Successful treatment with short-course Daptomycin lock and systemic therapy in two cases of catheter-related bloodstream infections due to uncommon pathogens

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Abstract

Treatment of catheter-related bloodstream infections (CRSBI) is one of current major challenges in management of long-term catheters. Daptomycin has proved its efficacy as lock therapy for treating CRSBI due to coagulase negative Staphylococci.Here we describe two cases of successful treatment with short course Daptomycin as lock and systemic therapy for CRSBI due to uncommon pathogens, thus bringing new insights about strategies for a conservative management of devices.

Introduction

Long-term in-dwelling catheters are commonly used devices, especially in cancer patients and in those receiving parenteral nutrition. Treatment of catheter-related bloodstream infections (CRSBI) is one of current major challenges in their management.

Indeed, CRSBI are associated with increased morbidity, mortality and costs (1-4).

Antimicrobial failure to treat CRSBI is essentially linked to microbial biofilms, which develop when bacteria adhere on the catheter surface, thus producing a matrix acting like a filter which reduces the capacity of antimicrobials to inhibit bacterial growth (5).

In the majority of cases, catheter removal is recommended, especially in case of *Staphylococcus aureus*, Fungal and Pseudomonas infections (6).

However, catheter salvage could be an option in situations when venous access is poor, especially in case of coagulase-negative Staphylococcal (Co-NS) infection, such as *Staphylococcus epidermidis*, *Staphyloccus hominis* and *Staphylococcus lugdunensis*. Indeed, the clinical course of CRSBI infections due to Co-NS is generally benign and both *in vitro* and *in vivo* data suggest the possibility of conservative management of the catheter when antibiotic-lock therapy (ALT) is associated with systemic treatment (6-12).

ALT consists in instilling antimicrobials in the catheter hub, in order to achieve antibiotic concentrations many-fold higher than the minimal inhibitory concentration (12-13). The antibiotic should remain in the hub for a specified duration, typically between 18 to 24 hours, and this strategy appears particularly useful for patients in whom reintroducing a catheter may be difficult (12).

Among antibiotics used as ALT, Daptomycin (DPT) appears to be one of the most promising agents (9, 10, 14). We recently showed that a short course of DPT as ALT, associated with systemic treatment, could allow high rates of success in case of CRSBI due to Co-NS infection(15).This strategy allows catheter reutilization after 3 days of treatment and has the potential to reduce hospital stay and costs.

Here we present two cases of successful treatment with short-course DPT as ALT for CRSBI due to uncommon bacteria.

Case 1

In August 2016, a 61 year-old man was admitted to our Department for fever. He had been followed for 2 months for lung cancer and had been receiving intravenous chemotherapy. His latest dose had been administered a few days before his transfer to our Department from a local Clinic.

Several blood cultures, withdrawn from the port-a-cath and from peripheral blood, grew *Staphylococcus condimenti*. CRSBI was defined according to the criteria described in current guidelines (16). In line with previously

published articles (15, 17, 18), our local guidelines suggest locking with DPT, diluted in Ringer's solution (5 mg/ml) (8, 17, 18). Five millilitres (19) of the prepared, heparin-free solution (i.e. 25 mg of DPT) are instilled in the catheter lumen for 18 hours daily, usually for 3 consecutive days (17). ALT is initially combined with systemic treatment, i.e. DPT (using the remaining quantity from the same vial) with Rifampin, due to their synergistic activity (20).Treatment may then be modified, commonly after 3-4 days, in order to achieve the recommended duration of systemic treatment of 10-14 days (6).The choice of antibiotic for the switch is guided by microbiological results and susceptibility testing and is preferentially administered orally. Rifampin is generally discontinued concomitantly with DPT, as its administration is mainly justified by its synergistic action with DPT on the biofilm.

The patient thus received 3-days' ALT with DPT, associated with systemic DPT and Rifampin. He rapidly became afebrile, and on day 4 antibiotic treatment was switched to oral linezolid in order to complete the total course of 14 days and the patient was discharged. Chemotherapy was resumed rapidly after he left our Department. One month after ending antibiotic treatment, he remained afebrile and the chemotherapy protocol was still ongoing.

Case 2

In June 2016 a 70 year-old female patient was admitted to our hospital for fever. She had been followed for metastatic anal cancer and had been receiving intravenous chemotherapy via a port-a-cath. She was transferred to our Department from a Cancer care center in Nice. Several blood cultures,from the port-a-cath and peripheral blood, were positive for *Corynebacterium sp*., with CRSBI-defining criteria .

She received the same antibiotic protocol as the previous patient, i.e. 3 days of systemic and ALT DPT, associated with systemic Rifampin. She rapidly became afebrile and on the basis of sensitivity testing of *Corynebacterium sp*., she continued treatment with levofloxacin orally from day 4, in order to complete two weeks' therapy. She was rapidly discharged and continued her chemotherapy protocol in the Cancer reference center. One month after ending antibiotic treatment she was still afebrile and the catheter was maintained.

Conclusions

We describe two cases of CRSBI due to very rare pathogens, successfully treated with a short-course of DPT as ALT.

Staphylococcus condimenti was first isolated from soy sauce mash in 1998 (21) and has never been reported as a human pathogen, until 2014, when Misawa *et al*. described the first case of CRSBI related to such bacteria(22).

Corynebacterium sp. has rarely been described as responsible for CRSBI (23-25). There are very few data available on conservative management of the device with antibiotic treatment (26, 27) and guidelines generally suggest catheter removal as the primary option in case of infection with *Corynebacterium*, *Bacillus* and *Micrococcus* species (6).

To our knowledge, these are the first cases of CRSBI due to such pathogens successfully treated with DPT and catheter salvage.

DPT has potent capacity to inhibit replication of gram-positive biofilm-forming bacteria, probably superior to Vancomycin, even for stationary-phase bacteria (11).

As a calcium-dependent antibacterial agent, DPT optimally works *in vitro* with levels of free calcium ions at physiological concentrations (50 μg/ml). Therefore, it is generally diluted in lactated Ringer's solution, containing 50–80 μg/ml of calcium (8, 17).

DPT has revealed its efficacy as ALT in a few clinical studies on CRSBI due to common Co-NS (18, 28).We recently showed that the duration of DPT can be shorter, with potential advantages in terms of costs and patient's quality of life (15).

We presented here two cases of successful treatment with short course DPT in case of CRSBI due to rare pathogens, thus bringing new insights about strategies for a conservative management of devices.

Key points

DPT has revealed its potency as a molecule for ALT in case of CRSBI due to common Co-NS, with the possibility of reducing the duration of therapy and allowing good rates of catheter salvage

In this case series, we showed the efficacy of short course DPT even in case of CRSBI due to uncommon pathogens.

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