Evaluation of a Positive Yeast-in-Blood Service

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Abstract: *Background:* The purpose of this study was to evaluate the effect of a novel "yeast-in-blood" surveillance service on the timeliness of antifungal chemotherapy for candidemia. *Methods:* Two hundred seven blood cultures positive for *Candida* species between July 1, 1994, and February 15, 2009, as identified by the microbiology positive culture log, were included in this retrospective chart review. Patients with a positive culture before July 1, 2008, were evaluated by the yeast-in-blood surveillance service and included as intervention cases (IC). After this time, those occurring after discontinuation of the service were included as nonintervention cases (NIC). The primary outcome measure was the time to antifungal therapy from the time of blood culture draw. Secondary outcome measures included antifungal selection and time to antifungal prescription order from culture positivity. *Results:* Median time to therapy was 58.9 ± 28.4 hours and 41.3 ± 30.5 hours for NIC and IC, respectively ($P = 0.001$). Median time to prescription order was 3.0 ± 6.9 hours for NIC versus 1.9 ± 3.9 hours for IC. *Candida albicans* was the predominant organism identified (45.3% of NIC and 54.6% of IC). Treatment agents included an azole in 57.4% of NIC and 47.4% of IC, an echinocandin in 33.3% and 27.3% and a polyene in 5.7% and 27.8%, respectively. *Conclusions:* Time to therapy and time to prescription were shorter in those evaluated by the surveillance service. These data suggest that a yeast surveillance service improves antifungal medication therapy initiation.

Key Indexing Terms: *Candida*; Fungemia; Microbiology. **[Am J Med Sci 2014;348(1):43–46.]**

Candida species are the most common nosocomial fungal pathogens.[1,2] According to the Centers for Disease Control and Prevention's National Healthcare Safety Network, fungi are responsible for 13% of all hospital-acquired infections. *Candida* species are responsible for 82.3% of nosocomial mycoses, and *Candida albicans* accounts for the majority (64%) of these isolates.[1] *Candida* species are the 4th leading cause of bloodstream infections. Crude mortality attributed to nosocomial bloodstream infections from all *Candida* species is 39%.[3] The prevalence of infections caused by fungal pathogens should be considered by clinicians when determining empiric therapy, potentially prompting the addition of antifungal therapy to initial regimens. Risk factors for candidemia include prolonged use of broad-spectrum antimicrobial agents and the presence of central venous catheters, especially in immunocompromised patients in an intensive care unit. According to the guidelines from the Infectious Diseases Society of America (IDSA), all bloodstream isolates of *Candida* species should be considered pathogenic and treated.[4]

The timing and appropriateness of antifungal therapy impact the mortality of patients with candidemia.[5–7] Without prospective monitoring of patients with suspected or confirmed candidemia, treatment could be delayed and patient outcomes adversely affected. No prior study has assessed the effect of a proactive, pharmacy-directed, collaborative service in improving the timeliness of administration for fungal bloodstream infections.

Although pharmacists have had the opportunity to participate with infectious diseases and microbiology colleagues in many aspects of care, interaction has usually taken the form of antibiotic surveillance services and antibiotic subcommittee activities of Pharmacy and Therapeutics Committees. The antiinfective surveillance system at this institution uses pharmacists as front-line advocates for optimal patient care, including medication therapy management. In this service, a member of the team is notified by the microbiology laboratory in addition to the primary care provider of the occurrence of blood cultures positive for *Candida* species. After notification, the pharmacist evaluates the patient's appearance, vital signs and clinical picture; reviews culture and laboratory results and performs a complete pharmacotherapy assessment. Verbal recommendations using the proposed and ultimately published IDSA candidemia guidelines were then made to the prescribers.[8] This allows the service to help assure use of best practices of care for candidemia. This study evaluated the effect of direct involvement of a yeast-in-blood monitoring service in securing timely antifungal therapy for a disease state that is responsible for significant hospital morbidity and mortality.

METHODS

This retrospective analysis of data from 2 time periods was completed at a 722-bed tertiary referral teaching hospital. Patients with a blood culture positive for yeast between July 1, 1994, and February 15, 2009, as identified by review of the positive blood culture log of the microbiology laboratory, were eligible for inclusion. Patients were divided into 2 groups: those who were evaluated by the yeast surveillance service from July 1, 1994, to June 30, 2008 (intervention cases [IC]) and those who were not evaluated, from July 1, 2008, to February 15, 2009 (nonintervention cases [NIC]). The primary outcome measure was the time to antifungal therapy from the time of culture. An assessment of the success of the surveillance service was made by comparing outcome data from IC with NIC. Finally, although a true correlation is difficult to determine, crude hospital mortality (calculated using individual patient outcomes) was described demonstratively as a statement to the effect on patient care. This study was approved by the institutional review board.

Patient Recruitment and Data Collection

Patients with a blood culture positive for yeast between July 1, 2008, and February 15, 2009, were not evaluated by this surveillance service and were identified as NIC. IC patients had a blood culture positive for yeast between July 1, 1994, and June 30, 2008, and were evaluated by the service. The first positive

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culture for each new species of *Candida* during the study period was included. New positive cultures collected greater than 30 days apart, including the same *Candida* species, were also included. If a repeat culture was performed and positive during the course of therapy or up to 7 days following therapy, it was considered a duplicate culture and excluded. In addition, patients during either time period were excluded from participation if medical records were incomplete or unavailable. Cultures repeated between 7 and 30 days were evaluated on an individual basis.

