Successful treatment of *Chromobacterium violaceum* sepsis in South Africa

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*Chromobacterium violaceum* sepsis is extremely rare and usually fatal. A very few cases of *C. violaceum* infection have been reported from Africa, but never from South Africa. As far as could be ascertained, this infection has never been reported in a patient with leukaemia. We describe what we believe to be the first such case of *C. violaceum* sepsis, in a 16-year-old female patient with acute biphenotypic leukaemia, which developed during the neutropenic phase after intensive chemotherapy. The infection was due to a non-pigmented strain of *C. violaceum* and was associated with a co-infection with *Candida parapsilosis*; both were successfully treated using broad-spectrum antibiotics, antifungals and removal of a Hickman line.

Introduction

*Chromobacterium violaceum* is an uncommon, but potentially life-threatening infection in humans with a very high fatality rate (Anah *et al.*, 2008). *Chromobacterium* is a genus of Gram-negative facultative anaerobic, slender, slightly curved, rod-shaped bacteria. The species *violaceum* typically grows as a dark violet, almost black colour colony on both blood and MacConkey agars (Ponté & Jenkins, 1992). Although non-pigmented strains are rare, both pigmented and non-pigmented strains exist (Ray *et al.*, 2004). The two strain types have similar pathogenicity (Sivendra & Tan, 1977). These bacteria are considered to be environmental organisms, occurring in water and soil in subtropical to tropical areas, but are not part of the normal flora of humans (Teoh *et al.*, 1977). From a review of the literature we could not find any previous case of *C. violaceum* in a patient with leukaemia, although it has been described in association with defective neutrophil function (Mamlok *et al.*, 1987). To the best of our knowledge, *C. violaceum* infection, pigmented or non-pigmented has never been described in South Africa and infection with the non-pigmented strain has never been described in Africa. Infection with the pigmented strain has been described in a case of gastro-enteritis with septicaemia in a young female from western Nigeria, as well as in a child with diarrhea from Senegal (Onile *et al.*, 1984; Dromigny *et al.*, 2002). More recently, a disturbing increase in cases of neonatal septicaemia due to *C. violaceum* has been noted in a teaching hospital in south-eastern Nigeria, which was attributed to a lack of a public water supply (Anah *et al.*, 2008). The organism has been cultured from water sources in Nigeria and Uganda before (Byamukama *et al.*, 2005; Ibibebele & Sokari, 1989). In this case report we review our experience with a *C. violaceum* infection in a neutropenic leukaemia patient receiving intensive chemotherapy.

Case report

In May 2007, a 16-year-old student, who was human immunosuppressive virus negative and known to have acute biphenotypic leukaemia since April 2006, presented at the haematology clinic with a relapse of her leukaemia at a routine follow-up visit. She was previously treated with an intensive acute lymphoblastic leukaemia (ALL) regimen followed by an acute myeloblastic leukaemia regimen with Cytosar and daunorubicin, after which she was in complete haematological remission. At the time of relapse she was on oral 6-mercaptopurine and methotrexate, which was given as maintenance treatment. She was admitted to the Leukaemia Isolation Unit and retreated with an intensive ALL regimen. On day 11 after chemotherapy was started she became neutropenic and a local infection (redness, swelling and discharge) at the Hickman-line skin entrance was noted. From a pus swab of this area *Staphylococcus epidermidis* sensitive to vancomycin was isolated. This

Abbreviation: ALL, acute lymphoblastic leukaemia.
infection was treated with local antiseptics and intravenous vancomycin.

Early on day 13 the patient complained of a non-productive cough, general myalgia and dizziness. On examination she was acutely ill with a pulse rate of 146 beats min\(^{-1}\), blood pressure of 57/26 mmHg and a temperature of 38.5 °C. Pulse oximetry revealed an oxygen saturation at room air of 98%. She was also pale with mild peripheral oedema. Examination of the throat revealed signs of pharyngitis. She was tachypnoeic and had right basal coarse crepitations on auscultation of the lungs. The rest of her physical examination was normal. Blood investigations showed a total leukocyte count of \(0.36 \times 10^9\) (with differential count unreliable due to the severe leucopenia), haemoglobin of 8.1 g dl\(^{-1}\) and \(20 \times 10^9\) platelets l\(^{-1}\). A chest X-ray revealed a right lower lobe consolidation, which supported the diagnosis of a pneumonia with septic shock (Fig. 1).

