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Repeat cultures in septic arthritis, do they change antibiotic management?

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ABSTRACT

Objectives: Septic arthritis is an orthopedic surgical emergency. Repeat cultures increase cost and patient discomfort; however, it is unknown whether repeat cultures have any merit in guiding treatment. The primary purpose of this investigation is to determine if repeat septic arthritis synovial fluid cultures alter antibiotic management. The secondary purpose is to identify independent risk factors that may alter subsequent antibiotic therapy.

Methods: Septic arthritis cases were retrospectively reviewed using the International Classification of Diseases, Ninth Revision codes between January 2011 and December 2015. Inclusion criteria were patients >18 years with >1 positive synovial culture taken >2 days apart.

Results: Two hundred and ninety-two synovial cultures were taken. Seventy were repeat cultures. Around 3 quarters (74.3%) yielded the same bacteria and 25.7% yielded different bacteria. Less than half (45.7%) of repeat cultures were associated with a change in antibiotics. Of the 18 repeat cultures that yielded different bacteria, six repeat cultures contained the same bacteria ± a different organism. Thirteen of the eighteen repeat cultures with different bacteria required a change in antibiotics. Patients who had their antibiotic therapy changed after repeat cultures were more likely to have diabetes mellitus (66.7% vs. 38.5%; $P = 0.04$, OR = 3.2 [1.04, 9.89]). Patients with hepatitis C more frequently required a different antibiotic regimen on repeat cultures (69.2% vs. 40.4%; $P = 0.06$, OR = 3.3 [0.91, 12.1]).

Conclusion: Repeat culture data in patients with septic arthritis changed antibiotic regimens in 45.7% of patients and yielded different bacteria in 25.7%. Patients with diabetes more frequently required alternate antibiotic regimens.

Keywords: Orthopedic surgery, Repeat culture, Septic arthritis, Stewardship, Synovial culture

INTRODUCTION

Septic arthritis is an orthopedic surgical emergency with an incidence of two cases per 100,000 people per year.[1] Untreated sequelae of septic arthritis may be severe, including chronic disability, joint destruction, and death, with a case-fatality rate of approximately 11%.[2] Even with antibiotic use, the in-hospital mortality rate for septic arthritis ranges from 7% to 15%.[3] The incidence of septic arthritis is increasing due to a number of factors, including an aging population, use of immunosuppressants, increased rates of intravenous drug use, and antibiotic

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resistance.[2] Proposed risk factors for septic arthritis include bacteremia, joint surgery, rheumatoid arthritis, diabetes, an immunocompromised state, intravenous drug abuse, trauma, recent tattoos, and long-term corticosteroid therapy.[1,4] When septic arthritis infects a native joint, chondral damage results from bacterial invasion, host inflammation, and tissue ischemia. Cartilage may rapidly be degraded after host matrix metalloproteinases are activated.[5] In addition, the diffusion of nutrients and oxygen to the cartilage through the synovial fluid is disrupted as purulent inflammatory tissue accumulates, thus increasing joint pressure and causing cartilage anoxia.[6]

Due to the devastating nature of this condition, prompt diagnosis and treatment of septic arthritis are paramount. The gold standard for the diagnosis of septic arthritis is joint arthrocentesis. Initial cultures are used to isolate the organism and establish antibiotic sensitivities for goal-directed treatment.[1] Organism identification and timely antibiotic sensitivity profiles are essential to narrowing the appropriate antibiotic regimen and eradicating infection while reducing antibiotic resistance. The rise of polymicrobial infections and emerging local antibiotic resistance patterns makes managing these infections increasingly challenging. Management of repeat upper extremity soft-tissue infections has been investigated, but these findings have never been duplicated in cases of septic arthritis.[7] These repeat cultures are frequently obtained in the operating room during definitive debridement procedures or on readmissions. Repeat cultures of septic arthritis increase health-care costs and patient discomfort; however, it is not known whether these repeated cultures have any merit in guiding treatment. Obtaining initial cultures is standard practice for the definitive management of treating septic arthritis, but repeat synovial cultures and their impact on antibiotic therapy have yet to be elucidated. No scientific publication, to the best of our knowledge, has described the outcomes and implications of repeat synovial cultures in septic arthritis.

