CASE REPORT

Relapse of Polymicrobial Endocarditis in an Intravenous Drug User

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A 26-year-old male intravenous drug user (IDU\textsuperscript{†}) presented twice within 6 months with relapsed polymicrobial infective endocarditis (IE) due to \textit{Eikenella corrodens} and \textit{Streptococcus constellatus} after completing two courses of appropriate antimicrobial therapy. This report points to relapsing endocarditis as a clinical entity that warrants attention in IDUs when \textit{E. corrodens} or \textit{S. constellatus} are causative agents of IE.

INTRODUCTION

Intravenous drug users (IDUs) are at increased risk for infective endocarditis (IE) with tricuspid valve involvement caused by a variety of organisms, including \textit{Staphylococcus aureus}, and both gram negative and/or gram positive oral flora [1]. The optimal treatment length for these patients is unknown, and some patients develop relapsing endocarditis despite appropriate antimicrobial therapy [2-4]. We report an instructive case of relapsing polymicrobial endocarditis in an IDU whose blood originally grew only \textit{S. aureus} but later grew multiple fastidious organisms once the \textit{S. aureus} had been treated. This case highlights: 1) the isolation of \textit{S. aureus} does not preclude the presence of other organisms; 2) polymicrobial endocarditis is a risk for relapse, especially with \textit{E. corrodens} and \textit{S. constellatus}, even with prolonged antimicrobial therapy; 3) \textit{E. corrodens} and \textit{S. constellatus} are synergistic for infection in animal models, and this may be relevant for human infections as well; and 4) as urine toxicology screens do not necessarily rule out active drug use, the distinction between re-infection and relapse can be difficult.

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\textsuperscript{†}Abbreviations: IDU, intravenous drug user; IE, infective endocarditis; LLSB, left lower sternal border; RIBA, recombinant immunoblot assay; HCV, hepatitis C virus; PICC, peripherally inserted central catheter.

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A 26-year-old male presented to the emergency department with a 2-week history of fevers, chills, myalgias, non-productive cough, episodes of non-bloody emesis, and a 10- to 15-pound weight loss. He was a habitual IV heroine user until a few months prior to admission. He reported acquiring syringes from pharmacies to inject heroine mixed with tap water into both arms, denied licking the needle before injecting heroine, and denied reusing syringes. The patient admitted that he was on probation for 3 years for a drug-related misdemeanor committed a year before he presented. Conditions for his probation included out-patient drug rehabilitation, which he reported completing a few weeks before he presented, and periodic urine toxicology screens.

On admission, the patent was afebrile. A 2/6 systolic murmur at the left lower sternal border (LLSB) was present on cardiac auscultation, but the lung fields were clear. No cutaneous abscesses, splinter hemorrhages, or Osler’s nodes were appreciated. A urine toxicology screen was not obtained upon initial presentation. Lab results included white blood cell count 15, 100 cells/μL (82 percent neutrophils), positive recombinant immunoblot assay (RIBA) for hepatitis C virus (HCV), and an undetectable HCV viral load assayed by PCR. Hepatitis A, B, and HIV serologies were negative. A chest CT of the thorax showed bilateral scattered nodules, some of which were cavitating, later presumed to be septic emboli. A transesophageal echocardiogram demonstrated a mobile 0.8 x 0.8-cm density on the tricuspid valve with moderate tricuspid regurgitation and mild pulmonary hypertension. Blood cultures were drawn, and the patient was treated empirically for endocarditis with vancomycin and piperacillin/tazobactam.

