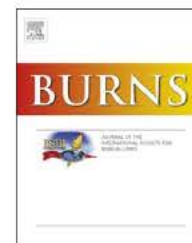


available at www.sciencedirect.comjournal homepage: www.elsevier.com/locate/burns

Case report

Nontuberculous mycobacterium infection in a burn ICU patient[☆]

Joseph M. Boyer^a, Peter J. Blatz^a, Kevin S. Akers^a, Jason F. Okulicz^a, Kevin K. Chung^b, Evan M. Renz^{b,c}, Duane R. Hospenthal^{a,c}, Clinton K. Murray^{a,c,*}

^a San Antonio Military Medical Center (SAMMC), United States

^b US Army Institute of Surgical Research (USAISR), United States

^c Uniformed Services University of the Health Sciences, United States

ARTICLE INFO

Article history:

Accepted 12 May 2010

1. Introduction

Infection is a leading cause of mortality in burn patients, typically due to bacterial pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*, less commonly fungi, and possibly viruses [1–4]. In non burn patients with underlying pulmonary or cutaneous disease, nontuberculous mycobacteria (NTM) have become an increasingly recognized cause of infection, especially in patients who are immunocompromised [5]. Patients with severe burns might have higher rates of NTM infections due to inherent risks associated with the burn injury: compromised skin integrity, immunocompromised state, inhalation injury, and frequent use of indwelling vascular catheters. To date there have been no reports describing the incidence of mycobacterial infections in burn patients. We describe a case of *Mycobacterium abscessus* bacteremia and clinical record review of patients admitted to the US Department of Defense burn center with severe burns for other evidence of NTM infections from 1 May 2000 to 30 April 2009.

2. Case report

A 52 year old male patient suffered a 65% total body surface area (TBSA) burn from an explosive device in Iraq. At the time of injury, he underwent an emergent cricothyroidotomy, was intubated, and transferred to Landstuhl Regional Medical Center (LRMC) in Germany. The patient was stabilized at LRMC and subsequently evacuated to the US Army Institute of Surgical Research (USAISR) burn intensive care unit at Brooke Army Medical Center (BAMC) for definitive care.

The patient had no significant past medical or surgical history, and was not taking any medications at the time of his injury. The patient underwent initial excision and grafting with available autograft, temporary coverage with homograft and subsequent serial autograft placement. Topical wound dressings utilized 5% sulfamylon soaks initially as well as silver nylon dressings following autograft placement; approximately 10% TBSA remained open following grafting operations. The patient's hospital course was complicated with multiple episodes of sepsis including sepsis with multidrug resistant *P. aeruginosa* and *Enterobacter cloacae* which required repeated courses of broad spectrum antibiotics including colistimethate, vancomycin, and imipenem. Central lines were changed to a new site at least every 7 days or earlier for suspected line related infection. Standard aerobic cultures of blood obtained on hospital days (HD) 72 and 79 produced growth of acid fast bacilli (AFB). Prior to this first recovery of

[☆] The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or reflecting the views of the Department of the Army, Department of the Air Force, Department of Defense or the US Government. This work was prepared as part of their official duties and, as such, there is no copyright to be transferred.

* Corresponding author at: Infectious Disease Service, San Antonio Military Medical Center, Brooke Army Medical Center, 3851 Roger Brooke Drive, Fort Sam Houston, TX 78234, United States. Tel.: +1 210 916 5554; fax: +1 210 916 5900.

E mail address: Clinton.Murray@amedd.army.mil (C.K. Murray).

0305 4179/\$36.00. Published by Elsevier Ltd and ISBI

doi:10.1016/j.burns.2010.05.014

Report Documentation Page

Form Approved
OMB No. 0704-0188

Public reporting burden for the collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to a penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.

1. REPORT DATE 01 NOV 2010		2. REPORT TYPE N/A		3. DATES COVERED -	
4. TITLE AND SUBTITLE Nontuberculous mycobacterium infection in a burn ICU patient				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Boyer J. M., Blatz P. J., Akers K. S., Okulicz J. F., Chung K. K., Renz E. M., Hospenthal D. R., Murray C. K.,				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX				8. PERFORMING ORGANIZATION REPORT NUMBER	
				10. SPONSOR/MONITOR'S ACRONYM(S)	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release, distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT					
15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 4	19a. NAME OF RESPONSIBLE PERSON
a REPORT unclassified	b ABSTRACT unclassified	c THIS PAGE unclassified			