The primary purpose of this study was to determine if repeat cultures of septic arthritis change antibiotic management. The secondary purpose of this study was to identify independent risk factors that may alter subsequent antibiotic management. Our hypothesis was that repeat synovial fluid culture data will change antibiotic regimen in more than 20% of cases.

MATERIALS AND METHODS

Following Institutional Review Board approval (27192, Temple University Hospital, 12/2021), codes associated with joint septic arthritis were applied to our institutional database using International Classification of Diseases, Ninth Revision codes for patients between January 2011 and December 2015. All data collection was in accordance with ethical standards of the Institutional Review Board and with the Helsinki Declaration of 1975, as revised in 2000. Inclusion criteria consisted of patients aged 18 years or older who had at least two positive synovial culture collections (either through joint aspiration or during intraoperative irrigation and debridement taken at least 2 days apart). Reasons for a repeat debridement procedure were left to the discretion of the attending surgeon. These indications included infection severity at the primary procedure, continued drainage through the previous incision or hemovac, and lack of clinical improvement despite previous irrigation and debridement. Exclusion criteria included patients <18 years old, pregnant patients, incarcerated patients, and patients with a prosthetic joint. The type(s) of bacteria were recorded, and the antibiotic prescribed at the time of discharge was defined as the definitive management. Patient demographics and comorbidities were also collected for analysis of independent risk factors associated with a change in the antibiotic regimen [Table 1].

Statistical analysis consisted of the Chi-squared and Fisher's exact tests for categorical variables (presence or absence of specific comorbidity). Unpaired *t*-test and standard deviations (SD) were used to compare the average time between cultures. $P < 0.05$ was considered to be statistically significant.

RESULTS

Over the 5-year period, 292 synovial fluid cultures were recorded, with a total of 120 positive cultures. Seventy of the total cultures were repeat cultures. Of the 70 repeat cultures, 52 (74.3%) yielded the same bacteria as the previous cultures and 18 (25.7%) yielded different bacteria than their previous cultures [Figure 1]. Thirty-eight (54.3%) repeat cultures did not change the antibiotic regimen. Thirty-two (45.7%) of the repeated cultures were associated with a change in antibiotic regimen. Of the total 18 repeat cultures yielded different bacteria, six contained the same bacteria ± a different organism due to polymicrobial cultures. Sixteen patients' repeat cultures did not have a change in organism, yet had a change in their antibiotics. Of these 2 (12.5%) were due to a change in sensitivity, 5 (31.3%) were transitioned to oral medication, 3 (18.8%) were changed to remove a broad-spectrum antibiotic, 3 (18.8%) were changed to add a broad-spectrum antibiotic, and three were changed for an unspecified reason. The average time between repeat cultures was 160.2 days (SD 287.1 days). The average time between repeat cultures that yielded different bacteria was 254.9 days (SD 367.6 days, $P = 0.24$). Of patients with septic arthritis, 38% were intravenous drug abusers, 6% had HIV, 22% had HCV, 16% had psychiatric diagnoses, 28% had diabetes mellitus, and 6% were immunocompromised.

Patients who had their antibiotic therapy changed after repeat cultures were significantly more likely to have diabetes

Table 1: Demographic and clinical variables.

