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Blood Culture Associations in Children With a Diagnosis of Cellulitis in the Era of Methicillin-Resistant *Staphylococcus aureus*

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INTRODUCTION

Cellulitis is defined as an “acute spreading infection of the skin that extends deeper than erysipelas and involves the subcutaneous tissues.”¹ In the last 2 decades, we have seen an increase in cellulitis and overall skin and soft tissue infection (SSTI) diagnoses. During this time, the rate of emergency department (ED) visits for SSTI has doubled, and overall there has been a 50% increase in ambulatory visits.^{2,3} In addition, an exponential rise in community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections has occurred.⁴

The cause of cellulitis or nondrainable SSTI is frequently attributed to staphylococcal and streptococcal species, although this is complicated by the difficulty in obtaining culture proof of an organism.^{5–13} The inability to obtain proof of bacterial etiology in patients with cellulitis is typically due to the absence of a specific nidus of infection from which to culture. Leading edge cultures and fine-needle aspiration of the infected area have fallen from favor, but blood cultures continue to be used despite several studies illustrating that they tend to be low yield.^{11–17}

Evaluative procedures of patients presenting with cellulitis may be physician-, hospital-, or region-dependent and tend to be variable. Previously published studies found that blood cultures in patients with cellulitis yield a low prevalence of bacteremia (0.7%–5%); however, most of these studies were completed before the recent surge in CA-MRSA and SSTIs.^{11–13} Due to increasing concern of CA-MRSA in cellulitis, antibiotic therapy directed toward methicillin-resistant *S aureus* (MRSA) has become standard, although it is not clear that the rise in cellulitis is attributable to CA-MRSA.¹⁸

The objective of the current study was to determine the incidence of clinically relevant blood cultures in an era of increasing MRSA prevalence. Secondary objectives include demographic features associated with blood culture ordering as well as previous antibiotic use, associated testing, and association with hospitalization.

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METHODS

We completed a retrospective chart review of ED visits at a single, urban tertiary care children's hospital between January 1, 2008, and December 31, 2008. During this period, there was an electronic health record (EHR) for laboratory and imaging studies and a separate EHR (IBEX) that the ED used; the inpatient documentation used paper records. Because ED evaluation of these patients was the focus, the laboratory and imaging EHR as well as IBEX were reviewed for this study.

IBEX required the physician to choose 1 or more diagnoses from a drop-down menu of codes from the International Classification of Diseases, Ninth Revision (ICD-9) or to free-text a diagnosis for the patient encounter. Because the database allowed the physician to free-text a diagnosis, the study used a key word search for the term "cellulitis" rather than the ICD-9 code, in an effort to identify as many of the cellulitis diagnoses as possible. The search identified subjects who had the key word "cellulitis" as 1 of their diagnoses or who had an ICD-9 code that included cellulitis (681.0–682.9).

We included children aged 2 months to 18 years with a final diagnosis of cellulitis at disposition from the ED. We excluded subjects with primary or secondary immunodeficiency, osteomyelitis, orbital or periorbital cellulitis, postoperative infection, dental-related infection, or infections involving foreign bodies. Some subjects were evaluated in the ED on multiple occasions during the study period. To help determine if a subsequent visit was related to the initial diagnosis of cellulitis or a completely new diagnosis, time between visits was evaluated. If the time between visits was ≥ 8 weeks, the subsequent visit was considered a new diagnosis.

The following information was abstracted from the chart during the review: age at encounter, race, month of the year, incision, and drainage. We also obtained information on complete blood cell count (CBC), blood culture, wound culture, history of administration of previous antibiotics, and subsequent hospitalization.

The primary outcome was the presence of a clinically relevant organism on blood culture obtained during the evaluation. Secondary outcomes included the rate of blood culture, grouped according to race, history of previous antibiotic exposure, and hospitalized versus nonhospitalized subjects. Associations between CBC and blood culture, as well as wound culture and blood culture testing, were also evaluated.

Susceptibility testing within this institution uses oxacillin, and methicillin resistance is inferred. The term MRSA as opposed to oxacillin-resistant *S aureus* is used because it is the more widely accepted term.

