

Phage-Loaded Hydrogel Combined with Systemic and Intra-Articular Phage Therapy for Chronic *Staphylococcus epidermidis* Periprosthetic Hip Infection: A Case Report

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Background and phage therapy rationale

Introduction
- Chronic PJI after multiple revisions may leave few viable surgical and antimicrobial options. - Bacteriophage therapy has potential as a biofilm-active adjunct, although clinical evidence remains limited and optimal administration route is unknown. - We report triple-route adjunctive phage therapy alongside salvage DAIR and systemic antibiotics for chronic multidrug-resistant <i>Staphylococcus epidermidis</i> hip PJI.

Case presentation
65 years old female - Upper limb phocomelia secondary to thalidomide (resulting in difficult peripheral venous access, precluding Dalbavancin as long-term suppression) - Congenital bilateral high dislocation (Crowe IV) dysplastic hips

Allergies - Penicillin anaphylaxis - Linezolid ophthalmopathy (blurred vision)
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Clinical picture while on Pristinamycin suppression: - Intermittent fevers / Significant fatigue - Painful left hip swelling - Declining mobility / Increased bed-dependance - High CRP (50-75mg/L) // Chronic anaemia (Hb 82g/L)
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UK National Phage MDT salvage treatment eligibility
- Recurrent MDR <i>Staphylococcus epidermidis</i> infection - Lack of oral options including resistances and multiple drug allergies - Phocomelia complexified prolonged IV administration - Current stable construct without loosening or migration - High revision risk due to custom acetabular cup

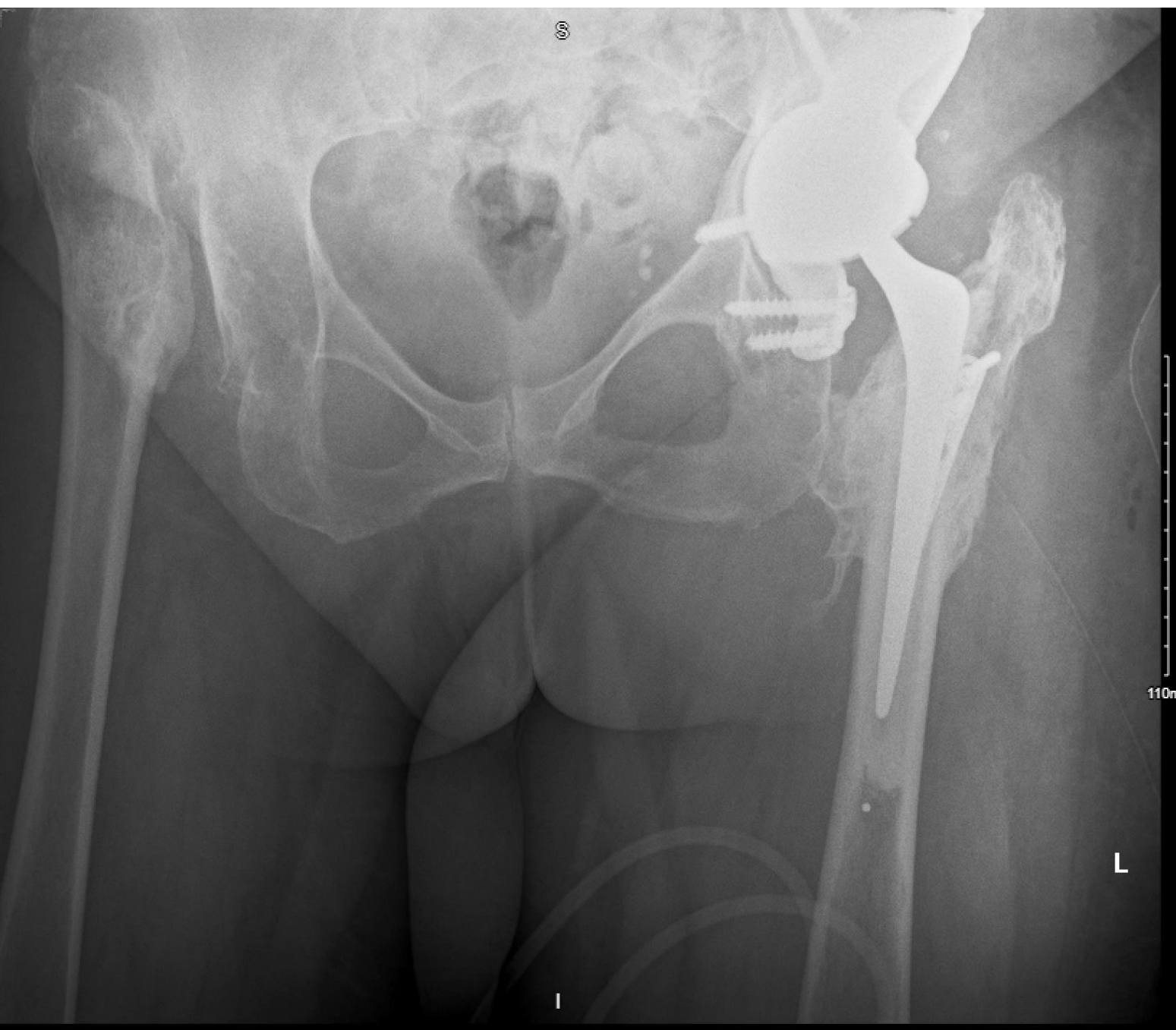
Ethics MDT → Informed consent obtained
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Decision
→ Salvage DAIR with adjunctive PT and systemic antibiotics