Variable	Same antibiotic treatment, No. (%)	Different antibiotic treatment, No. (%)	Odds ratio (95% confidence interval)	*P*-value
Gender			1.04 (0.37, 2.95)	0.94
M	27 (38.6)	23 (32.9)		
F	11 (15.7)	9 (12.9)		
Age, year			0.96 (0.34, 2.72)	0.94
<45	11 (15.7)	9 (23.9)		
>45	27 (38.6)	23 (32.9)		
Race/Ethnicity			1.54 (0.06, 41.08)	0.19
Caucasian	20 (28.6)	10 (14.3)		
Hispanic	6 (8.9)	6 (8.9)		
African American	11 (15.7)	16 (22.9)		
Other	1 (1.4)	0 (0)		
IVDU			0.74 (0.28, 1.94	0.54
Y	17 (24.3)	12 (17.1)		
N	21 (30)	20 (28.6)		
HCV			3.33 (0.91, 12.1)	0.06
Y	4 (5.7)	9 (12.9)		
N	34 (48.6)	23 (32.9)		
Psychiatric history			2.20 (0.64, 7.56)	0.2
Y	5 (7.1)	8 (11.4)		
N	33 (47.1)	24 (34.3)		
Diabetic			3.20 (1.04, 9.89)	0.04
Y	6 (8.6)	12 (17.1)		
N	32 (45.6)	20 (28.6)		
HIV			2.47 (0.21, 28.54)	0.6
Y	1 (1.4)	2 (2.9)		
N	37 (52.9)	30 (42.9)		
Immunosuppressed			2.47 (0.21, 28.54)	0.6
Y	1 (1.4)	2 (2.9)		
N	37 (52.9)	30 (42.9)		

IVDU: Intravenous drug abuser; HCV: Hepatitis C virus, HIV: Human immunodeficiency virus

mellitus (66.7% vs. 38.5%; $P = 0.04$, OR = 3.2 [1.04, 9.89], [Table 1]). Patients with a psychiatric history were more likely to yield the same bacteria on repeat culture (92.3% vs. 70.2%; $P = 0.16$, OR = 0.2 [0.02, 1.63]). Patients with hepatitis C more frequently required a different antibiotic regimen on repeat cultures (69.2% vs. 40.4%; $P = 0.06$, OR = 3.3 [0.91, 12.1]). There was no significant difference in patient demographics and comorbidities, including age, gender, and race, intravenous drug use, HIV, and immunosuppression in terms of different cultures or antibiotic regimens.

Of the total 120 cultures, methicillin-resistant Staphylococcus aureus (MRSA) containing cultures were the most prevalent with 65 (54.1%), followed by methicillin-susceptible Staphylococcus aureus (MSSA) in 35 (29.2%) cultures [Table 2]. Fourteen (11.7%) of the total 120 cultures were polymicrobial. Eight of the repeat cultures that required antibiotic change contained polymicrobial bacteria either in the first culture or repeated culture. Sites of septic arthritis in the study included 23 knees, five ankles, ten hips, five shoulders, one tarsometatarsal joint, one sternoclavicular joint, one elbow, three wrists, one pubic symphysis, and one metatarsophalangeal joint. Five (7.14%) of the 70 repeat cultures yielded septic arthritis in a different location than their respective previous cultures.

DISCUSSION

Septic arthritis has significant morbidity and requires prompt diagnosis and treatment. The value of repeat intraoperative or aspirate cultures and their effects on antibiotic regimens has yet to be elucidated. The outcomes of repeat cultures have only been studied in the upper extremity infections. Repeat cultures in the upper extremity infections yielded different bacteria in 16.4% of patients and changed antibiotic treatment in only 7.1% of patients.[7] In our study, repeat cultures of septic arthritis were both more likely to yield different bacteria and change antibiotic regimens. Our study demonstrated that 25.7% of repeat septic arthritis cultures yielded different bacteria. Interestingly, our study

