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Patients with *Acinetobacter baumannii* bloodstream infections are colonized in the gastrointestinal tract with identical strains

Kerri A. Thom, MD, MS, **William W. L. Hsiao, PhD**, **Anthony D. Harris, MD, MPH**, **O. Colin Stine, PhD**, **David A. Rasko, PhD**, and **J. Kristie Johnson, PhD**
University of Maryland School of Medicine, Baltimore, MD

Abstract

In this study, we identified critically ill patients with *Acinetobacter baumannii* bacteremia and examined perirectal surveillance cultures for the presence of genetically related *A baumannii* strains using pulsed-field gel electrophoresis to determine whether gut colonization preceded clinical infection. Seven patients with imipenem-resistant *A baumannii* bacteremia were identified from January to June of 2008. Six of 7 (86%) patients were colonized in the gastrointestinal tract with genetically similar strains preceding their bacteremia.

Keywords

Acinetobacter baumannii; hospital epidemiology

Acinetobacter baumannii has emerged as an important nosocomial pathogen.[1] Nosocomial transmission is well documented from outbreak investigations[2]; however, it is unclear whether transmission leads directly to infection through breaches in normal host defense mechanisms or whether *A baumannii* first establishes colonization in turn leading to infection. This is an important distinction because infection control interventions would vary in either scenario. We investigate critically ill patients with imipenem-resistant *A baumannii* (IRAB) bacteremia and examine perirectal surveillance cultures for the presence of genetically related *A baumannii* strains to determine whether gut colonization precedes clinical infection.

PATIENTS AND METHODS

This study utilized an ongoing prospective cohort of adult patients admitted to the medical intensive care unit at the University of Maryland Medical Center (UMMC), who have routine (admission, weekly, and discharge) perirectal surveillance cultures obtained. Patients within the cohort who had IRAB bacteremia from January 1, 2008, to June 30, 2008, were identified using the UMMC computerized central data repository.

For those patients with IRAB bacteremia, previously obtained perirectal cultures were plated onto MacConkey agar (Remel, Lenexa, KS) supplemented with 6 μg/mL of imipenem and incubated at 37°C for 24 to 48 hours. Antimicrobial susceptibility testing was performed by disk diffusion and interpreted in accordance with Clinical and Laboratory Standards Institute

Address correspondence to Kerri A. Thom, MD, MS, Division of Healthcare Outcomes Research, Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, 100 N Greene St, Lower Level, Baltimore, MD 21201. kthom@epi.umaryland.edu.

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guidelines.[3] *A baumannii* was identified from the blood in the UMMC microbiology laboratory following standard protocol.

Pulsed-field gel electrophoresis (PFGE) was performed on all blood isolates and the corresponding perirectal surveillance cultures if they grew IRAB. PFGE was performed following the protocol described at http://www.cdc.gov/pulsenet/protocols.htm with modifications.[4] Briefly, DNA was digested with *Apa*I according to the manufacturer's recommendations (New England Biolabs, Beverly, MA). DNA was separated in 1% agarose on a contour-clamped homogeneous-field machine (CHEF-DR II; Bio-Rad, Hercules, CA). Interpretation of PFGE was done using criteria outlined by Tenover et al.[5]

RESULTS

From January 1, 2008, until June 30, 2008, 610 people entered the cohort and had perirectal surveillance cultures obtained. Of these, 7 (1.1%) had a blood culture positive for IRAB, mean age was 58.9 years, and 29% (2/7) were men. Four patients (57%) died during their hospital admission. Among the 3 survivors, postbacteremia length of stay was 7, 20, and 21 days. In total, 50 perirectal surveillance cultures were collected from these 7 patients, 26 of which were positive for growth of IRAB (27 isolates; one swab had 2 different isolates).