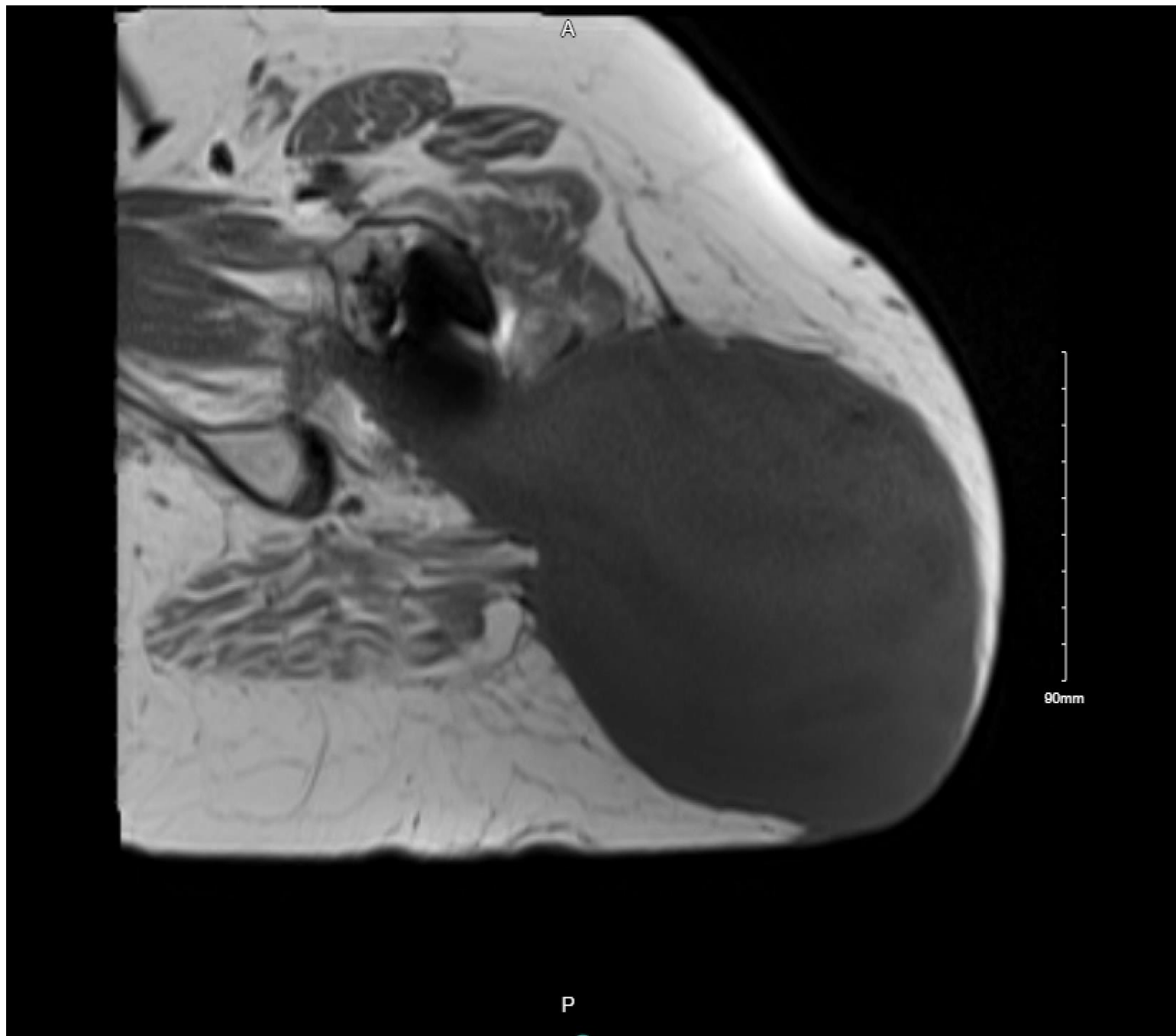
Phage preparation
- A fixed lytic 5-phage anti-staphylococcal cocktail was selected to target the patient’s <i>S. epidermidis</i> isolate 2.5 × 10⁹ PFU per 10 mL dose; equivalent to 2.5 × 10⁸ PFU/mL total cocktail
Why a cocktail? - Broader host range : risk factors for heterogenous bacterial population - Reduced emergence of phage-resistant mutants - Was one GMP available option “off the shelf”



