

High-Grade *Staphylococcus lugdunensis* Bacteremia in a Patient on Home Hemodialysis

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Background: *Staphylococcus lugdunensis* (*S lugdunensis*) is a species of coagulase-negative *Staphylococcus* and a constituent of human skin flora. *S lugdunensis* has gained notoriety for its virulence, which resembles *Staphylococcus aureus* (*S aureus*). *S lugdunensis* is now recognized as an important nosocomial pathogen and cause of prosthetic device infections, including vascular catheter infections.

Case Presentation: A 60-year-old man with a history of uncontrolled type 2 diabetes mellitus and end-stage renal disease on home hemodialysis via arteriovenous fistula (AVF) presented to the emergency department for evaluation of subacute progressive low back pain. Initial laboratory tests were notable for elevated inflammatory markers. Magnetic resonance imaging with contrast of the thoracic and lumbar spine revealed abnormal marrow edema in the T11-T12 vertebrae with abnormal fluid signal in the T11-T12 disc space. Cultures grew

methicillin-sensitive *S lugdunensis*. The patient's antibiotic regimen was narrowed to IV oxacillin. He was transitioned to IV cefazolin dosed 3 times weekly after hemodialysis and an outpatient dialysis center.

Conclusions: Treatment of bacteremia caused by *S lugdunensis* or *S aureus* should be managed with prompt initiation of IV antistaphylococcal therapy, a thorough evaluation for the source of bacteremia as well as metastatic complications, and consultation with an infectious disease specialist. This case highlights AVF as a potential source for infection even without localized signs of infection. The buttonhole method of AVF cannulation was thought to be a major contributor to the development and persistence of our patient's bacteremia. This risk should be discussed with patients using a shared decision-making approach when developing a dialysis treatment plan.

Staphylococcus lugdunensis (*S lugdunensis*) is a species of coagulase-negative *Staphylococcus* (CoNS) and a constituent of human skin flora. Unlike other strains of CoNS, however, *S lugdunensis* has gained notoriety for virulence that resembles *Staphylococcus aureus* (*S aureus*). *S lugdunensis* is now recognized as an important nosocomial pathogen and cause of prosthetic device infections, including vascular catheter infections. We present a case of persistent *S lugdunensis* bacteremia occurring in a patient on hemodialysis (HD) without any implanted prosthetic materials.

CASE PRESENTATION

A 60-year-old man with a history of uncontrolled type 2 diabetes mellitus (T2DM) and end-stage renal disease on home HD via arteriovenous fistula (AVF) presented to the emergency department (ED) for evaluation of subacute progressive low back pain. His symptoms began abruptly 2 weeks prior to presentation without any identifiable trigger or trauma. His pain localized to the lower thoracic spine, radiating anteriorly into his abdomen. He reported tactile fever for several days before presentation but no chills, night sweats, paresthesia, weakness, or bowel/bladder incontinence. He had no re-

cent surgeries, implanted hardware, or invasive procedures involving the spine. HD was performed 5 times a week at home with a family member cannulating his AVF via buttonhole technique. He initially sought evaluation in a community hospital several days prior, where he underwent magnetic resonance imaging (MRI) of the thoracic spine. He was discharged from the community ED with oral opioids prior to the MRI results. He presented to West Los Angeles Veterans Affairs Medical Center (WLAVAMC) ED when MRI results came back indicating abnormalities and he reported recalcitrant pain.

On arrival at WLAVAMC, the patient was afebrile with a heart rate of 107 bpm and blood pressure of 152/97 mm Hg. The remainder of his vital signs were normal. The physical examination revealed midline tenderness on palpation of the distal thoracic and proximal lumbar spine. Muscle strength was 4 of 5 in the bilateral hip flexors, though this was limited by pain. The remainder of his neurologic examination was nonfocal. The cardiac examination was unremarkable with no murmurs auscultated. His left upper extremity AVF had an audible bruit and palpable thrill. The skin examination was notable for acanthosis nigricans but no areas of skin

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erythema or induration and no obvious stigmata of infective endocarditis.

