

SURGERY

CASE REPORT: CLINICAL CASE

Successful Investigational Phage Therapy for Pan-Resistant Bacterial Mediastinitis Following Type II Hybrid Aortic Arch Replacement



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ABSTRACT

A 47-year-old woman presented to our hospital with Stanford type B aortic dissection with retrograde arch extension. The decision was made to undergo hybrid arch repair with thoracic endovascular aortic repair. The patient underwent surgery, but her intraoperative course was complicated by delayed sternal closure and mediastinitis requiring flap reconstruction. Recurrent pan resistant *Klebsiella* sternal wound infection (SWI) was observed, for which successful investigational bacteriophage therapy initiated through mediastinal drains. She remains infection-free at 2-year follow-up. SWI is a morbid complication following cardiac surgery, particularly when colonized by pan-resistant bacterium. Phage therapy refers to the therapeutic use of modified bacteriophages and have been previously described for use in mediastinitis. We report the use of phage therapy to treat *Klebsiella* SWI in our patient. This case report adds to the current evidence supporting the use of phage therapy for treatment of complicated mediastinal wound infection following aortic arch surgery. (JACC Case Rep. 2024;29:102816) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

HISTORY OF PRESENTATION

A 47-year-old morbidly obese woman presented to the emergency department with acute breakthrough upper chest and back pain. The symptoms had begun that morning after she woke up to go to work.

PAST MEDICAL HISTORY

Past medical history was significant for morbid obesity (body mass index 56 kg/m²), type 2 diabetes (on insulin), and hypertension. Additionally, surgical

TAKE-HOME MESSAGES

- When present, complex mediastinal wound infection requires extensive multidisciplinary collaboration between surgeons and infectious disease specialists to optimize patient outcomes.
- This case report contributes to the growing literature showing the utility of phage therapy for treating persistent, pan-resistant mediastinal infection.

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ABBREVIATIONS
AND ACRONYMS

- CT = computed tomography
- DSC = delayed sternal wound closure
- LSCA = left subclavian artery
- TEVAR = thoracic endovascular aortic repair
- PET = positron emission tomography
- POD = postoperative day
- VAC = vacuum-assisted closure

history was significant for hysterectomy and endovascular infrarenal abdominal aortic aneurysm repair.

DIFFERENTIAL DIAGNOSIS

Plausible differential diagnoses for the patient’s presentation included acute aortic dissection, aneurysm rupture and myocardial infarction.

INVESTIGATIONS

Computed tomography (CT) angiography confirmed a Stanford type B aortic dissection with zone II arch extension to the level of an infrarenal endoprosthesis from prior endovascular repair of abdominal aortic aneurysm (Figure 1). Also, we noted a dominant left vertebral artery originating from the aortic arch. After discussion with patient and family, the decision was made to undergo complex type II hybrid aortic arch repair with great vessel debranching and thoracic endovascular aortic repair (TEVAR).

MANAGEMENT

In preparation for TEVAR, the patient underwent left carotid-subclavian bypass using an 8-mm interposition graft (Terumo Corporation). Next day, the patient underwent type II hybrid arch repair. After aortic cross-clamping, the ascending aorta was resected just above the sinotubular junction, and a 28-mm Lupiae graft was anastomosed above the sinotubular junction. Upon initiating deep

hypothermic circulatory arrest with retrograde cerebral protection, transverse hemiarch replacement with debranching of the innominate artery and left subclavian artery (LSCA) performed using 10-mm and 8-mm grafts of the Lupiae graft. The left vertebral artery was debranched using a saphenous vein conduit. Upon completion of the aortic reconstruction and rewarming, the patient was taken off cardiopulmonary bypass successfully. However, due to loss of domain, chest closure was not possible (Figure 2).

On postoperative day (POD) 2, the patient successfully underwent retrograde TEVAR with endovascular LSCA coil embolization (Figure 3). Completion aortogram confirmed patent great vessels and proper graft positioning no endoleak. After serial chest washouts, on POD-10, the patient underwent bilateral pectoralis major flap reconstruction with wound vacuum-assisted closure (VAC) successfully. Two superficial drains were placed underneath the muscle flaps.