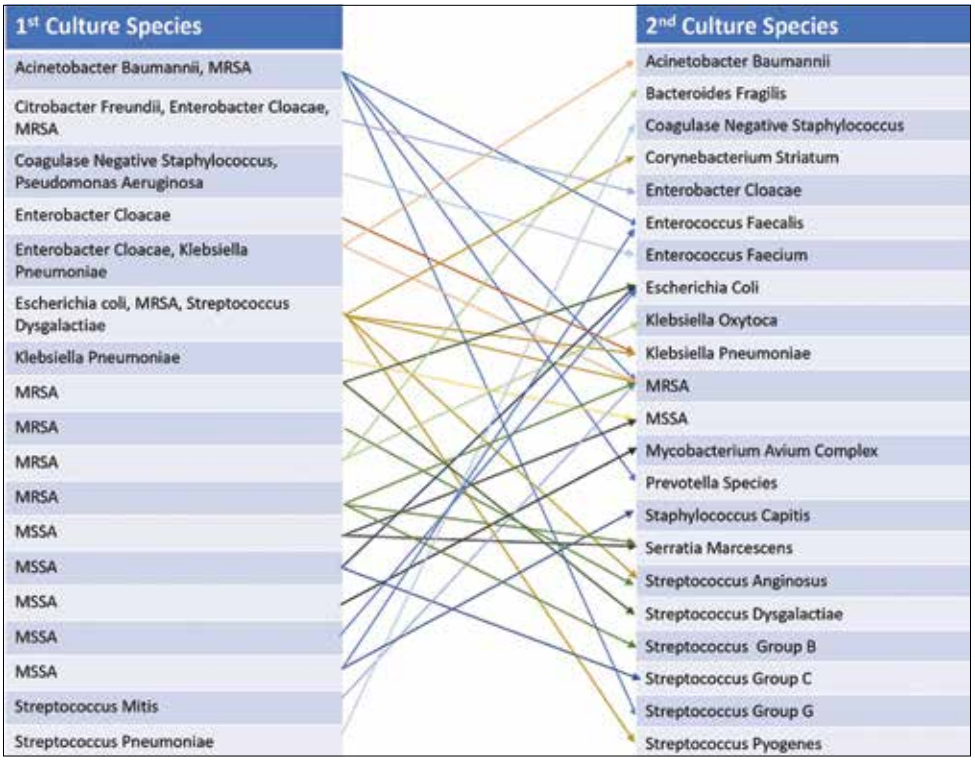

Figure 1: First versus repeat cultures in septic arthritis.

Table 2: Prevalence of organisms in septic arthritis culture.

Prevalence of organisms	Number
Methicillin-resistant Staphylococcus aureus	65
Methicillin-susceptible *Staphylococcus aureus*	35
Escherichia coli	6
Enterobacter cloacae	4
Klebsiella pneumoniae	4
Enterococcus faecalis	3
Enterococcus faecium	1
Proteus mirabilis	4
Pseudomonas aeruginosa	3
Acinetobacter baumannii	2
Streptococcus anginosus	2
Streptococcus group b	3
Bacteroides fragilis	1
Serratia marcescens	1
Prevotella species	1
Streptococcus dysgalactiae	1
Streptococcus mitis	1
Streptococcus group c	1
Streptococcus group g	1
Streptococcus pneumoniae	1
Streptococcus pyogenes	1
Corynebacterium striatum	1
Mycobacterium avium complex	1
Citrobacter freundii	1
Staphylococcus capitis	1

demonstrated that 45.7% of repeat cultures were associated with a change in antibiotic management. Reasons why patients had a change in antibiotic management despite not having a change in culture results were attributed to a change in antibiotic sensitivity, a conversion to oral medication or to add or remove a broad-spectrum antibiotic.

Our study showed no association between hepatitis C and different bacteria following repeat culture. There was, however, a trend toward significance for patients with hepatitis C requiring a change in their antibiotics after repeat cultures. Diabetes mellitus was identified as an independent risk factor for a change in an antibiotic regimen with repeat cultures. As diabetes is a clinical factor predictive of failure after a single surgical debridement, this frequent change in antibiotics may reflect an effort for more aggressive antibiotics on discharge.[3] Diabetes has been shown to be a risk factor for the development of septic arthritis, which corresponds to the prevalence of 15% of patients in the study. Immunosuppression is also a risk factor for developing septic arthritis; however, this was not shown to be a significant risk factor for changing antibiotic regimen in this study.