Data collected included demographics, primary and secondary diagnoses, medical and surgical history, Acute Physiology and Chronic Health Evaluation (APACHE) II score (calculated on the day blood cultures were drawn), patient location (intensive care versus ward), species of *Candida* obtained from blood culture, antifungal therapy and risk factors for candidemia (assessed at the time of culture). Risk factors included presence of central venous catheters, immune-suppressing medications or disease states including any corticosteroid use or documented history of diabetes, concomitant antibiotic use of any type or duration except preoperation surgical prophylaxis and receipt of total parenteral nutrition. Time of culture, time to culture positivity, time of provider notification, time of antifungal therapy order and time of administration of first dose of antifungal medication (as determined from the medication administration record) were also recorded. Time to therapy was chosen as the primary objective and defined as the interval between culture collection and medication administration to the patient based on consensus definitions in similar studies.[5,6] Time to prescription order was defined as the time from provider notification of a positive culture to the time an order was written for antifungal therapy. Time to identification of the positive yeast in the blood was defined as the time the culture was drawn until positive culture results were reported. Patients receiving prophylactic (before culture) or empiric (before culture results) therapy were included in time to identification calculations but excluded from calculations of time to therapy and time to prescription order. All data collection was completed by clinical pharmacists with training in infectious diseases.

Microbiology

Blood samples for culture were drawn by nurses or hospital-trained phlebotomists following standard procedures. According to normal procedures, cultures were drawn from 2 sites (2 peripheral or 1 peripheral and 1 through a central venous catheter, if present). All blood samples were inoculated into aerobic and anaerobic bottles and processed by the BACTEC 9240 blood culture system (Becton Dickinson, Sparks, MD) for 5 days. On notification of a positive sample, a Gram stain was performed, and the sample was cultured on blood, chocolate and MacConkey agar according to usual practice. Any growth was identified by Vitek 2 (bioMerieux, Inc, Durham, NC).

Statistical Analysis

The measured time to therapy was calculated for each group as median ± 25%. These data were not normally distributed; so, Mann-Whitney's rank sum test was performed to assess differences in time to therapy (SYSTAT Software; Systat, Richmond, CA). An alpha = 0.05 was selected for this statistical comparison. All other data collected are represented descriptively.

RESULTS

Fifty-three positive cultures were identified for inclusion as NIC and nearly 2,200 cultures were identified as IC. Of the NIC, 8 of 53 (15%) represented a 2nd positive *Candida* culture in a patient. A new positive culture in these patients was a mean of 34 days after the first culture, and 4 of these 8 (50%) cases had a positive culture with a different *Candida* species. In view of the above, the 8 cultures were included with the original data for a total of 53 cultures. Of the nearly 2,200 positive blood cultures in the IC, 534 were randomly selected for inclusion. Of these, 380 were duplicates or repeat culture results for patients. These were removed from the 534, leaving 154 IC for analysis.

Demographics for the NIC and IC groups are listed in Table 1. In both groups, *C albicans* was the predominant organism identified (47.1% of NIC and 54.6% of IC). Other organisms identified in more than 1 patient were *C glabrata* (20.8% versus 16.9%), *C parapsilosis* (20.8% versus 18.2%) and *C tropicalis* (7.6% versus 7.8%). One NIC and 4 IC cultured more than 1 *Candida* species simultaneously.

In patients who were not treated prophylactically or empirically, the median time to therapy was significantly longer in the NIC than IC (58.9 ± 26.2 hours versus 41.3 ± 23.9 hours [$P = 0.001$]; Table 2). Twenty-two of 52 (42%) antifungal orders for the NIC were written before receiving the culture results, and 30 (58%) orders were written after notification of the positive culture. Forty-one of 147 (28%) orders for the IC were written before receiving the culture results, and 106 (72%) orders were written after notification of the positive culture. Patients receiving prophylactic or empiric therapy were not included in the time to prescription order analysis.

Median time to identification of all positive yeast was 47.5 ± 21.9 hours and 31.1 ± 26.2 hours for NIC versus IC, respectively. In the NIC versus IC, 5 of 53 (9.4%) versus 26 of 154 (16.9%) were identified in less than 24 hours, 27 (50.9%) versus 127 (82.5%) were identified within 24 to 48 hours and

TABLE 1. Patient demographics

	Nonintervention (NIC), n (%)	Intervention (IC), n (%)
Age (yr), median ± 25%	40.3 ± 20.8	31.4 ± 27.7
Male	28 (53)	79 (51)
Race		
African American	29 (55)	89 (58)
Caucasian	20 (38)	62 (40)
Other	4 (8)	3 (2)
Patient location		
Children's hospital	5 (9)	18 (12)
Intensive care unit	31 (58)	74 (48)
Medicine floor	17 (32)	52 (34)
Specialty area	0	10 (6)
APACHE II score		
<20	40 (75)	112 (73)
≥20	8 (15)	35 (23)
NA	5 (9)	7 (5)
Other risk factors		
Central venous catheters	45 (85)	122 (79)
Diabetes	10 (19)	18 (12)
Medications		
Corticosteroids	17 (32)	26 (17)
Antibiotics	45 (85)	139 (90)
TPN	22 (42)	60 (39)

Data are presented as median ± 25% or n (%), rounded to the nearest whole number.