Novel bacteriophage therapy for treatment of left ventricular assist device infection

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We report the case of a 65-year-old male with non-ischemic cardiomyopathy requiring left ventricular assist device (LVAD) implantation in 2014. He developed a Staphylococcus aureus (SA) device infection complicated by sternal osteomyelitis and bacteremia, leading to multiple hospitalizations, surgical debridements, and prolonged intravenous (IV) antibiotics (refer to Table S1 in the Supplementary Material available online at www.jhltonline.org). He was considered ineligible for heart transplant because of ongoing infection and presented to our center for a second opinion. We elected to use IV bacteriophage therapy (BT) as an adjunct to antibiotics for improved suppression and possible cure of the infection.

Bacteriophages are viruses that infect specific bacteria but not human cells and penetrate SA biofilm efficiently.1,2 There has been recent interest in exploring BT for various clinical applications (refer Supplementary Material online), including a case report for treatment of an aortic graft infection.3 AB-SA01 (NCT03395769; AmpliPhi Biosciences), a combination of 3 anti-staphylococcal bacteriophages, was used after in-vitro bactericidal activity against the patient’s clinical isolates was confirmed.

Before BT initiation, the patient had an open chest wound with a visible device (Figure 1) that repetitively grew methicillin-sensitive SA (MSSA) despite 2.5 months of antibiotics (see Supplementary Material online). After informed consent, the patient received IV AB-SA01 (3 × 10^9 plaque-forming units) every 12 hours for 28 days as an outpatient under U.S. Food and Drug Administration authorization (emergency IND #18133). Cefazolin 2 g IV every 8 hours and minocycline 100 mg orally twice daily were continued.

BT was administered without adverse clinical or laboratory events. By Week 1, and thereafter, the patient noted continued improvements in his energy level. Hemoglobin rose from 10.5 to 12.3 g/dl. Calculated panel-reactive antibody levels remained unchanged. Sternal cultures became negative for MSSA at Weeks 1, 2, and 4 (end of therapy, EOT); Week 3 culture grew MSSA and S epidermidis. At EOT, wound appearance had improved with reduced purulence and healthy granulation tissue. The patient underwent heart transplantation 1 week later. Intra-operative cultures of the graft pocket, LVAD pocket, pericardial tissue, left rib tissue, sternal bone, GoreTex patch, inflow cannula pocket, and inflow graft pocket were obtained. The latter 2 samples grew scant MSSA; all others were negative. Given positive surgical cultures, the patient received an additional 8 weeks of cefazolin. MSSA isolates after BT initiation showed no changes in antibiotic resistance profile and remained sensitive to AB-SA01. The patient is now 7 months post-transplant and doing well clinically with no infection recurrence.

We have reported the first successful use of BT as an adjunct to antibiotics for LVAD infection. The combined treatment resulted in negative sternal wound and intra-operative samples, except for the inflow cannula pocket and inflow graft pocket. The latter 2 positive cultures may have been related to poor blood flow and phage delivery to the external surface of the exposed device. We believe AB-SA01’s bacterial specificity, safety profile, and biofilm activity make it attractive to study as a treatment of staphylococcal device infections. We plan to conduct a pilot study to evaluate the effects of adjunctive AB-SA01 with IV antibiotics for treatment of staphylococcal LVAD infections.

Disclosure statement

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Supplementary data

Supplementary data associated with this article can be found in the online version at www.jhiltonline.org/.

Supplementary materials

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References


Figure 1  Sternal wound at baseline (A) and at end of bacteriophage therapy (B) with visible ventricular assist device. (A) Wound with purulence and poorly granulating tissue. (B) Healthy red granulation tissue and reduced purulence.