Epidemiology of Rapidly Growing Mycobacteria Bloodstream Infections

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ABSTRACT

Background: Rapidly growing mycobacteria (RGM) bloodstream infections (BSI) are an emerging problem often associated with therapeutic challenges. We review the epidemiology, treatment and outcomes over a 5-year period of a heterogeneous group presenting to our institution with RGM BSI.

Materials and Methods: A retrospective cohort study of patients with primary RGM BSI from January 2006-December 2011 was conducted. Patient characteristics (age, race, sex and comorbidities), infection characteristics (catheter associated, hospital acquired, microbiology and antimicrobial susceptibilities), therapy and outcomes were recorded and compared by species.

Results: Among 32 patients, 33 RGM BSI occurred. Patients had an average of 3-4 comorbidities, most commonly malignancy (45.5%). Most isolates (30.3%) were *Mycobacterium fortuitum* or *Mycobacterium mucogenicum* (27.2%), followed by *Mycobacterium abscessus/chelonae* (18.2%) and *Mycobacterium immunogenum* (12.2%). In all, 85% were catheter associated and 27.3% were hospital acquired. Empiric therapy was started in 19 (57.6%) patients and among these, it was adequate (at least 2 active agents based on susceptibilities) in 12 (63.2%). Among 21 patients with outcome data, cure was assumed for 14 (66.7%). One death was attributable to RGM BSI. Cure rates were higher among those who received adequate empiric therapy compared to those who did not (83.3% versus 42.9%). In general, antibiotic susceptibility was favorable across species for clarithromycin, amikacin and imipenem.

Conclusions: RGM BSI occurred in a population with multiple comorbidities, most commonly malignancy, and most were catheter associated. Higher cures were seen among those who received adequate empiric therapy and based on susceptibility data, a broad empiric regimen of clarithromycin, amikacin and imipenem would be expected to be adequate.

Key Indexing Terms: Rapidly growing mycobacteria; Bloodstream infection; Antimicrobial susceptibilities; Empiric therapy; Clinical outcomes. **[Am J Med Sci 2016;351(3):253–258.]**

INTRODUCTION

Rapidly growing nontuberculous mycobacteria (RGM), both pigmented and nonpigmented species, produce mature growth on culture media within 7 days. The major groups are: *M. fortuitum*, *M. chelonae/abscessus*, *M. mucogenicum*, *Mycobacterium smegmatis* and early pigmenting RGM such as *Mycobacterium flavescens, Mycobacterium neoaurum, Mycobacterium cosmeticum* and *Mycobacterium phlei*.[1,2] Even though RGM are ubiquitous in the environment, they have generally only been described as a cause of disease among special patient populations, especially the immunosuppressed or those with conditions which lead to disruption of normal anatomic barriers.[3-8]

Historically, even among high-risk patient populations, the incidence of RGM infections has been low, reported as less than 1% in a large case series of the patients who have undergone hematopoietic stem cell transplant.[6] However, over the past decade there has been an increase in the number of reports of RGM bloodstream infections (BSI). Not unexpectedly, treatment strategies have been disparate as there is no evidence-based consensus to guide therapy. These have ranged from line removal only (with no antimicrobial therapy) to combination antimicrobial therapy with 2 or 3 agents. Most RGM BSI have been described among patients with neoplastic disease and these represent the largest case series to date.[4-8] Few studies describe risk factors associated with RGM BSI and these include neutropenia, concurrent corticosteroid therapy, graft versus host disease, chemotherapy, radiation therapy, hemodialysis, surgery, total parenteral nutrition and human immunodeficiency virus.[5,6,9-11]

We review here the epidemiology, treatment plans and clinical outcomes over a 5-year period of a heterogeneous group of patients presenting to our institution with an episode of RGM BSI.

METHODS

Patient Population and Study Setting

We conducted a retrospective cohort study of all patients who had an episode of BSI due to a RGM based on blood culture data obtained between January 1, 2006 and December 31, 2011 at the Medical University of South Carolina. Medical University of South Carolina is a 750-bed academic medical center, located in Charleston, South Carolina, which provides all medical and surgical care (including solid organ and stem cell transplantation) for South Carolina residents as well as referrals from surrounding states.

Data Collection and Analysis

We reviewed the charts of all patients in the previously described cohort using a standardized data collection form. Patient demographics such as age, race and sex were recorded as comorbidities, presence of a central venous catheter, receipt of antimicrobials or antifungals within 30 days of the BSI episode, infection characteristics such as whether or not the BSI was hospital acquired, type of empiric and definitive antimicrobial therapy, susceptibility patterns of the organism(s), duration of antimicrobial therapy and outcome at least 6 months post-treatment. These characteristics were described for the overall cohort and then by RGM species.