Procedures before PT (years prior to phage therapy)			
Time	Procedure	Cultures	Treatment
8 years	1. Primary Left THA + shortening osteotomy. 2. Left THR revision to captive cup for early dislocation 3. Left THR augmant and re-fixation of the captive cup for loosening	-	-
6 years	Aspiration for PJI workup (chronic pain, broken screw and acetabular cup augment migration and loosening)	<i>Staphylococcus epidermidis</i> R : Flucloxacillin, Rifampicin, Co-Trimoxazole, Fusidic acid I : Ciprofloxacin S : Tetracycline, Clindamycin, Teicoplanin, Gentamicin, Linezolid, Daptomycin	-
5.5 years	Left THR single stage revision with a custom-engineered acetabular cup (3D-printed titanium salvage implant to match severe, irregular bone defects) for PJI	<i>S. epidermidis</i> (idem)	IV Teicoplanin → Linezolid → Doxycycline (total 12 weeks)
5 years	DAIR	<i>S. epidermidis</i> (idem)	IV Teicoplanin → Doxycycline (total 12 weeks)
4.5 years	Left hip aspiration (rapid relapse with a sinus)	<i>S. epidermidis</i> (idem)	Doxycycline suppression
4 years	Limited washout (700-800mL of pus around and communicating with joint)	<i>S. epidermidis</i> New R to Clindamycin and Doxycycline	Started on Pristinamycin
1.5 years	Debulking, washout without change of mobile components, rotational flap (large 1L collection of pus around and communicating with joint and skin)	<i>S. epidermidis</i> 1) Clindamycin S/ Tetracycline R 2) Clindamycin R/ Tetracycline S Quinu-Dalfo MIC = 0.125mg/L	IV Dalbavancin x 3 → Pristinamycin suppression
0.5 years	Hip fluid therapeutic aspiration	-	IV Teicoplanin → Pristinamycin suppression



Pre-op X-ray



Pre-op MRI : large solid cystic mass in the gluteal region communicating with the femoral head.

Treatment modalities and results

Intravenous	Intra-articular	Hydrogel
2.5 × 10 ⁹ PFU per administration in 0.9% saline to a final 60mL volume twice a day , infused over 30 minutes	2.5 × 10 ⁹ PFU per administration in 0.9% saline to a final 30mL volume	2.5 × 10 ⁹ PFU per administration in 0.9% saline to a final 30mL volume of hydrogel applied once intraoperatively

Figures created using Microsoft CoPilot (AI-assisted image generation) and subsequently reviewed by the authors.

Safety
No immediate adverse effects Transient eosinophilia (0.94 x10 ⁹ /L), from day 10 → 35 possibly due to IV phages Transient neutropenia (0.96 x10 ⁹ /L) at day 45 due to Teicoplanin (managed by ↓ dose)

Outcomes at 6 months of follow-up
Clinical : - Wound healed / No fistula / Pain decreased / Joint function improved and more stable - No fevers / Less fatigue - Left hip seroma recurrence by month 4
Biochemical: - CRP remained normal at 3 months, but increased by month 6 (8 → 20 → 37mg/L) - Chronic anemia improved (Hb 82 →118)
Quality of life – EQ-5D-5L score at baseline , then at 6 months : - Mobility: 3 → 3 - Usual activities: 2 → 3 - Anxiety/depression: 2 → 2 - Self-care: 1 → 1 - Pain/discomfort: 3 → 2 - Health today score 40 → 50
*Score at 6 months influenced by painful native right hip

	Day 0	Day 7	Day 14	//	Day 90	Day 180	...
Left hip DAIR (Dual mobility head not exchanged) + removal of femoral plate + surface VAC + Calcium sulfate beads (Vancomycin and Gentamicin)	X						
Ultrasound-guided left hip aspiration (300-400mL seroma)		X	X				
Intra-articular phages	X	X	X				
Hydrogel-loaded phages	X						
Twice-daily IV phages							
IV Teicoplanin							
Oral Doxycycline							
Microbiology cultures	+	-	-				

4/5 samples grew *S. epidermidis* : **R – Flucloxacillin, Clindamycin, Rifampicin, Co-Trimoxazole, Fusidic acid**
// I – Ciprofloxacin // **S – Tetracycline, Linezolid, Gentamicin, Vancomycin, Teicoplanin, Daptomycin, Tigecycline, Quinu/Dalfo 0.125mg/L**

Conclusion
- We describe adjunctive triple-route phage therapy (intravenous, topical hydrogel, and intra-articular) for chronic MDR PJI with otherwise limited treatment options. - Phage administration was feasible, well coordinated across multidisciplinary teams, and generally well tolerated, with only transient low-grade eosinophilia possibly related to IV phage treatment. - At 6 months, the patient demonstrated wound healing, reduced pain, improved joint stability, increased energy levels, and modest improvement in health-related quality of life. - However, recurrent seroma formation and rising inflammatory markers may indicate persistent or recurrent infection. - Ongoing long-term follow-up will help determine the durability of clinical response and the role of multimodal phage therapy in complex PJI management.