Ultrasound-guided local administration of personalized cocktail of bacteriophages followed by suppressive antibiotherapy as salvage therapy in patients with relapsing total femur prosthetic joint infection (PJI)

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INTRODUCTION

Lytic bacteriophages are of interest to treat patients with PJI based on their synergistic activity with antibiotics on bacteria in biofilm. In patients with relapsing total femur PJI, disarticulation is often unfortunately the only final option. In such a population, suppressive antimicrobial therapy is sometimes used after performing an open “DAIR” procedure, but the skin closure may be not possible and the success rate of this conservative approach is so low in such patients.

MATERIALS- METHODS

In our reference regional center “CRIOAc Lyon” ultrasound-guided (**panel A**) local administration of personalized cocktail of bacteriophages of anti-*S. aureus* or anti-*P. aeruginosa* bacteriophages followed by suppressive antibiotherapy is proposed for relapsing total femur PJI with no therapeutic option or therapeutic dead-end (**panel B, C**).

Each case was discussed with the French health authority. Bacteriophages were produced following the Good Manufacturing Practice (GMP) guidelines and were selected by Pherecydes, according to their activity (**panel D**). Hospital pharmacist mixed each phage (1 ml of $1x10^{10}$ PFU/ml) extemporaneously as “magistral” preparation (final dilution $1x10^{8}$ PFU/mL).

RESULTS

Two patients (55 and 84 yo) experiencing a relapsing *S. aureus* or *P. aeruginosa* total femur PJI following previous debridement and implant retention procedure, were treated with personalized cocktails. One patient had soft-tissue defect with suppurative discharge (**panel C**).

At the time of injection, both patients had already received targeted antibiotics, cefoxitin (for *S. aureus*) and ceftazidime (for *P. aeruginosa*), respectively. After the phage injection, antibiotics were switched to daptomycin-levofloxacin followed by doxycycline for the first one, and ceftazidime was maintained for the second.

After a follow-up of 8 months, clinical signs of infection were improved, as systemic biologic markers of infection, in the first patient (**panel E**). Superinfection with *C. albicans* was unfortunately discovered at the time of phage injection, with *C. albicans* persistence and unfavorable outcome in the second one.

CONCLUSIONS

Ultrasound-guided local administration of personalized cocktail of GMP bacteriophages followed by suppressive antibiotherapy in patients with relapsing total femur PJI has the potential to be used as salvage therapy to control the infection and avoid disarticulation. Dramatic superinfection could be diagnosed at the time of phage administration.

A

Panel A
ultrasound-guided local administration of cocktail of bacteriophages

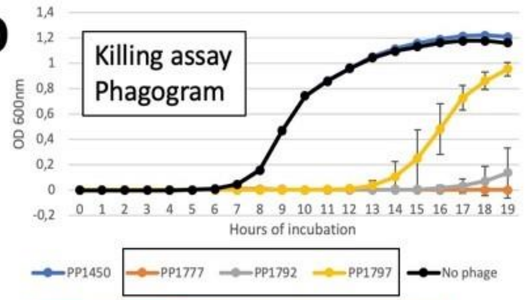
B

Panel B
X-ray of the right total femur without loosening

C

Panel C
Relapsing total femur PJI: soft-tissue defect with suppurative discharge

D



Panel D
Phagogram

E

Panel E
Improvement of clinical signs of infection