The initial laboratory workup was remarkable for a white blood cell (WBC) count of $10.0 \times 10^3/\mu\text{L}$ with left shift, blood urea nitrogen level of 59 mg/dL, and creatinine level of 9.3 mg/dL. The patient's erythrocyte sedimentation rate (ESR) was 45 mm/h (reference range, ≤ 20 mm/h) and C-reactive protein level was > 8.0 mg/L (reference range, ≤ 0.74 mg/L). Two months prior the hemoglobin A_{1c} had been recorded at 9.9%.

Given his intractable low back pain and elevated inflammatory markers, the patient underwent an MRI of the thoracic and lumbar spine with contrast while in the ED. This MRI revealed abnormal marrow edema in the T11-T12 vertebrae with abnormal fluid signal in the T11-T12 disc space. Subjacent paravertebral edema also was noted. There was no well-defined fluid collection or abnormal signal in the spinal cord. Taken together, these findings were concerning for T11-T12 discitis with osteomyelitis.

Two sets of blood cultures were obtained, and empiric IV vancomycin and ceftriaxone were started. Interventional radiology was consulted for consideration of vertebral biopsy but deferred while awaiting blood culture data. Neurosurgery also was consulted and recommended non-operative management given his nonfocal neurologic examination and imaging without evidence of abscess. Both sets of blood cultures collected on admission later grew methicillin-sensitive *S lugdunensis*, a species of CoNS. A transthoracic and later transesophageal echocardiogram did not show any valvular vegetations. The patient's antibiotic regimen was narrowed to IV oxacillin based on susceptibility data. It was later discovered that both blood cultures obtained during his outside ED encounter were also growing *S lugdunensis*.

The patient's *S lugdunensis* bacteremia persisted for the first 8 days of his admission despite appropriate dosing of oxacillin. During this time, the patient remained afebrile with stable vital signs and a normal WBC count. Positron emission tomography was obtained to evaluate for potential sources of his persistent bacteremia.

Aside from tracer uptake in the T11-T12 vertebral bodies and intervertebral disc space, no other areas showed suspicious uptake. Neurosurgery reevaluated the patient and again recommended non-operative management. Blood cultures cleared and based on recommendations from an infectious disease specialist, the patient was transitioned to IV cefazolin dosed 3 times weekly after HD, which was transitioned to an outpatient dialysis center. The patient continued taking cefazolin for 6 weeks with subsequent improvement in back pain and normalization of inflammatory markers at outpatient follow-up.

DISCUSSION

CoNS are a major contributor to human skin flora, a common contaminant of blood cultures, and an important cause of nosocomial bloodstream infections.^{1,2} These species have a predilection for forming biofilms, making CoNS a major cause of prosthetic device infections.³ *S lugdunensis* is a CoNS species that was first described in 1988.⁴ In addition to foreign body-related infections, *S lugdunensis* has been implicated in bone/joint infections, native valve endocarditis, toxic shock syndrome, and brain abscesses.⁵⁻⁸ Infections due to *S lugdunensis* are notorious for their aggressive and fulminant courses. With its increased virulence that is atypical of other CoNS, *S lugdunensis* has understandably been likened more to *S aureus*.

Prior cases have been reported of *S lugdunensis* bacteremia in patients using HD. However, the suspected source of bacteremia in these cases has generally been central venous catheters.⁹⁻¹² Only 2 cases reported in the medical literature suspected the patient's AVF to be the source of bacteremia (Table).^{10,11} Both our patient and the Conner and colleagues case report received HD at home.¹¹ In a retrospective study of dialysis patients with AVFs, bacteremia may be attributable to the AVF even in the absence of localized erythema or induration if no alternative source for the bacteremia is found.¹³ Our patient lacked any central venous catheters, and after a thorough investigation, the only remaining source for bacteremia was his left upper extremity AVF.