Definitions

A list of all patients with positive blood cultures for RGM over the study period was provided to the investigators by the Clinical Microbiology Laboratory. Patients were included in the study if they met the definition for a primary RGM BSI. A primary RGM BSI was defined as a RGM isolated from 1 or more blood cultures and not related to an infection at another site. The presence or absence of infection at another site was determined by review of physician notes, radiology data and pathologic data in the patient's medical record. A hospital-acquired BSI was defined as one that was not present or incubating at the time of admission to the hospital (typically more than 72 hours postadmission). Empiric therapy was defined as the initiation of antimicrobials without the knowledge of the antibiotic susceptibility profile. Definitive therapy consisted of the antibiotic(s) chosen to complete the treatment course once the susceptibility profile was available. Adequate therapy was defined as receipt of at least 2 active agents based on the susceptibility profile of the organism. Cure was defined as no relapse of bacteremia after at least 6 months follow-up in surviving patients.

Clinical Microbiology and Susceptibility Testing

Blood culture specimens were analyzed using the BacT/Alert blood culture system (bioMerieux, Inc, Durham, NC). Positive blood cultures were Gram stained and subcultured to bacterial media according to standard microbiological practices. Cultures demonstrating beaded Gram-positive organisms were stained by both modified and full acid-fast stain and subcultured to buffered charcoal yeast extract agar (BD, Franklin Lakes, NJ) and incubated at 35°C. Once acid-fast growth was present in pure culture on solid media, the isolate was sent for further testing at ARUP Laboratories, Salt Lake City, UT, for partial 16 rRNA gene sequencing. Isolates identified as *M. chelonae/abscessus* by sequencing were separated into species by PCR. Susceptibility testing was performed in accordance with current CLSI methods.[12] The following antimicrobials were tested: amikacin (except *M. chelonae*), tobramycin (*M. chelonae* only), clarithromycin, ciprofloxacin, moxifloxacin, cefoxitin, imipenem, linezolid, minocycline, trimetroprim-sulfamethoxazole, doxycycline and tigecycline (by request only).

RESULTS

Clinical Characteristics

A total of 33 primary RGM BSI occurred over the study period among 32 patients (1 patient had 2 RGM BSI). Among our study cohort of cases, 16 (48.5%) were men, 20 (60.6%) were White and the mean age was 51.2 years (range: 12-88 years). There was an average of 3-4 comorbidities per patient and the most common was malignancy, which occurred in 15 (45.5%) cases. The second most common comorbidity was chronic gastrointestinal pathology, which was present in 9 (27.3%) cases, including inflammatory bowel disease and chronic pancreatitis. Other comorbidities included diabetes, autoimmune disease, chronic kidney disease on hemodialysis, intravenous drug use and sickle cell disease (Table 1).

Among the 33 primary RGM BSI episodes, 26 (78.8 %) patients had received antibiotic therapy within 30 days of the BSI, 13 (39.4 %) received antifungal therapy within 30 days of the RGM BSI, 5 (15.2%) received a blood transfusion, 7 (21.2 %) received total parenteral nutrition, 10 (30.3%) received immunosuppressive therapy other than chemotherapy, 10 (30.3%) received chemotherapy and 5 (15.2%) were on hemodialysis. Most of the RGM BSI, 28 (84.8%), were catheter associated and 9 (27.3%) were hospital acquired. One case was complicated by endocarditis.

Microbiologic Characteristics

M. fortuitum (10 isolates) and *M. mucogenicum* (9 isolates) were the most common species isolated. This was followed by *M. abscessus/chelonae* (6 isolates) and *M. immunogenum* (4 isolates). In all, 2 isolates were not speciated and 2 others were less common species, *M. cosmeticum* and *Mycobacterium goodii*. In all, 2 patients had more than 1 species isolated from blood, 1 with *M. immunogenum* and *M. mucogenicum*, and 1 with *M. mucogenicum* and *M. abscessus. M. immunogenum* was always associated with multiple positive blood cultures and was always hospital acquired. Mean time to positivity of blood culture with a RGM was 4.7 days (range: 2–5 days); mean time to RGM species identification was 29.9 days (range: 11–173 days). A total of 14 (42.4%) patients had multiple positive blood cultures for RGM.

Treatment and Outcomes

Overall, 19 (57.6%) cases had documentation of receiving antimicrobial therapy for their RGM BSI. Average duration of therapy was documented for 14 of these and was 47.6 days (range: 10–180 days). Of the 28 cases with catheter-associated RGM BSI, 20 (71.4%) had their catheter removed as part of the treatment