The patient was recovering well until approximately a month later, when she developed a large aortic bleeder in her chest requiring laparoscopy-assisted reconstruction of the infected graft with pericardial patch and delayed omental flap reconstruction of the chest. The patient went on to recover stably over the coming weeks and was ready for hospital discharge.

On POD-25 after omental flap reconstruction, the patient developed an enlarging infectious hematoma with presence of gram-negative bacilli. The decision

VISUAL SUMMARY. Timeline	
Date	Events
POD 0	A 47-year-old woman presented with acute breakthrough back/chest pain and found to have a Stanford type B aortic dissection with retrograde arch extension. The decision was made to undergo left carotid-subclavian bypass followed by type II hybrid arch repair. The sternotomy incision was left open due to loss of domain.
POD 2	The patient successfully undergoes retrograde TEVAR with endovascular LSCA coil embolization.
POD 10	Patient undergoes bilateral pectoralis major flap reconstruction with wound vacuum-assisted closure.
POD 39	Patient develops a large aortic bleeder in her chest, which is successfully managed with laparoscopy-assisted reconstruction of infected graft with pericardial patch and delayed omental flap reconstruction.
POD 64	Patient develops an enlarging infectious hematoma with cultures positive for gram-negative bacilli. She is managed with incision/drainage of the hematoma with negative pressure VAC therapy. Operative specimen culture grew multi-drug resistant <i>Klebsiella pneumoniae</i> , which was managed with systemic ertapenem.
POD 76	Patient presents with acute onset chest pain and increased active contract extravasation from proximal arch into presternal hematoma requiring retrograde zone 0 TEVAR.
POD 77-80	Patient develops intermittent fevers, inflammatory markers, positive <i>Klebsiella</i> culture with PET scan showing increased uptake at graft site concerning for mycotic aneurysm.
POD 80-83	Investigational phage therapy is initiated systemically via IV route and locally via 24 Fr Blake drain. Patient remains afebrile during this time.
POD 86	Patient is discharged to subacute care with systemic antibiotic therapy.
2-month follow up	Repeat PET/CT scan show improvement in chest wall collection and decreased graft hypermetabolism.
2-year follow-up	Patient seen in clinic and is doing well with intact hybrid arch reconstruction with positive aortic remodeling.
CT = computed tomography; PET = positron emission tomography; POD = post-operative day; TEVAR = thoracic endovascular aneurysm repair; VAC = vacuum-assisted closure.	

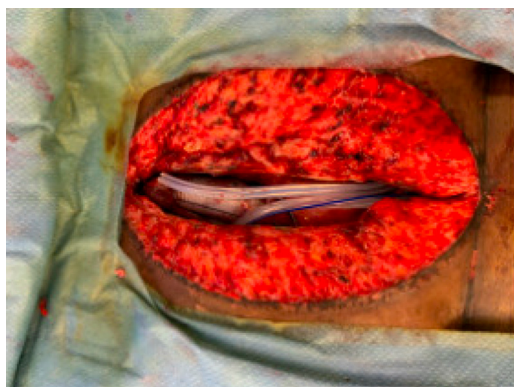
FIGURE 1 Patient Presented With Radiating Back Pain



Computed tomography angiography confirmed descending aortic dissection.

was made to perform an incision/drainage and initiate negative-pressure VAC therapy. The patient was brought into the operating room and started on broad spectrum antibiotic therapy. The cavity was copiously irrigated followed by placement of a 24-Fr Blake. The fascia/skin incisions were sutured close, and a black foam wound VAC dressing was placed over the incision. All fluid and clot from the operation were sent to culture, which revealed multidrug-

FIGURE 2 Delayed Closure of Patient Sternal Wound Leading to Complex Mediastinitis



Delayed closure of patient sternal wound lead to complex mediastinitis which indicated the use of vacuum-assisted closure therapy.

FIGURE 3 Computed Tomography Angiography Post-Great Vessel Debranching and Thoracic Endovascular Aortic Repair



No evidence of endoleak was present.

resistant *Klebsiella pneumoniae*. The patient was sent to the intensive care unit in stable condition and administered systemic ertapenem.