χ^2 and Fischer exact tests, as appropriate, were used to examine factors associated with the primary and secondary outcomes. Multivariable regression analysis was completed, adjusting for race, previous antibiotic use, wound culture, CBC, and hospitalization. SPSS version 17.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) was used for analysis. This study received approval from the institutional review board of Saint Louis University.

RESULTS

There were no clinically relevant organisms found on blood culture over the study period. There were 4 blood cultures obtained that resulted in growth of typical contaminants: 3 cultures resulted in coagulase-negative staphylococci and 1 culture had >3 organisms.

Over the study period, there were 473 patients who presented to the ED with a final diagnosis of cellulitis and who met inclusion criteria. Eighty-eight subjects were excluded, leaving 385 subjects with a mean $\pm$ SD age of 6.9 ± 5.9 years; 58% were African American, and 51% were male (Table 1).

There were 88 subjects excluded after chart review because of the following: 46 subjects had periorbital or orbital cellulitis, 29 subjects had dental-related infection, 7 subjects had postsurgical infections, 3 subjects were diagnosed with osteomyelitis, 2 subjects had foreign bodies, and 1 subject was immunosuppressed. Of the 385 subjects meeting inclusion criteria, 22 had multiple encounters over the study period. Each of the subsequent encounters occurred <8 weeks after the initial encounter; therefore, only the first encounter was evaluated and reported, resulting in 385 subjects each with 1 encounter in the ED.

There are many factors associated with blood culture testing (Table 2). The most significant factors were CBC testing and subsequent hospitalization after ED evaluation (Table 3).

There were 187 subjects (49%) who underwent a procedure that included incision into the affected area and drainage if a fluid collection was encountered, although this procedure was not always clearly or consistently reported in the EHR of the ED. A total of 146 of these subjects had a wound culture, and it is unclear from the records if a wound culture was simply not completed or there was no fluid collection from which to culture.

The subjects who underwent incision into the affected area had significant differences compared with those who did not undergo the procedure. The subjects undergoing an incision and possible drainage were significantly more likely to have a CBC compared with the subjects who did not undergo this procedure (43% vs 32%; $P = .035$). The subjects who underwent an incision procedure were more likely to receive antibiotics before arrival (62% vs 44%; $P = .003$) and to be hospitalized (59% vs 43%; $P = .003$). There was no significant difference in the rate of blood culture testing between the group who underwent an incision and possible drainage procedure and the group that did not (37% vs 31%; $P = .17$).

In our institution, the charge for a blood culture is \$212, with \$124 added for each organism isolated and \$184 for each susceptibility test. In this cohort, there were \$28 780 in charges for blood cultures, which included \$2280 for the contaminated blood cultures.

DISCUSSION

Before the recent increase in MRSA, several studies concluded that blood cultures in patients with cellulitis were of little clinical value.¹¹⁻¹³ Despite the increased incidence of MRSA and cellulitis, blood cultures do not provide evidence of the causative organism in the diagnosis of cellulitis.

Blood cultures are still frequently ordered in children diagnosed with cellulitis. There were no clinically significant organisms isolated in the blood culture of patients with cellulitis, yet they were completed on one-third of the subjects diagnosed with cellulitis. The blood cultures did lead to 4 contaminated cultures. It does not appear from the records obtained that these subjects had any further blood work obtained in the immediate period after their admission, and it is unknown if the subjects had prolonged or expanded antibiotic coverage, prolonged length of stays, or elevated patient status or increase in monitoring.

The significant association between blood cultures and hospitalization may represent the practitioners' perception of the overall appearance of the child; however, this study did not specifically examine that relationship. The association may also be secondary to practitioners' perceived obligation to obtain laboratory tests when they are admitting a child. Laboratory orders seem to be ordered simultaneously, as evident by close timing of the placement of CBC and blood culture orders.

In the subjects who underwent incision into the affected area, it is assumed that the practitioner felt an abscess was present. Only 78% of these subjects had a wound culture obtained. This finding may be due to the absence of fluid to culture (no abscess) or the practitioner may have decided a wound culture was not needed. Almost one-half of subjects with a wound culture also had a blood culture. A wound culture provides information from the source of the infection and identifies the cause. A blood culture samples fluid distant from the immediate area of infection and would be an inferior test when looking for a causative organism. It is interesting that despite having a wound culture, practitioners opted to also obtain blood cultures in these individuals. This action leads one to assume that the blood culture had less to do with identification of an organism causing the SSTI and was more likely due to another reason.

