile fluid cultures cannot be over-emphasized. We need to know the clinical spectrum of this disease as it is a disease of the tropics. Awareness of its presentation and its potential to cause fatal disease is important since this disease can mimic melioidosis and should be recognised and treated early so as to prevent mortality. The association with immune dysfunction needs to be studied further.

ACKNOWLEDGEMENT

Dr Diana Teo from the National Blood Centre for her valuable interpretation of the T and B cell markers.

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