Approximately 2 weeks later, the patient presented with acute-onset chest pain. CT showed active contrast extravasation from the proximal arch into the presternal hematoma. Given chest re-entry was prohibitive, retrograde zone 0 TEVAR was performed with successful coverage of the extravasation, and patient was transferred to the floor 4 days later to recover. During this time, the patient developed intermittent fever and elevated proinflammatory markers, and positron emission tomography (PET) scan showed increased uptake at the graft site. Culture showed pan-resistant *Klebsiella* infection, which was susceptible to minocycline, ertapenem, and gentamicin, intermediately resistant to piperacillin/tazobactam and ciprofloxacin, and resistant to ceftriaxone, trimethoprim + sulfamethoxazole. In coordination with the infectious disease team, we initiated investigational phage therapy systemically and locally due to unavailability of antibiotic susceptibility. The patient consented to the experimental therapy and institutional review board/Food and Drug Administration approval was obtained for eIND (28188) phage therapy, which was initiated for 4 days systemically by intravenous route at a rate of 1×10^8 phage cocktail diluted into 100 mL of

normal saline, and locally via 24-F Blake drain of 1×10^9 phage cocktail diluted into 30 mL of normal saline. The patient remained afebrile during this time and C-reactive protein reached nadir levels.

OUTCOME AND FOLLOW UP

The patient was discharged to subacute care within 3 days after the conclusion of phage treatment. Two months later, repeat PET/CT scan showed improved chest wall collection and decreased graft hypermetabolism. She was recently seen in clinic at 2-year follow-up from her index hospitalization and is doing well. The hybrid aortic arch reconstruction and TEVAR remained intact, with pristine aortic remodeling.

DISCUSSION

Delayed sternal wound closure (DSC) is a rare complication following cardiac surgery, which predisposes patients to mediastinitis and increased morbidity.¹ Although several therapies are helpful in facilitating complex sternotomy wound closure, including debridement, drainage, and flap reconstruction, obesity further complicates management and increases risk for dehiscence.² We report the successful management of a 47-year-old morbidly obese woman requiring DSC following hybrid aortic arch repair with subsequent infective hematoma requiring adjunctive investigational therapy.

Following HAR and TEVAR deployment, the patient developed severe right ventricular domain loss due to her body habitus, including short stature and body mass index of 56. Recently, the use of VAC therapy in patients presenting with DSC-associated mediastinitis following aortic arch surgery has been described.³ Through the development of a negative-pressure system, VAC therapy helps reduce edema, whereas increasing blood flow and neovascularization, promoting wound healing. The management of this patient's DSC following hybrid arch repair with VAC-therapy and bilateral fascio-cutaneous pectoralis flaps was complicated by the development of an aortic bleeder. We theorize that this was due to a tear from grating of her ascending aortic graft against her inferior

mediastinum due to movement of the heart. After repair of her aortic hematoma, the patient underwent omental flap reconstruction of her sternal wound, which was complicated this time by development of mediastinal infection.

Despite attempts at drainage and systemic antibiotic therapy, the patients' graft developed persistent pan-resistant *Klebsiella* graft infection requiring adjunctive therapy. Phage therapy refers to the therapeutic use of modified bacteriophages for treatment of persistent bacterial infections. Previously the use of needle-injected OMKO1 phage therapy for treatment of a *Pseudomonas*-infected aortic Dacron graft has been described.⁴ In this case, the patient's mediastinal culture grew pan-resistant *Klebsiella* that persisted despite a full course of systemic ertapenem. We initiated phage therapy systemically and locally. Following discharge to subacute care, systemic antibiotic therapy was continued until 2 months. After imaging confirmed improvement in graft metabolism, we were able to safely transition the patient to oral antibiotics at home. She remains infection-free at 2 years, maintaining good quality of life.

CONCLUSIONS

This case report adds to the current literature on management of complicated mediastinitis wound infection following complex aortic arch surgery using investigational phage therapy for fighting persistent, pan-resistant infection. When faced with such complex patients, multidisciplinary collaboration, specifically between cardiac surgery and infectious disease is critical for facilitating investigational therapies for complex mediastinal wound infection.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS aortic dissection, hybrid arch repair, phage therapy, TEVAR