Notably, our patient's AVF was accessed

TABLE *Staphylococcus lugdunensis* Bacteremia Cases Affecting Patients on Chronic HD

Source	Age, y	Home HD	AVF location	Localized infection at AVF?	Bacteremia sequelae	Outcome
Shuttleworth and Colby, ¹⁰ 1992	60	No	Left upper extremity	Yes	Native mitral valve endocarditis	Died
Conner et al, ¹¹ 2012	45	Yes	Right upper extremity	No	Native tricuspid valve endocarditis; emboli causing pulmonary infarction and pneumonia	Survived
Current case	60	Yes	Left upper extremity	No	Vertebral osteomyelitis and discitis	Survived

Abbreviations: AVF, arteriovenous fistula; HD, hemodialysis.

using the buttonhole technique for his home HD sessions, which involves cannulating the same site along the fistula until an epithelialized track has formed from scar tissue. At later HD sessions, duller needles can then be used to cannulate this same track. In contrast, the rope-ladder technique involves cannulating a different site along the fistula until the entire length of the fistula has been used. Patients report higher levels of satisfaction with the buttonhole technique, citing decreased pain, decreased oozing, and the perception of easier cannulation by HD nurses.¹⁴ However, the buttonhole technique also appears to confer a higher risk of vascular access-related bloodstream infection when compared with the rope-ladder technique.^{13,15,16}

The buttonhole technique is hypothesized to increase infection risk due to the repeated use of the same site for needle entry. Skin flora, including CoNS, may colonize the scab that forms after dialysis access. If proper sterilization techniques are not rigorously followed, the bacteria colonizing the scab and adjacent skin may be introduced into a patient's bloodstream during needle puncture. Loss of skin integrity due to frequent cannulation of the same site may also contribute to this increased infection risk. It is relevant to recall that our patient received HD 5 times weekly using the buttonhole technique. The use of the buttonhole technique, frequency of his HD sessions, unclear sterilization methods, and immune dysfunction related to his uncontrolled T2DM and renal disease all likely contributed to our patient's bacteremia.

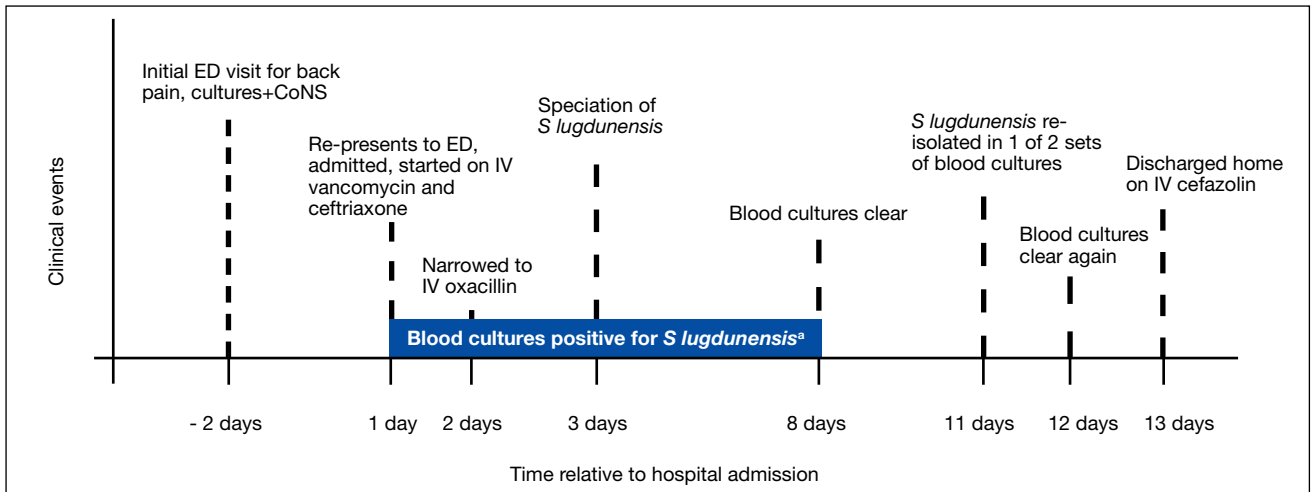
Using topical mupirocin for prophylaxis at the intended buttonhole puncture site has shown promising results in decreasing

rates of *S aureus* bacteremia.¹⁷ It is unclear whether this intervention also would be effective against *S lugdunensis*. Increasing rates of mupirocin resistance have been reported among *S lugdunensis* isolates in dialysis settings, but further research in this area is warranted.¹⁸

