

Right-sided endocarditis from *Staphylococcus lugdunensis* in a patient with tetralogy of Fallot

Bradford Becken III,¹ Jacob Kilgore,¹ Elizabeth Thompson,² M. Anthony Moody¹

¹Division of Pediatric Infectious Diseases, ²Department of Pediatrics, Duke University Children's Hospital, Durham, NC, USA

Abstract

Infective endocarditis is often caused by bacterial pathogens and can affect native and prosthetic tissue. Common pathogens in pediatric patients include *Staphylococcus aureus*, viridans group streptococci, enterococcal species and coagulase-negative staphylococci, though culture-negative cases are not uncommon. Coagulase-negative staphylococci present a conundrum to clinicians due to the potential of culture contamination. While *Staphylococcus lugdunensis* is a coagulase-negative staphylococcus, it is an emerging cardiotropic pathogen that presents similarly to *Staphylococcus aureus*. Here we report a case of a child with repaired tetralogy of Fallot found to have right-sided infective endocarditis caused by *Staphylococcus lugdunensis*.

Introduction

Infective endocarditis (IE) is a significant concern in febrile patients with a history of prosthetic issue. Bacterial pathogens, predominantly Gram-positive organisms, are the most common cause of infective endocarditis, with *Staphylococcus aureus*, viridians group streptococci, and enterococcal species being the most common organisms.¹ However, coagulase-negative staphylococci cause a significant proportion of infective endocarditis. Coagulase-negative staphylococci are grouped together based on their biochemical properties, but their ability to invade and destroy native tissue widely varies. *Staphylococcus lugdunensis* was first described in 1988, and while it is a coagulase-negative staphylococcus, it behaves more similarly to *S. aureus* than to the more commonly isolated coagulase-negative staphylococci *S. epidermidis* and *S. hominis* species, thus necessitating more aggressive management.^{2,3}

Case Report

A 14-year-old male with a known history of tetralogy of Fallot (TOF) status post placement of a 10 mm right ventricle (RV) to pulmonary artery (PA) conduit at one year of age presented to the pediatric cardiologist for one month of fevers to 39°C and fatigue. Prior to evaluation, he had been treated with non-steroidal anti-inflammatory drugs (NSAIDs) as well as a one-week course of trimethoprim/sulfamethoxazole for a presumed urinary tract infection with only temporary relief of his symptoms. Over the resulting weeks, he developed a non-productive cough, non-bloody diarrhea, and worsening abdominal pain. He subsequently presented to the pediatric cardiologist for further evaluation despite being previously lost to subspecialty follow up for two years. No relevant social or exposure history was identified including denial of recent dental procedures or intravenous drug use. His exam was notable for a grade III/VI systolic ejection murmur loudest at the left upper sternal border with radiation to both axillae, documented to be louder than previous exams. There was no evidence of splinter hemorrhages, retinal hemorrhages, or distal cutaneous findings consistent with sequelae of infective endocarditis. The patient underwent a transthoracic echocardiogram that showed multiple vegetations in the right ventricular outflow tract, pulmonary valve, and PA conduit. The largest vegetation measured 20 × 12 mm with smaller vegetations measuring 9 × 9 mm and 7 × 3 mm, respectively. Subsequent chest CT imaging re-demonstrated cardiac vegetations in addition to revealing bilateral pulmonary nodules concerning for septic emboli (Figure 1).

He was admitted to the hospital and pediatric infectious diseases was consulted. The patient was empirically started on intravenous vancomycin and gentamicin therapies. Initial labs were significant for a C-reactive protein (CRP) of 13.78 mg/dL (reference range <0.60 mg/dL), erythrocyte sedimentation rate (ESR) of 34 mm/hr (reference range 0-13 mm/hr), a creatinine of 0.9 mg/dL (reference range 0.3-0.8 mg/dL), a sodium of 127 mmol/L (reference range 135-145 mmol/L), and an INR of 1.4. The white blood cell count was normal; however, the differential revealed a neutrophilic predominance with mild bandemia. Vancomycin troughs were kept between 11.5 and 14.5 µg/mL. Blood cultures ultimately grew pan-sensitive *Staphylococcus lugdunensis*. On hospital day 6, the patient was transitioned to intravenous cefazolin 150 mg/kg/day and rifampin 600 mg/day due to lack of central access preventing continuous nafcillin use.

Correspondence: Bradford Becken, Division of Pediatric Infectious Diseases, Duke University Medical Center, T915 Children's Health Center, Box 3499 Durham, NC 27710, USA.
Tel: +1.919-684-6335 - Fax: +1.919-668-4859.
E-mail: bradford.becken@duke.edu

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Despite the aforementioned antibiotic treatment, blood cultures remained persistently positive for 10 days. On hospital day 11, he underwent cardiothoracic operative repair in addition to central line placement. Per the intraoperative report, the anterior portion of the conduit wall was compromised by infection, leaving the conduit thinned and with a pseudo-aneurysm formation. Additionally, the conduit valve had been destroyed. The compromised portions of the conduit were removed and vegetations were debrided. A 25 mm pulmonary homograft was installed in place of the old conduit with a portion of the re-anastomosis being augmented with de-cellularized

bovine pericardium (CardioCel). The patient tolerated the procedure well and was extubated in the operating room. Following surgical intervention and central line placement the patient was transitioned to continuous infusion nafcillin monotherapy with clearance of repeat blood cultures. Prior to discharge the patient operative pace right internal jugular line was removed and a peripherally inserted central catheter (PICC) was placed. He was discharged home 6 days after surgical intervention to complete a planned 6-week course of a nafcillin 8 grams/day via continuous infusion, which based on the patient's weight, was 175 mg/kg/day. Though the patient clinically improved during his planned course, owing to persistently elevated inflammatory markers after 6-weeks of therapy, the nafcillin course was extended for an additional two weeks for a total of eight weeks of therapy. At his 8-week outpatient follow up with pediatric infectious diseases, inflammatory markers had normalized and his clinical examination was reassuring. A follow up echocardiogram demonstrated normal cardiac function and no residual vegetations. The patient's PICC line was removed, and he continued with close interval follow up with pediatric cardiology.

