EP CASE REPORT

Successful bacteriophage treatment of infection involving cardiac implantable electronic device and aortic graft: a Trojan horse concept

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Introduction

Device-associated infections are difficult to cure as standard antibiotic treatment cannot eradicate biofilms. Removal of the device is usually the only successful therapy, however, removal is not always possible or is associated with high mortality.[1] We report a successful bacteriophage therapy case with chronic recurrent CIED and carotid subclavian bypass infection.

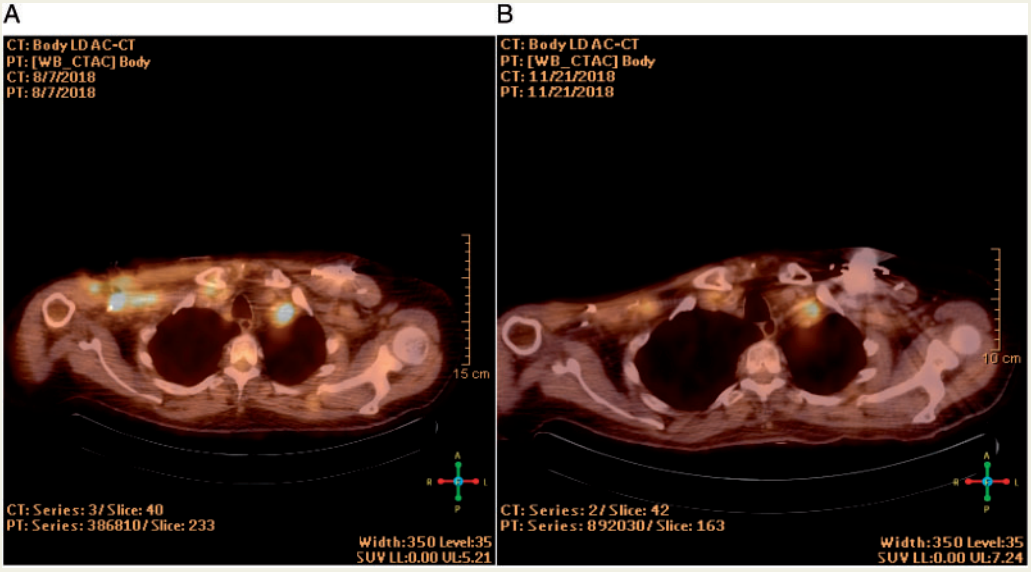

Figure 1 ^{18}F-fluorodeoxyglucose positron-emission tomography computed tomography before phage therapy (*A*) and 3 months later (*B*) showing reduced glucose uptake.

Case report

A 41-year-old man with a cardiac resynchronization therapy with defibrillator (CRT-D) (implanted 2016) presented with suspicion of a CIED pocket infection. The patient was diagnosed with Marfan syndrome and had undergone extensive cardiovascular surgery, including aortic root, ascending aorta (05/2000), and total aortic arch replacement, along with a right carotid-subclavian bypass (08/2013).

On admission, the patient was in reduced general health with significantly increased inflammatory biomarkers. The CIED pocket showed signs of infection, yet no wound discharge. No vegetations were seen in the transoesophageal echocardiography and blood cultures were negative. The CRT-D system was explanted and empiric intravenous antibiotic therapy was started (Meropenem 1 g/8 h and Daptomycin 700 mg/24 h). During device explantation, a connection to the carotid subclavian bypass was found, surrounded with pus. A vacuum assisted closure (VAC) therapy was initiated. A positron-emission tomography–computed tomography (PET-CT) showed extensive inflammation involving the complete vascular graft (*Figure 1A*). Intraoperative specimens (from the bypass) grew *Staphylococcus aureus* and *Cutibacterium acnes* and antibiotics were changed to Flucloxacillin (2 g/4 h), Fosfomycin (5 g/8 h). Intraoperative swabs from the device pocket remained negative. Despite the combined VAC (18 days) and intravenous antibiotic therapy (36 days), the surgical wound showed continuous discharge, microbial cultures remained positive.

Due to high operative risk and severely impaired left ventricular function; an 'ultima ratio' treatment attempt with bacteriophages was proposed with the patients informed consent.

During surgical debridement, no antiseptics were used. Bacteriophages were applied as a loading dose of bacteriophage solution (10 mL) containing 1:1 mixture of PYO bacteriophage at $\approx 10^6$ plaque-forming units (PFU)/mL (R-022600) and Staphylococcal bacteriophage Sb-1 at $\approx 10^7$ PFU/mL (R-022876), both from ELIAVA Institute of Bacteriophage, Tbilisi, Georgia. After surgery, a drain was placed into the surgical site before wound closure, through which 5 mL of bacteriophage solution was instilled every 8 h for 14 days. After 21 days, intravenous antibiotics were switched to oral Levofloxacin (500 mg/12 h) and Rifampicin (450 mg/12 h) for 3 months.

At follow-up after 3, 6, and 12 months, no local or systemic signs of infection were observed. Blood cultures remained negative, serum C-reactive protein was low, and the 3 months PET-CT showed reduced glucose uptake (*Figure 1B*).

Discussion

Bacteriophages invade bacterial cells and use their replication system to kill them;[2] they mainly replicate at the site of infection, which is associated with low risk of adverse events.[2] Some phages have the ability to penetrate deeper as they produce lytic enzymes against extracellular matrix of the biofilm.[3] Moreover, studies revealed that phages can eradicate biofilm infections by working synergistically with antibiotics.[3]

Bacteriophages could become the Trojan horse in treating device-associated infections that are untreatable by conventional therapy. However, currently no data exists about short- and long-term adverse events.

Conflict of interest: none declared.

References

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