

Soft tissue infection caused by *Burkholderia cepacia* in a child with polyarteritis nodosa

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Burkholderia cepacia belongs to a family of Burkholderia species previously described as *Pseudomonas cepacia*, especially in patients suffering from cystic fibrosis. There are also many studies about this agent in the last decade due to their life-threatening infections and ability to invade mucosal and cellular surfaces. Here, we report a case of soft tissue infection caused by *B. cepacia* in a child with an underlying condition of polyarteritis nodosa. Her complaints started at two months of age and she was on cyclosporine therapy. She was treated several times because of soft tissue infections especially in her extremities. The most common causative agents were *Pseudomonas* spp. and *Escherichia coli*, but recently, another soft tissue infection accompanied by fever and signs of sepsis had developed. All blood, urine and tissue (debrided from the necrotic area) specimens were incubated. Empirical antibiotherapy with clindamycin was started and cyclosporine therapy was discontinued. *B. cepacia* was grown in the tissue specimen culture and was only susceptible to carbapenems. Meropenem therapy was administered throughout 14 days with a daily dosage of 60 mg/kg, and she was treated successfully at least in this attack of soft tissue infection, which caused more severe sepsis and tissue damage than the previous infections with other agents.

Key words: *Burkholderia cepacia*, deep tissue infection, polyarteritis nodosa, antimicrobials.

We report a case of soft tissue infection caused by *Burkholderia cepacia* in a child with an underlying condition of polyarteritis nodosa (PAN). Her complaints had started at two months of age, and she was treated because of recurrent soft tissue infections especially in her extremities. Recently, she was infected again and treated successfully for *B. cepacia* infection and sepsis.

Case Report

A one-year-old girl was admitted to the hospital because of fever, erythema and cyanosis on her upper and lower extremities from two months of age. In her first examination, necrotic debris and concomitant vascular changes in capillaroscopy revealed signs of a vasculitic disease. According to the EULAR (European League Against Rheumatism) criteria, she was diagnosed with PAN¹. Treatment was started with appropriate immunosuppressive therapy, in this case, with steroids. Recurrent

soft tissue infections were also treated several times with different antibiotics over the course of the disease. However, reactivation of the disease necessitated the administration of immunosuppressive drugs like cyclosporine to control progressive worsening. Once again, soft tissue infection accompanied by fever and signs of sepsis developed, and empirical antibiotherapy with clindamycin was started, and cyclosporine therapy was discontinued. Nevertheless, her condition worsened, and she was admitted to the Pediatric Intensive Care Unit because of sepsis. Complete blood count revealed leukopenia (1830/mm³; normal range: 4000-7500/mm³), anemia (8.9 g/dl; normal range: 12-15 mg/dl), platelet count of 235000/mm³ (150000-400000/mm³), and C-reactive protein of 23.7 mg/dl (normal value: <0.5 mg/dl). All blood, urine and tissue biopsy (debrided from the necrotic area) specimens were cultured. Supportive fluid replacement and positive inotropes were used to treat



Fig. 2. Soft tissue necrosis and damage in lower extremities.



Fig. 1. Signs of soft tissue infection.

septic shock. After hemodynamic stabilization, she was evaluated for the specific focus of infection. There were severe changes due to vasculitis in her extremities, and recently, she was re-infected, and deep wound tissue had to be debrided to diminish the area with no circulation (Figs. 1, 2). Blood and urine cultures were negative, but *B. cepacia* was grown in the tissue biopsy specimen culture, which was debrided from both extremities in the operating room. Empirical therapy was changed according to antibiogram results because there was a multi-drug-resistant species that was only sensitive to carbapenems. Meropenem therapy was administered throughout 14 days with a daily dosage of 60 mg/kg, and she was treated successfully, at least in this attack of soft tissue infection.

Discussion

Burkholderia cepacia has been recognized as a group of highly virulent organisms known as *B. cepacia* complex (Bcc), which is associated mainly with infections in patients with cystic fibrosis (CF) and chronic granulomatous disease (CGD)²⁻⁵ as well as in other immunocompromised and hospitalized patients^{6,7}. There have been reports as well documenting Bcc as being responsible for endocarditis in drug addicts⁸ or patients with prosthetic heart valves⁹, eye infections following surgery^{10,11}, and infections or abscesses of the central nervous system¹²⁻¹⁴. A review and analysis of cases infected with *Burkholderia* spp. showed especially pulmonary infections in immunosuppressive and CF patients. However, it can be seen in previously healthy persons even if it has a poorer course in immunosuppressive patients¹.

The prevalence of these pathogens varies geographically and regionally. *B. cenocepacia*

predominates in North America, while *B. multivorans* is predominant in Europe¹⁵. Illustrating this regional variation in Bcc species predominance, 85% of the Bcc isolates from patients who attended the major cystic fibrosis center in Lisbon (Portugal) belonged to the *B. cepacia* species¹⁶. In our region, several species were reported with different clinical presentations of nosocomial infections like pneumonia, bloodstream infections, surgical site infections, urinary tract infections, and skin-soft tissue infections, usually caused by *B. cepacia*^{10,11,17-19}. Virulence factors utilized by *B. cepacia*, which are only beginning to be defined, are mainly the ability to invade deeper tissues of the lung and ultimately become blood-borne. *B. cepacia* is known to produce a number of extracellular products, including hemolysins, proteases, and lipases²⁰. The ability of *B. cepacia* to adhere and invade cultured respiratory epithelial cells is consistent with clinical manifestations of *B. cepacia* infection in CF patients.

Adherence of *B. cepacia* to host mucosal and cellular surfaces may contribute to bacterial persistence in the CF lung, while penetration of epithelial cells would promote systemic spread of the bacterium to deeper tissues. Even though the studies are mostly about CF patients and lung epithelium, it can be hypothesized that similar changes can occur in subcutaneous deep tissues, as in our patient, and can be responsible for the delay in wound healing and tissue regeneration.

Treatment options depend on the clinical condition and suspected species of microorganisms. Many studies are reported with several antibiotherapy strategies with ceftazidime alone or combined with other antimicrobial agents like aminoglycosides,

piperacillin, aztreonam, cotrimoxazole. Many cases have been treated with meropenem either as monotherapy or combined with other antibiotics. However, the suggested treatment options for Bcc infection are generally limited. In combination with clinical data, ceftazidime and cotrimoxazole are suggested as the drugs of choice²¹. In an analysis of clinical characteristics and outcome of case reports on Bcc infections, the main finding was reported as: when the administration of cotrimoxazole is inappropriate or ineffective, there are alternative therapies like ceftazidime, meropenem and penicillins, mainly piperacillin, either as monotherapy or in combination. As combination therapy did not lower mortality rates, it was not considered necessary, but a more recent study suggests administration of meropenem in combination with at least one of the following: minocycline, amikacin or ceftazidime²².

In this case, the causative microorganism was *B. cepacia*, and the patient was treated successfully with meropenem monotherapy according to the antibiogram. The main underlying condition was the presence of PAN, but it is hypothesized that adherence of *B. cepacia* to host mucosal and cellular surfaces worsened her condition. Immunosuppressive treatment with the previously used steroids and cyclosporine was another risk factor for the development of sepsis. Discontinuation of immunosuppressive therapy and use of appropriate antibiotherapy were the main influential factors for recovery.

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