MRSA and septic arthritis of the knee were the most commonly isolated organism and location of septic arthritis, which is consistent with the current literature.[3] However, the incidence of MRSA in repeat cultures was higher in our

study than in the previous reports of 25% in other urban areas.[1] Streptococcus species were the next most commonly isolated organisms. Of all intravenous drug abusers, this accounted for 4.2% of cases of septic arthritis. Streptococcal species are commensal organisms of the oral cavity and are often present in bacterial infections of people who inject drugs after cleaning injection paraphernalia with saliva.[8] These organisms are responsible for a recent decrease in the proportion of MRSA infections among patients who inject intravenous drugs.[9] Polymicrobial cultures also made up a sizable portion of all infections in the study, at 11.7%. Polymicrobial infections represent a significant challenge for eradication, due to concerns of antibiotic resistance and insufficient treatment. Treating these patients may require multiple operations and cultures to finalize a definitive antibiotic regimen, which is critical as these patients tend to present sicker and ultimately have worse outcomes.[10]

In 2012, the U.S. had 13,714 hospitalizations with septic arthritis as the primary diagnosis. The total hospital charges were $759 million. Less than half (44%) of these patients needed additional care in the form of a skilled nursing facility or home health. This is a 26% increase from 2009, which had 13,087 septic arthritis hospital cases and $601 million in total hospital charges.[11] Roughly 23% of all patients with septic arthritis report intravenous drug abuse.[12] Our study has a slightly higher incidence of intravenous drug abuse among patients with septic arthritis. The economic impact of intravenous drug abuse on urban tertiary-care and safety-net hospitals can be staggering. The average cost of an inpatient admission for an extraspinal orthopedic complication of intravenous drug abuse is $9,524.[12] The average cost for a complete synovial fluid analysis at our hospital is $5240.22 (cell count, crystals, acid-fast bacillus culture, aerobic culture, anaerobic culture, and fungal culture). Unnecessary repeat cultures that do not lead to more targeted antibiotic management may unnecessarily add to the total cost of septic arthritis. Knowledge of this cost is crucial for orthopedic surgeons when repeating repeat debridement procedures. However, repeated cultures in high-risk groups like patients with diabetes or hepatitis C may lead to more targeted treatment plans, thereby reducing overall cost.

Limitations of this study include its retrospective nature, lack of culture standardization, and small sample size. In some instances, reasons for changing the antibiotics were not well-documented in the electronic medical record. Some of the reasons for switching antibiotics that may not be readily appreciable include cost to the patient, variations among infectious disease specialist treatment practices, and availability of antibiotics. In addition, cultures were collected both by arthrocentesis and intraoperatively. Because the cultures were obtained by various attending, residents, in the operating room, in the emergency department and on inpatient floors, the environment and personnel were not identical. Due to the small incidence of repeat septic arthritis, statistical significance was not able to be achieved in some analyses. Finally, the large discrepancy in duration between repeat cultures with different bacteria and those with the same bacteria may reflect a new disease process rather than insufficiently treated primary septic arthritis. This large diastasis in the two groups has yet to be explored in the literature. Further multicenter studies with larger study groups may help reach statistical significance and explore the gap between repeat cultures of almost 8 months. To the best of our knowledge, this is the first study to examine the effects of repeat cultures on the management of patients with septic arthritis.

CONCLUSION

Repeat cultures yielded different bacteria than their respective previous cultures at a frequency of 25.7% and changed antibiotic management in 45.7% of patients. Repeat synovial cultures of diabetic patients were significantly more likely to have a change in their antibiotic therapy. Our study supports that repeat cultures of septic arthritis may be beneficial for adequate antibiotic management of septic arthritis in patients with diabetes.

AUTHORS' CONTRIBUTIONS

RPJ conceived and designed the study, performed the literature search, data analysis, and wrote the manuscript. MG performed the literature search, performed the statistical analysis, and wrote the manuscript. JMS designed the study, supervised the study, and wrote and edited the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content.

ETHICAL APPROVAL

This investigation was approved by the Institutional Review Board at Temple University Hospital on January 18, 2021, as protocol number 27192.

DECLARATION OF PATIENT CONSENT

Consent was waived for patients by the Institutional Review Board, given that the study meets minimal risk criteria and meets all five criteria for waiving consent under Common Rule 45 CFR 46.116(f) as defined by the United States Department of Health and Human Services.

FINANCIAL SUPPORT AND SPONSORSHIP

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICTS OF INTEREST

There are no conflicting relationships or activities.

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