She was immediately resuscitated with intravenous fluids, including colloids (Tetrastarch), and inotropes and was started on empirical broad-spectrum antibiotics (2 g cefepime intravenous infusion twice daily for 8 days, 1 g amikacin intravenous infusion daily for 4 days) according to unit protocol. Filgrastim (300 µg subcutaneously daily for 4 days), a granulocyte colony stimulating factor, was added. Two units of leuco-depleted red blood cell concentrates and 1 single donor apheresis unit of apheresis platelets were given to the patient by transfusion. From a blood culture taken from the Hickman catheter, a Gram-negative bacillus, \(C. \) violaceum, and a yeast, \(C. \) parapsilosis, sensitive to fluconazole and amphotericin B, were cultured. The Hickman catheter was removed and treatment with 400 mg intravenous fluconazole once daily was initiated. Culture of the Hickman catheter tip also revealed the presence of \(C. \) parapsilosis, but not the \(C. \) violaceum. The isolated \(C. \) violaceum was not violacein producing and was therefore a non-pigmented strain. The organism was sensitive to cefepime, amikacin, piperacillin/tazobactam, imipenem, gentamicin and tobramycin, and was resistant to ampicillin, amoxicillin, cefazolin, cephalixin, cefuroxime, co-amoxi-clavulanic acid, co-trimoxazole and ertapenem.

In an effort to determine the source of this organism, it was discovered that the patient ate a fast-food sandwich on the evening of day 12. The sandwich was brought into the unit (against unit policy) by friends. According to the nursing staff this sandwich looked like it ‘had a layer of mould’ on top of it. The nurses tried to stop the patient from eating it, but she absolutely refused to discard it and consumed it before it could be taken away. The oral route has previously been described as a rare route of \(C. \) violaceum infection (Ponte & Jenkins, 1992). Sputum microscopy and culture did not reveal any pathogenic bacteria and specifically not \(C. \) violaceum.

Final identification of the organisms (\(C. \) violaceum and \(C. \) parapsilosis) was made using an automated microdiffusion identification system (Microscan) and API 20E system. Furthermore, the \(C. \) parapsilosis species that was isolated from blood culture and the Hickman catheter tip was identified as \(C. \) parapsilosis, which was sensitive to fluconazole and amphotericin B. Sensitivity to fluconazole and amphotericin B was assessed using the Kirby-Bauer method according to the guidelines of the Clinical Laboratory Standards Institute.

The patient made a remarkable clinical recovery and was discharged 2 weeks later. On follow up 2 weeks later the patient was still clinically well. However, a repeat chest X-ray still showed a right lower lobe consolidation with an area of cavitation. A follow-up bone marrow analysis revealed that she was not in remission and she was retreated with an aggressive ALL regimen (HyperCVAD) (Cortes et al., 1995).

One week after restarting treatment, a follow up computed tomography scan of her chest showed segmental consolidation in the right lateral basal segment, mediastinal lymphadenopathy with collateral circulation, possibly secondary to a left subclavian thrombus, and widespread nodules in the left and right lung, which was in keeping with leukaemic infiltration (Fig. 2). The patient died 3 months later due to progressive leukaemia, despite maximal treatment.

**Discussion**

To the best of our knowledge, this is the first case of \(C. \) violaceum isolated from a blood culture in the Universitas Academic Complex, the largest academic facility in the central region of South Africa, and also the first human case described from South Africa that could be identified in the literature. As far as could be determined, this is also the first described case of sepsis with the non-pigmented strain of \(C. \) violaceum in a patient from Africa, and the first case described of \(C. \) violaceum septicemia in an adult with acute leukaemia. As to the origin of this infection, the sputum

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**Fig. 1.** Chest X-ray showing right lower lobe pneumonia.
analysed was negative for the presence of *C. violaceum*, but this does not definitively exclude the pneumonia as a possible cause of the septicaemia. Unfortunately, at that stage of the patient’s disease history, it did not seem appropriate to culture stool specimens, but in retrospect stool cultures may have been valuable in determining the origin of this infection. The only growth from the Hickman line was that of *S. epidermidis*, which was never cultured from the blood. One could postulate further that contamination of the Hickman line itself was the source of the infection, as the organism was cultured from blood cultures taken from the line. Furthermore, although impossible to prove, it is not unlikely that this patient was infected via the oral route by the sandwich that she ate, which in itself would be very rare.

*C. violaceum* is supposed to be confined to tropical and subtropical regions and generally geographically restricted between latitudes 35° N and 35° S. In this case it was diagnosed in Bloemfontein in the Free State province (longitude 26 12:00, latitude 29 08:00 S), known for its hot and arid climate, with weather typical of an interior plateau (altitude of about 1300 m above sea level) with summer rains, chilly winters and plenty of sunshine. This case presented in mid-winter when the mean temperature is about 8 °C.

*C. violaceum* is a very uncommon infection and only a few cases have been reported in the literature over the past few decades. The most common clinical picture is that of abscesses with or without septicaemia developing after exposure to stagnant water. This case confirms what has been shown previously, namely that the non-pigmented strain of *C. violaceum* may be just as pathogenic as the pigmented strain. Because this is such a rare infection, there are no set guidelines on the management of this infection. Most of the described cases were treated with ciprofloxacin or gentamicin although in this case amikacin and cefepime were appropriate for controlling this infection in this severely immunocompromised patient. It is of interest to note that depsipeptide (FR9012280), a fermentation product isolated from *C. violaceum*, is currently in clinical trials for evaluation of its anticancer efficacy (Mori et al., 2004).

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**References**


