Gentamicin–vancomycin–colistin local antibiotherapy in a cement spacer in a 54-year-old haemophilic patient with relapsing plurimicrobial severe prosthetic joint infection

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DESCRIPTION

A 54-year-old patient with haemophilia and hepatitis C virus infection experienced acute left prosthetic joint infection due to *Klebsiella pneumoniae* and *Staphylococcus aureus* following unipolar exchange in September 2015. As the outcome was not favourable with bloody discharge despite haemophilic factor substitution, a new local debridement was performed in May 2016 and multidrug-resistant *Enterobacter asburiae* (only susceptible to imipenem, colistin, amikacin and fosfomycin) and *Corynebacterium striatum* (only susceptible to vancomycin, rifampin and linezolid) grew in cultures. As explantation was considered too risky due to the potential bleeding, systemic intravenous treatment was proposed with imipenem (3 g/day), vancomycin (2.5 g/day) and fosfomycin (12 g/day). After 3 months of therapy, the bloody discharge persisted. One month after discontinuation of antibiotics, the patient presented a large 'bourgeon charnu' with impressive bloody discharge (figure 1A). X-ray revealed trochanter osteolysis, without prosthesis loosening (figure 1B). Prosthesis explantation was performed, and a commercial articulated spacer was inserted. We used the COPAL G+V, which delivers locally a high amount of gentamicin and vancomycin. To have an activity against the Gram-negative pathogen, we decided to add 6 MUI of Colimycine to each dose of cement even if few data were available on this practice.[1] A total of five doses were required to do the articulated spacer (figure 1C), leading to a total local dose of 30 MUI of colimycin. Additionally, the patient received as empirical therapy meropenem (6 g/day) and daptomycin (700 mg/day). Colistin (the active form of Colimycine) concentrations were measured locally from suction drainage fluid and in plasma (to ensure that there is no systemic diffusion) using liquid chromatography. High concentrations of colistin were measured locally during several days, 32 times (at day 1) and 5 times (at day 4) above the *E. asburiae* colistin minimum inhibitory concentration (MIC=0.125 mg/L). Cultures of per operative samples yielded the same *E. asburiae*, but not the *Corynebacterium*. Colistin concentration in plasma was below the limit of quantification set at 0.04 mg/L. Colistin was then administered systemically at day 5, taking over the local administration. The outcome was initially favourable, but

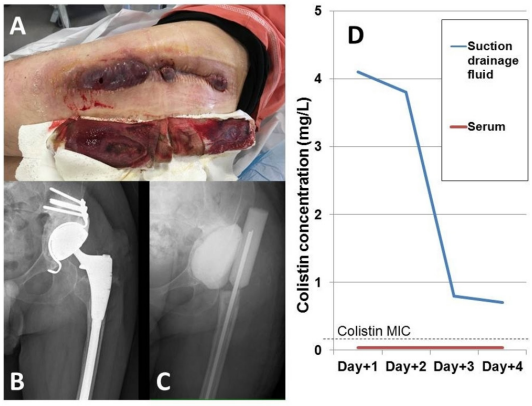

Figure 1 Local (A) and radiological (B) aspects before prosthesis explantation; radiological aspect of the antibiotic-loaded articulated spacer, after prosthesis explantation (C); colistin concentrations in the suction drainage fluid and in plasma (D). MIC, minimum inhibitory concentration.

debridement and spacer explantation were required several weeks later as haematoma with bloody discharge occurred. Superinfection with *Enterococcus faecalis* and *Candida albicans* was detected and treated. The *E. asburiae* was never found again. Nine months later, a small intermittent haemorrhagic discharge was still observed, making prosthesis reimplantation impossible.

Articulated spacers are currently used in patients with knee prosthesis infection, as they are associated with significant improvement of clinical results and knee functionality after reimplantation.[2] Moreover, in prosthetic joint infections, there is growing evidence concerning the potential efficacy of antibiotic-loaded spacer that provides a high local concentration of antibiotic.[3] Commercially or locally

Learning points

- Antibiotic-loaded spacer delivers high concentrations of colistin locally, without systemic diffusion.
- Combination of local antimicrobials could be useful for the treatment of multidrug-resistant prosthetic joint infection.

made gentamicin or vancomycin spacers are usually used in this indication. Facing polymicrobial prosthetic joint infection with multidrug-resistant pathogens, it could be useful to use a combination of antibiotics in the spacer. Gentamicin and vancomycin are synergistic against staphylococci and might also prevent superinfection with these pathogens. Here, awaiting the culture results, the addition of colimycin in the spacer allowed high local concentrations of colistin, with no potential of systemic toxicity.

Contributors TF designed the management of the patient with the antibiotic-loaded spacer and wrote the draft of the manuscript. All authors (TF, RD, SM and FV) participated in the patient care, the literature review and the improvement of the manuscript. SM performed the measurements of colistine.

Competing interests None declared.

Patient consent Obtained.

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