Four out of four blood culture sets obtained on the day of admission were positive for methicillin-sensitive S. aureus. Two out of four blood culture sets were positive for S. constellatus susceptible to clindamycin, penicillin (MIC of 0.094 µg/ml), ceftriaxone, and vancomycin. The patient was given oxacillin (2 g every 4 hours) and gentamicin (80 mg every 8 hours), but his fevers persisted. Daily blood cultures over the next 14 days grew Prevotella intermedia, Eikenella corrodens, and Hemophilus parainfluenzae (Figure 1).
His antibiotic regimen was changed to ceftriaxone, metronidazole, and oxacillin. He improved and completed 6 weeks of antibiotic therapy administered by a home nursing service via a peripherally inserted central catheter (PICC). Blood cultures obtained 3 weeks after discharge were negative. However, blood cultures were not obtained after the patient completed the prescribed antibiotic regimen.

The patient was readmitted 6 weeks after the completion of antibiotics with a palpable, non-tender, 2 x 2 inch mass in the right thigh, right hip pain that worsened with joint movement and weight bearing, malaise, fever, chills, night sweats, watery diarrhea, nausea, and vomiting. Blood cultures were again positive for *E. corrodens* and *S. constellatus*. Bilateral hip MRIs with and without intravenous contrast revealed a linear tear of the anterior-superior labrum in his right hip and a rim-enhancing fluid collection in the left obturator internus muscle that was sterile when an aspirate was cultured. A trans-esophageal echocardiogram revealed a 1.3 x 1.2 cm echodensity on the anterior leaflet of the tricuspid valve and an interval increase in degree of tricuspid regurgitation. A chest CT revealed almost complete resolution of the multiple pleura-based cavitary lesions. The patient reported that during the interval between his two hospitalizations, he had been subject to periodic urine toxicology screens that were negative for opiates. A urine toxicology screen performed when he presented was negative for cocaine, oxycodone, opiates, barbiturates, amphetamine, methadone, and phencyclidine and positive only for benzodiazepines. The patient was treated with vancomycin and piperillin/tazobactam, later switched to ampicillin/sulbactam. Blood cultures were positive only for *Sphingomonas paucimobilis*. The patient responded to therapy, discharged, and was not readmitted in the following 6 months.

**DISCUSSION**

A repeat episode of IE caused by the same species within 6 months of the initial episode is traditionally defined as a relapse, whereas a repeat episode 6 months after the initial episode is defined as recurrent IE or reinfection [3-6]. IDU is a known risk factor for recurrent or relapsing IE with incidences reported as high as 41 percent [3]. While in this case urine toxicology screens were negative, continued intermittent drug use cannot be conclusively eliminated as a cause of re-infection rather than relapse. Urine immunoasays detect >300ng/ml of 6-acetyl-morphine, typically picking up drug use within 54 hours, depending on dose of heroine. Active drug use should always be considered when evaluating patients for a repeat episode of IE [7]. IDUs are also at increased risk for polymicrobial IE with rates in one series of 8 percent
[8]. While *S. aureus* is the most common cause of IE in IDUs, its presence does not rule out polymicrobial infection [8,9]. This case illustrates how once the *S. aureus* is treated, more fastidious organisms can be recovered from the blood stream. *Prevotella intermedia*, *Hemophilus parainfluenzae*, *S. constellatus*, and *E. corrodens* are fastidious oral bacteria that cause IE in IDUs after salivary contamination of drug paraphernalia due to licking or blowing into needles or licking injection sites [10-14].

*E. corrodens* is often cultured with other bacteria and when recovered should alert the physician to the possibility of polymicrobial IE. *S. constellatus* and *E. corrodens* IE are enhanced by synergism between *E. corrodens* and streptococci hypothesized to be due to coinciding metabolic niches [15-17]. These organisms co-aggregate during in vitro growth, and 76 percent of *S. anginosus* group clinical isolates are recovered as part of a mixed culture. In animal models, infections result when *E. corrodens* is inoculated with streptococci, but not when *E. corrodens* is inoculated alone [15-17]. *E. corrodens* is also associated with clinical relapse as observed for this patient. *S. constellatus* blood stream infections are also a risk for embolic complications as observed in this case. This report demonstrates that physicians should be alert for relapse and embolic complications when *E. corrodens* and *S. constellatus* are isolated together during IE, even if past therapy was appropriate.

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