The term "abscess" was not included in the search for subjects because it was felt that these subjects had a specific nidus of infection that is easily cultured, whereas patients with cellulitis do not. There were 187 subjects (49% of all subjects) with a diagnosis including cellulitis at their discharge from the ED who underwent an incision into the affected area with possible drainage, and 146 of these subjects had a culture obtained from this area. Despite searching for subjects with cellulitis, there were many subjects identified who may have had an abscess. There was no statistical difference in blood culture ordering between subjects with an incision procedure with possible drainage and those who did not undergo this procedure.

Finally, each contaminated blood culture may significantly increase cost and charges. In 2 separate adult studies, which can have different causes and costs compared with pediatric studies, it was revealed that these contaminated cultures could result in \$6000 to \$9000 in additional charges.^{19,20} In the current study, the 4 subjects with contaminated blood cultures did not have any repeat blood work obtained during their hospitalization, but it is unknown from ED records if the subjects had prolonged length of stays, elevated status, broadened antibiotic coverage, or increased monitoring.

This study was a retrospective review at a single institution. It was meant to evaluate children diagnosed with cellulitis, and we found that one-half of patients underwent an incision into the affected area with most having a wound culture obtained; this calls into question the diagnosis of cellulitis. Other factors that may be associated with further laboratory evaluation and management of the subjects, including presence of fever, clinical appearance, and size of cellulitis, were not obtained and may add value to future studies. Such studies are needed to evaluate the extent of the impact that obtaining a blood culture has on length of stay, cost, and future decisions made by the health care provider.

CONCLUSIONS

In this study, blood culture results never revealed a clinically significant organism in these children diagnosed with cellulitis. Despite the increasing prevalence of MRSA, these data continue to support the recommendation that blood cultures should not be routinely obtained in the laboratory evaluation of children with cellulitis. Future studies would benefit from incorporating a multicenter design, evaluating subjects with a diagnosis of abscess, evaluating the impact of wound cultures on antibiotic selection, studying the impact of resource utilization (including blood cultures), and improving quality of care with pathway development incorporating these findings.

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ABBREVIATIONS

CA-MRSA	community-acquired methicillin-resistant <i>Staphylococcus aureus</i>
CBC	complete blood cell count
ED	emergency department
EHR	electronic health record
ICD-9	International Classification of Diseases, Ninth Revision
MRSA	methicillin-resistant <i>S aureus</i>
SSTI	skin and soft tissue infection

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TABLE 1

Demographic Characteristics of Subjects

Characteristic	Blood Culture	CBC	Hospitalized	Total Number
Age				
2–12 mo	24 (19)	27 (19)	29 (21)	54 (14)
>1–5 y	48 (37)	50 (35)	48 (34)	143 (37)
>5–10y	19 (15)	21 (14)	26 (19)	63 (16)
>10–15y	22 (17)	24 (17)	19 (14)	68 (18)
>15 y	16 (12)	22 (15)	18 (13)	57 (15)
Male gender	67 (52)	77 (53)	71 (51)	196 (51)
Race				
White	63 (49)	71 (49)	70 (50)	135 (35)
African American	54 (42)	61 (42)	58 (41)	223 (58)
Other	12 (9)	12 (8)	12 (9)	27 (7)

Data are presented as *n* (%).

TABLE 2

Nonadjusted Data for Subgroup Analysis of Blood Culture Testing

Individuals With Blood Culture Testing	Blood Culture	No Blood Culture	Percent
Race			
White	63	71	47
African American	54	169	24
Other	12	16	43
Previous antibiotics	47	37	56
Wound culture testing	62	83	43
CBC testing	126	18	88
Hospitalization	112	28	80

TABLE 3

Multivariable Regression Analysis Based on Bivariate Analysis and Adjusted for Race, Previous Antibiotics, Wound Culture Testing, CBC Testing, and Hospitalization

Characteristic	Odds Ratio	95% Confidence Interval	
		Lower Limit	Upper Limit
White race	2.8	1.8	4.5
Previous antibiotic use	3.5	2.1	5.8
Wound culture testing	1.9	1.2	2.9
CBC testing	502	144	1751
Hospitalization	53	27	102