Discussion

Infective endocarditis (IE) occurs when there is an infection of the cardiac endothelium or prosthetic material associated with the heart. Bacterial pathogens are implicated in the majority of cases, with *Staphylococcus aureus*, viridians group streptococci, and enterococcal species being the most common organisms isolated – though pathogens do vary by patient age and underlying cardiac disease.¹ However, coagulase-negative *staphylococci* cause a

significant proportion of infective endocarditis of both native and prosthetic valves. Though coagulase-negative staphylococci are grouped together based on their biochemical properties, their ability to invade and destroy native tissue widely varies with *S. lugdunensis* known to be more aggressive than the more commonly isolated *S. epidermidis* and *S. hominis* species. Characterized in 1988, *S. lugdunensis* is believed to have been previously misidentified as *S. aureus* because it is able to produce clumping factor and a positive DNase test. Additionally, its colony morphology closely resembles that of *S. aureus*.^{2,3}

Reports of *S. lugdunensis* infections are rare, especially regarding infective endocarditis in pediatric patients.^{4,6} One hypothesis regarding the dearth of pediatric cases is that colonization of the skin from *S. lugdunensis* occurs later in life.⁷ Another reason for the paucity of cases is that given the rarity of the organism, even when solely compared to other species of coagulase-negative staphylococci, it may be erroneously regarded as a contaminant.^{3,8} Despite the aggressive nature of *S. lugdunensis*, it is typically more sensitive to β -lactams than other strains of coagulase-negative staphylococci. However, as was the case with this patient, surgical intervention is often required. In a retrospective review of patients with IE from The Cleveland Clinic, patients with *S. lugdunensis*, when compared to those with *S. aureus*, were more likely to have bulky vegetations, and the affected patients were more likely to have had native valves but with pre-existing cardiac disease. Additionally, 13% of all isolates of *S. lugdunensis* were from patients who met the modified Duke's criteria for IE.⁸

As with any patient with prosthetic cardiac material, prompt evaluation of unexplained fevers is necessary. Presenting

symptoms of IE are often vague including a variety of somatic complaints such as fever, fatigue, weight loss, headaches, pallor, cough, abdominal pain, and myalgias. Physical examination findings characteristic of IE include a new and/or worsening cardiac murmur, retinal hemorrhages (Roth's spots), dark, non-painful distal extremity skin lesions (Janeway lesions), and painful swollen macules on the distal extremities (Osler's nodes).⁹ With respect to our patient, his history of unexplained and prolonged fevers, nonspecific fatigue, cough, and abdominal pain, and worsening cardiac murmur were quite suggestive of IE. And, while he didn't have other typical extracardiac manifestations of IE, these findings are significantly less common in children than adults.¹⁰

Conclusions

The patient was treated according to the 2015 American Heart Association (AHA) guidelines update for treatment of infective endocarditis in pediatric patients with de-escalation of therapy once source control was achieved with surgical intervention.¹ Note that due to the possible cardiotropic virulence of *S. lugdunensis*, based on the data from prior case series, patients in whom this organism is isolated often require surgical intervention in addition to antimicrobial therapy similar to that of *S. aureus*, be it vancomycin or an anti-staphylococcal beta-lactam.¹ In the setting or prolonged bacteremia, we emphasize the importance of early cardiothoracic evaluation and intervention. This case was further complicated by a delay in seeking appropriate care with previous loss to specialized follow up. This likely resulted in prolonged bacteremia, contributed to the degree of conduit destruction, and ultimately influenced the length of antimicrobial duration. To help prevent similar occurrence, our case emphasizes the importance of routine specialized care in patients with complex cardiac disease

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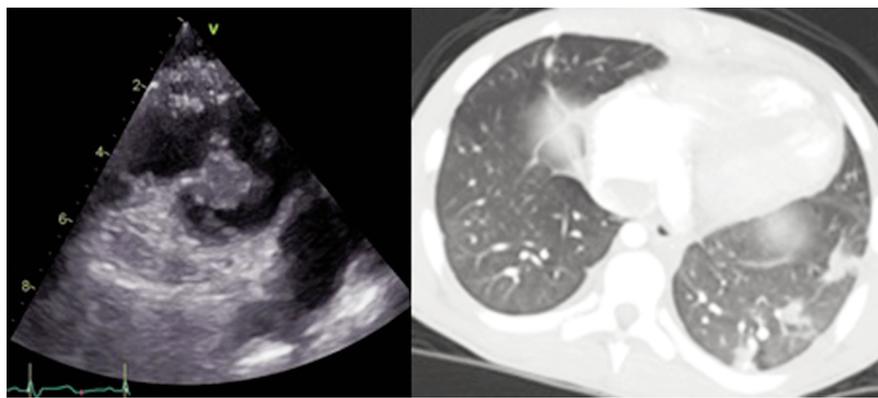


Figure 1. Transthoracic echocardiogram demonstrating the largest mobile mass on pulmonary valve (20 × 12 mm) and companion chest computed tomography showing subsequent pulmonary emboli.

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