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INTRODUCTION

As lytic phages act synergistically with antibiotics on biofilms, they could be a potent adjunct treatment for bone and joint infections (BJI). Currently, phage Active Pharmaceutical Ingredients (APIs) production follows minimal requirements of quality and safety, which guarantee adequate composition and acceptable levels of residual contaminants.

MATERIALS- METHODS

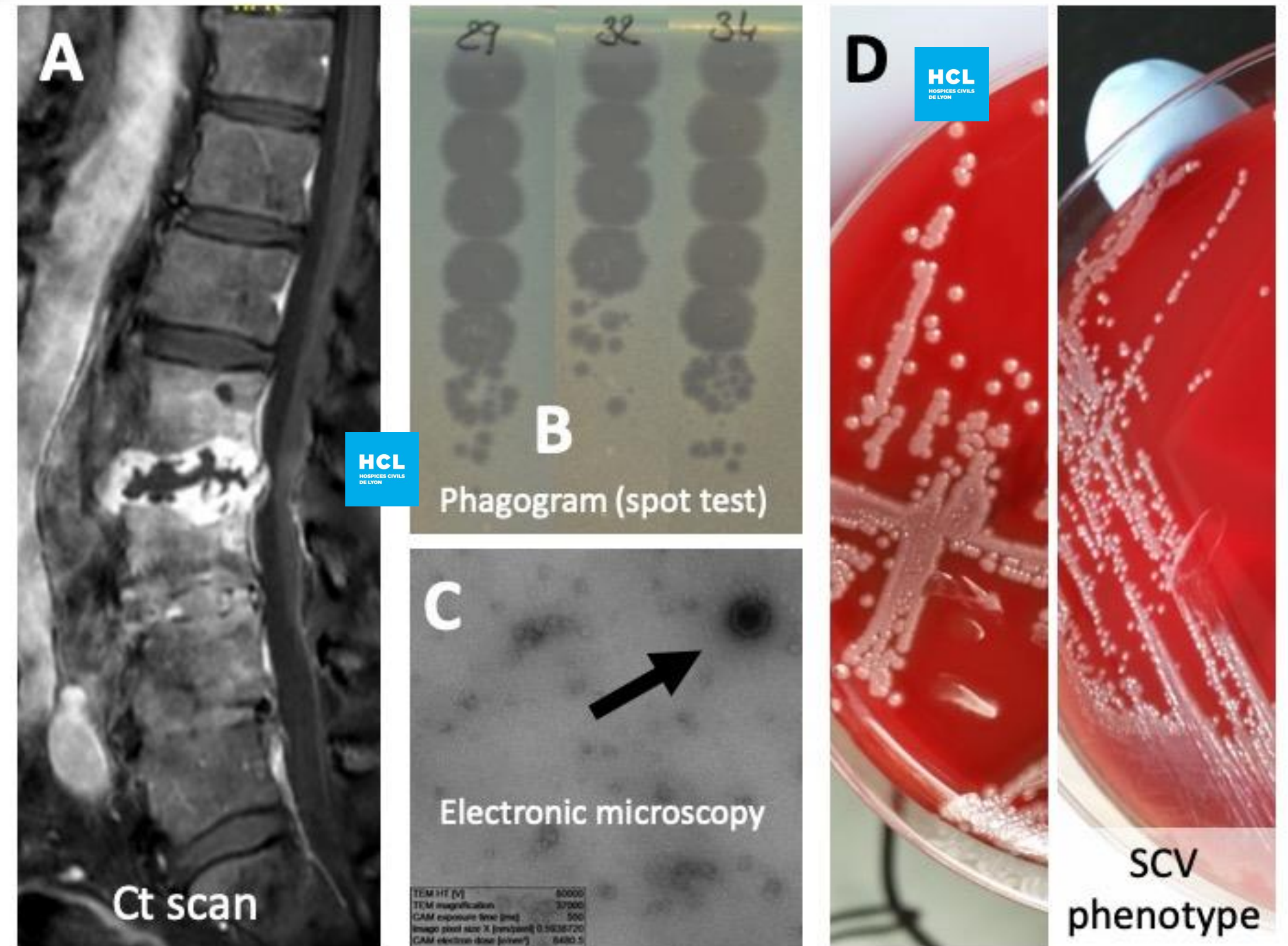
A 74-year-old man experienced *P. aeruginosa* bacteremia in January 2018. In summer 2018, spondylodiscitis with spinal abscess due to pandrug-resistant *P. aeruginosa* was diagnosed (**panel A**). Industrial phages under development were inactive, but 3 active phages (Phi4029, Phi4032 and Phi4034) were identified by the laboratory of G. Resch (**panel B, C**). Dedicated production of the APIs, in compliance with a monograph describing the production process and Quality Control (QC) system for incorporation in magistral preparations, was done at Queen Astrid military hospital in Brussels under the supervision of the French National authority (ANSM) in collaboration with the hospital pharmacist.

RESULTS

The patient was treated by open debridement and one local application of the phage cocktail after magistral preparation (dilution in 7 mL; final titer of 107 PFU/mL). Cefiderocol was started after the surgery for a duration of 6 weeks. One month after, a new surgery, corporectomy for stabilization, was performed. The patient had no systemic (no fever, CRP 10 mg/L) nor clinical signs of infection. The same phage cocktail with same dilution and titer was locally used. Cefiderocol was pursued pending the culture results. Unfortunately, *P. aeruginosa* still grew in culture from bone biopsies with small colony variant phenotype (**panel D**), but remained susceptible to the phage cocktail and cefiderocol. Colistin was added and phages were administered i.v. in 3-hours infusions (30 mL, phage titers 10⁸ PFU/mL) every day during 28 days. Antibiotics were stopped at 3 months. The outcome was favorable after 6 months, and the patient is walking without pain.

CONCLUSIONS

Personalized phage therapy is a potential adjunct treatment for patients with complex BJI due to pandrug-resistant bacteria. In addition to industrial phages under development, academic collaborative research is crucial to develop personalized phage therapy.



Panel A
 MRI showing podylodiscitis with spinal abscess due to pandrug-resistant *P. aeruginosa*

Panel B
 Phagogram of the 3 active phages
Panel C
 Electronic microscopy of one of the active phage

Panel D
P. aeruginosa still grew in culture with small colony variant phenotype