A catheter-related bloodstream infection caused by *Chryseobacterium indologenes* successfully treated with antibiotic-lock rescue therapy

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*Chryseobacterium indologenes* is a gram negative bacteria commonly distributed in nature and in the hospital environment such as mechanical ventilator circuits (Serkan et al., 2016). Infections due to this microorganism are rare and generally affect infants, hospitalized patients with immunocompromised conditions or with medical device implants. *C. indologenes* is resistant to many antimicrobial agents including carbapenems (Chang et al., 2015) and produces biofilm. Due to this characteristic, removal of the central venous catheter (CVC) appears to be the most reasonable treatment for CVC infection.

We describe a case of sepsis from an uncommon and multi-resistant pathogen in a pediatric patient with a long-term vascular access device placed for chemotherapy treatment. The infection was successfully treated with ciprofloxacin antibiotic-lock therapy. This is the first report on successful salvage of a long-term device colonized by multi-resistant *Chryseobacterium indologenes*.

**SUMMARY**

We report the case of a catheter-related bloodstream infection caused by *Chryseobacterium indologenes*, an uncommon and multi-resistant pathogen, in a pediatric patient with a long-term vascular access device placed for chemotherapy treatment. The infection was successfully treated with ciprofloxacin antibiotic-lock therapy. This is the first report on successful salvage of a long-term device colonized by multi-resistant *Chryseobacterium indologenes*.

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At the end of chemotherapy the catheter was electively aspirated and antibiotic-lock therapy the catheter was administrated while the catheter was not in use between venous therapy) for about 12 hours/day, plus intravenous ciprofloxacin for 9 days, then switched to an oral formulation at discharge. The volume used for the lock therapy was twofold the volume of the dead space of the single-lumen of the catheter and the antibiotic-lock was administered while the catheter was not in use between administrations of systemic therapy. After each cycle of antibiotic-lock therapy the catheter was aspirated and washed with saline as provided by internal guidelines. The clinical course was positive: the child remained afebrile and in good clinical condition. CRP levels and blood cultures, repeated on days three and seven of the lock-protocol, remained negative meeting our rescue endpoints. The remaining scheduled cycles of chemotherapy were completed without additional infections or complications. Surveillance blood cultures drawn from the CVC were negative after 1 and 2 months. At the end of chemotherapy the catheter was electively removed and the tip culture was negative. Twenty-four months after the end of therapy, the child is well and still in complete remission.

DISCUSSION

Pediatric patients with hematological malignancies or solid tumors are at high risk of infections. In this population, bacteremia still has an incidence of 10-40%, and is associated with serious complications and even death, with fatality rates ranging from 9 to 24% (Celkan et al., 2002; Zakhour et al., 2016). Susceptibility to infections results from the effects of high-dose chemotherapy or radiotherapy (Lv et al., 2013), and from several host factors, including surgical procedures, alteration of normal intestinal and skin flora and the use of invasive devices such as Long-Term Vascular Access Devices (LTVADs) (Celkan et al., 2002). CVCs are essential in the management of cancer, particularly in children, because they provide a reliable access site for chemotherapy, apheresis, transfusions, parenteral nutrition and blood sampling. However, the catheter hub and lumen are often colonized and the development of biofilm facilitates the adhesion of microorganisms and acts as protection against antibiotics (Mermel et al., 2010). Moreover positioning a new device can be a difficult and risky procedure because access sites are often limited and patients are frequently pancytopenic. Identification of effective procedures to eradicate CRBSI, while retaining the catheter, is therefore an important challenge. The Infectious Diseases Society of America (IDSA) guidelines for CRBSI emphasize that short-term devices must be removed, but long-term devices may be retained if the infection is not complicated and the pathogen can be treated with a reasonable chance of success (Mermel et al., 2009). The rescue procedure consists of both systemic antibiotics and lock-therapy, a technique that consists of an antibiotic-containing flush solution directly instilled into the lumen of the CVC (Henrickson et al., 2000). Recently, the unconventional use of ethanol as lock therapy has also been suggested.

The bacteria isolated in our patient, Chryseobacterium indologenes (previously named group IIb organisms by the Centers for Disease Control and Prevention, and later renamed as Flavobacterium) is an uncommon pathogen, normally not present in human microflora (Hsueh et al., 1996), that can survive in chlorinated waters (water systems or on wet surfaces) that act as a reservoir of infection. Chryseobacterium is a nonfermentative, non motile, aerobic, gram-negative bacillus. It is catalase, oxidase and indole positive and produces a distinctive yellow to orange pigment. The colonies are circular and smooth, making them difficult to remove from solid media. The clinical significance of Chryseobacterium indologenes has not been fully established, because this bacterium is infrequently identified in clinical specimens, is often erroneously identified by microbiology laboratories or is considered a culture contaminant because most strains do not grow on MacConkey’s agar; but grow well on blood agar after 24 hours incubation at 37°C.

Reported cases of Chryseobacterium indologenes bacteremia have been associated with nosocomial pneumonia, biliary tract infection, peritonitis, urinary tract infection, surgical wound infection, cellulitis, intravascular catheter-related bacteremia, and primary bacteremia (Chen et al., 2013; Mukerji et al., 2016). Most cases in the literature describe patients who had received long-term broad-spectrum antibiotics, with a severe underlying disease, such as malignancy or diabetes mellitus, or with indwelling devices (Esposito et al., 2014; Deng et al., 2015). Due to the increasing clinical usage of Colistin and Tigecyclin against emerging Carbapenem-resistant pathogens, multi-drug resistant Chryseobacterium species have caused significant problems in the critical healthcare setting. Moreover, effective empiric treatment for Chryseobacterium indologenes is unclear due to its variable and broad drug resistance. Accurate management of CRBSIs caused by Chryseobacterium indologenes is still debated. Hsueh et al. (1996), basing their conclusions on five patients, stated that CVC in-
fection caused by *Chryseobacterium indologenes* does not always require removal of the device, while Lin *et al.* (2010) suggested that indwelling devices should be removed as soon as possible if a *Chryseobacterium indologenes* infection is suspected due to the wide range of antibiotic resistance and difficulty in determining optimal therapeutic regimens. Chen *et al.* (2013), on the basis of results from 18 patients with a CVC and 6 with CRBSIs, claimed that removal of devices colonized by *Chryseobacterium indologenes* is not always necessary because eradication is possible with correct systemic antibiotic therapy, but with a very high 30 day mortality (33.3% vs 61.5% in appropriate vs. inappropriate antibiotic therapy).

Our case suggests that, in a stable patient under strict monitoring (CRP and blood cultures), LTAVDs can be retained using a combination therapy of systemic plus lock antimicrobials, based on susceptibility testing. In our patient, systemic therapy alone was not sufficient to clear *Chryseobacterium indologenes* from the contaminated CVC, as shown by infection relapses, probably because of the presence of biofilm that plays an important role in the virulence of *Chryseobacterium indologenes*. On the contrary, lock-therapy was effective in sterilizing the CVC, as shown by infection relapses, probably because of the presence of biofilm that plays an important role in the virulence of *Chryseobacterium indologenes*. In our patient, systemic therapy alone was not sufficient to clear *Chryseobacterium indologenes* from the contaminated CVC, as shown by infection relapses, probably because of the presence of biofilm that plays an important role in the virulence of *Chryseobacterium indologenes*. In conclusion, we suggest that an appropriate antibiotic-lock therapy, guided by susceptibility testing, may be considered an alternative to catheter removal even in LTAVDs colonized by *Chryseobacterium indologenes*.

**Disclosure statement**

The authors have no conflicts of interest to declare.

**References**