There are no established treatment guidelines for *S lugdunensis* infections. In vitro studies suggest that *S lugdunensis* is susceptible to a wide variety of antibiotics. The *mecA* gene is a major determinant of methicillin resistance that is commonly observed among CoNS but is uncommonly seen with *S lugdunensis*.⁵ In a study by Tan and colleagues of 106 *S lugdunensis* isolates, they found that only 5 (4.7%) were *mecA* positive.¹⁹

Vancomycin is generally reasonable for empiric antibiotic coverage of staphylococci while speciation is pending. However, if *S lugdunensis* is isolated, its favorable susceptibility pattern typically allows for de-escalation to an anti-staphylococcal β -lactam, such as oxacillin or nafcillin. In cases of bloodstream infections caused by methicillin-sensitive *S aureus*, treatment with a β -lactam has demonstrated superiority over vancomycin due to the lower rates of treatment failure and mortality with β -lactams.^{20,21} It is unknown whether β -lactams is superior for treating bacteremia with methicillin-sensitive *S lugdunensis*.

Our patient's isolate of *S lugdunensis* was pansensitive to all antibiotics tested, including penicillin. These susceptibility data were used to guide the de-escalation of his empiric vancomycin and ceftriaxone to oxacillin on hospital day 1. Interestingly, our patient's bacteremia persisted for the first 8 days of his hospitalization despite

FIGURE Illness Presentation Timeline

Abbreviations: CoNS, coagulase-negative *Staphylococcus*; ED, emergency department.

^aBlood cultures positive for *S lugdunensis*.

appropriate dosing of oxacillin (Figure). This phenomenon of prolonged bacteremia has been well described with *S aureus*.^{22,23} To our knowledge, only 1 other case report has been published detailing such high-grade bacteremia with *S lugdunensis*. Duhon and colleagues described a case of persistent *S lugdunensis* bacteremia that lasted 7 days and was complicated by native aortic valve endocarditis.²⁴ Their patient was initially started on empiric vancomycin and ceftriaxone but later switched to ceftazolin on hospital day 4. The authors proposed that the persistent bacteremia may have been from an “inoculum effect,” which is seen when ceftazolin loses efficacy against *S aureus* in vitro when there is a relatively high bacterial burden. However, our patient was not switched to ceftazolin until the day of discharge, when his bacteremia had already cleared. We hypothesize instead that continued use of AVF for HD during hospitalization was likely a major contributing factor to our patient’s persistent bacteremia. As his AVF was the suspected source for bacteremia, there was concern that repeated cannulation of the fistula intermittently introduced additional bacteria into the bloodstream between antibiotic doses.

Due to their virulence, bloodstream infections caused by *S aureus* and *S lugdunensis* often require more than timely antimicrobial treatment to ensure erad-

ication. Consultation with an infectious disease specialist to manage patients with *S aureus* bacteremia has been proven to reduce mortality.²⁵ A similar mortality benefit is seen when infectious disease specialists are consulted for *S lugdunensis* bacteremia.²⁶ This mortality benefit is likely explained by *S lugdunensis*’ propensity to cause aggressive, metastatic infections. In such cases, infectious disease consultants may recommend additional imaging (eg, transthoracic echocardiogram) to evaluate for occult sources of infection, advocate for appropriate source control, and guide the selection of an appropriate antibiotic course to ensure resolution of the bacteremia.

CONCLUSIONS

S lugdunensis is an increasingly recognized cause of nosocomial bloodstream infections. Given the commonalities in virulence that *S lugdunensis* shares with *S aureus*, treatment of bacteremia caused by either species should follow similar management principles: prompt initiation of IV antistaphylococcal therapy, a thorough evaluation for the source(s) of bacteremia as well as metastatic complications, and consultation with an infectious disease specialist. This case report also highlights the importance of considering a patient’s AVF as a potential source for infection even in the absence of localized signs of

infection. The buttonhole method of AVF cannulation was thought to be a major contributor to the development and persistence of our patient's bacteremia. This risk should be discussed with patients using a shared decision-making approach when developing a dialysis treatment plan.

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Ethics and consent

Written informed consent was obtained from the patient.

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