Six of the 7 (86%) patients with IRAB bacteremia had a perirectal culture that also grew IRAB at any time during their intensive care unit stay. Among these 6 patients, 4 had at least 1 positive perirectal culture that preceded the positive blood culture (days from the first positive perirectal culture to blood culture ranged from 2 to 76). In 3 of 4 patients, perirectal and blood isolates were indistinguishable by PFGE criteria; in the fourth patient, the isolates were classified as closely related (1 band difference). For the remaining 2 patients, the first *A baumannii*-positive perirectal and blood cultures were collected on the same day. In one of these patients, the perirectal and blood isolates were indistinguishable, and, in the other, the isolates were closely related. Data are summarized in Fig 1.

DISCUSSION

Among critically ill patients with IRAB bacteremia, we identified the proportion perirectally colonized with the same organism and compared perirectal and blood isolates using PFGE to determine genetic relatedness. Our results suggest that gut colonization with *A baumannii* frequently precedes bacteremia in this population.

Infection caused by IRAB has been linked to increased mortality, length of stay, and hospital costs.[1] Colonization with *A baumannii* has been shown to precede infection, with 17% to 26% of patients colonized at 1 or multiple sites (eg, skin, oropharynx, rectum) developing infection.[6–8] These studies, however, are limited by the lack of molecular typing to determine genetic relatedness between colonizing and infecting organisms. Because it is possible that patients are colonized and infected with 2 different isolates of a particular bacterium, molecular typing showing genetically similar strains gives further support to the possibility of a causal relationship between colonization and subsequent infection.

Early recognition of colonization has several potential advantages. Recognition of colonization by multidrug-resistant strains may assist in early treatment decisions when infection does occur. Knowledge of colonization status prior to infection has been associated with higher rates of appropriate antibiotic use for bacteremia caused by gram-negative bacilli.[9] Conflicting data exist in the literature, however, regarding the benefit of early appropriate antibiotic use for gram-negative bacteremia, and, to our knowledge, no studies specifically examined *A baumannii* bacteremia.[10,11] In addition, early detection of colonization allows for the implementation of infection control strategies, such as barrier

precautions, aimed at reducing transmission. The frequency of nosocomial outbreaks because of *A baumannii* suggests that nosocomial transmission because of this organism is high, likely because of patient-to-patient transmission via the hands of health care workers from a common environmental source.[2] Future investigators may choose to study potential interventions, such as decolonization, aimed at prevention of infection and spread in persons known to be colonized. Identification of colonization prior to clinical infection, however, relies on costly and time-consuming active surveillance strategies. Definitive knowledge regarding the frequency of colonization prior to infection, along with knowledge regarding the most common site of colonization and the outcome benefits related to early detection would be needed prior to implementation of such a strategy.

This study is limited by a small sample size; large studies similar to this would be needed to determine the true frequency with which colonization precedes clinical infection. In addition, because of the difficult nature of classifying clinical infections retrospectively and differentiating from colonization, this study was limited only to bacteremia and did not consider infections of the respiratory tract, urinary tract, wounds, or other sites. Furthermore, because we only considered colonization at the perirectal site, it is possible that the single patient in this study who was not found to be colonized in the perirectal sample was colonized at an alternate site (eg, respiratory tract) or that the perirectal culture was not sensitive enough to detect intestinal colonization.

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PFGE Pattern	Patient	No. of PR cultures obtained prior to BSI	No. of PR cultures positive for *A. baumannii*	No. days from first positive PR culture to BSI	PFGE results of PR compared to Bloodstream Isolate
	1	13	7	76	Closely Related
	2	2	1	0	Indistinguishable
	3	5	3	6	Closely Related*
	4	5	3	17	Indistinguishable
	5	6	1	0	Closely Related
	6	3	1	2	Indistinguishable
	7	4	0	--	--

Fig 1.

Patients with *Acinetobacter Baumannii* bacteremia. Description of perirectal cultures and comparison with bloodstream isolates. *Patient 3 had 3 perirectal cultures positive for *A baumannii*. PFGE results from these 3 cultures included 1 isolate possibly related to the bloodstream isolate, 1 isolate closely related (6 days prior to the positive blood culture), and the third isolate indistinguishable (1 day prior to the positive blood culture). The indistinguishable isolates are shown in the Figure. PR, perirectal; BSI, bloodstream infection. This figure is available in color online at www.ajicjournal.org.