AFB from blood culture obtained on HD 72, a total of 9 cutaneous tissue specimens performed on HD 2, 6 and 14 were negative for AFB by specific staining and culture. Multiple tracheal aspirates and bronchial alveolar lavages (BAL) specimens grew various bacteria but did not reveal evidence of AFB. On HD 87, preliminary laboratory testing from one of the blood AFB isolates revealed a suspected rapid growing mycobacterium and empiric antimicrobial therapy with tobramycin and azithromycin was added to his current imipenem. Tracheal aspirates cultured on HD 89 and 90 also produced AFB. Unfortunately, the patient succumbed to his injuries and complications on HD 100. The blood cultures from HD 72 and 79 as well as tracheal aspirate cultures from HD 89 and 90 grew *M. abscessus*, which was confirmed by biochemical and mycolic acid analysis performed at National Jewish Health, Denver, CO. Antimicrobial susceptibility testing of the isolate revealed susceptibility to amikacin and clarithromycin, but resistance to ciprofloxacin, linezolid, and tobramycin. The imipenem MIC was 8 µg/mL (no interpretive criteria available). Autopsy revealed diffuse interstitial pulmonary fibrosis as well as extensive pulmonary hemorrhage, but no organisms were seen on microscopy. Integumentary pathology revealed intraepidermal gram positive and gram negative bacterial colonies focally invading the dermis, with multiple organisms cultured from the burn wounds including *Stenotrophomonas maltophilia*, *P. aeruginosa*, *S. aureus*, *Micrococcus* sp., and Group B *Streptococcus*. Mycobacteria did not grow from post mortem cultures. AFB staining was not performed on specimens obtained at autopsy; however, standard stains of all autopsy samples did not identify any pathogen consistent with a mycobacterial species.

3. Review of the incidence of mycobacterial infections

After obtaining institutional review board approval, we performed a retrospective electronic records review of patients admitted to the USAISR burn center for treatment of thermal burns for those demonstrating culture growth of mycobacteria; patients without thermal burns were excluded from the study. The standard approach to care of burn patients at our institution includes early burn wound excision and grafting, early bronchoscopy for suspected inhalation injury and aggressive infection control interventions [6].

Using electronic medical records, culture results for the period of 1 May 2000 through 30 April 2009 were screened for *Mycobacterium* species. Culture sites included sputum, BAL fluid, blood, urine, skin, and cerebrospinal fluid. Demographic data, comorbid conditions and potential risk factors were characterized for patients with culture growth of mycobacteria. To differentiate between colonization and infection, the clinical and microbiologic criteria set forth by the American Thoracic Society (ATS) and Infectious Disease Society of America (IDSA) were used [5]. Clinical criteria include pulmonary symptoms, nodular or cavitary opacities on chest radiograph or multifocal bronchiectasis seen on high resolution computed tomography and appropriate exclusion of other diagnoses [5]. Microbiologic criteria include either culture results from at least two expectorated samples, culture from at

least one BAL, or lung histopathology demonstrating mycobacterial organisms and NTM growth in culture. Criteria for disseminated disease included growth from blood or bone marrow cultures [5].

During the study period, 2428 patients with thermal burns were admitted to the USAISR burn center. The median TBSA burn was 9% (range 0.1–99%), median age was 31 (range 15–100) and the median injury severity score (ISS) was 4 (range 0–75). The majority of the patients were male (2051, 84%). Inhalational injury was seen in 287 patients (11.8%).

From this cohort, only 8 patients (including our case report), with a total of 14 cultures, had growth of NTMs (Table 1). Of these, 7 were male. The median TBSA burn was 24.8% (range 4.5–72.5%) with a median age of 50 years (range 18–79). Inhalational injury was diagnosed in 3 patients and only 2 patients sustained burns during military operations. Nontuberculous mycobacteria were isolated from the sputa of 7 patients, one patient had NTM recovered in gastric aspirate culture and one patient had NTM isolated from blood culture. The most common NTM were *Mycobacterium avium* complex (MAC) and *Mycobacterium simiae*: isolated in 5 and 4 patients, respectively. *M. goodii*, *M. fortuitum*, and *M. abscessus* were each isolated in single patients. Of the 8 total patients with NTM isolates, 5 patients had a documented history of active tobacco use at the time of admission. Two patients reported active recreational drug use (1 heroin, 1 marijuana) and two patients had a history of chronic obstructive pulmonary disease (COPD). One patient reported a history of treated pulmonary tuberculosis. With exception to our case patient, no other patient met ATS/IDSA criteria for NTM infection.

4. Discussion

Infections are the primary cause of mortality among burn patients after recovery from the initial burn injury. Although patients with severe burns have risk factors that may increase their risk of developing NTM infections, our 9 year review of 2428 admissions to a single burn unit revealed only 1 patient with definite NTM infection. To our knowledge, this is the first reported case of NTM infection in a burn patient.

Mycobacteria are gram positive, acid fast bacteria, which can cause a wide variety of clinical syndromes including pulmonary disease, skin and soft tissue infection, and rarely bacteremia. *M. tuberculosis*, *M. kansasii*, *M. avium* complex and *M. chelonae* are typically associated with pulmonary disease while *M. marinum*, *M. ulcerans* and the rapidly growing mycobacteria (*M. fortuitum*, *M. abscessus*, and *M. chelonae*) are typically associated with skin and soft tissue infections. Rapidly growing mycobacteria are of great interest as these NTM are a group of environmental organisms which can cause disease in humans. These organisms commonly cause localized skin and soft tissue infections [7], intravascular catheter infections [8], disseminated infection, osteomyelitis, peritonitis [9,10], endocarditis [11], and bacteremia [12]. Although infections with this group of organisms may occur sporadically, outbreaks have also been reported. Nosocomial outbreaks due to *M. abscessus* are most commonly described; the majority of which have been traced to contaminated

Table 1 – Characteristics of burn patients with culture growth of nontuberculous mycobacteria from 1 May 2000 through 30 April 2009.

Case	Age/gender	% TBSA	Inhalational injury	Comorbid conditions	Specimen cultured	Species recovered	Number of positive cultures	Pulmonary imaging	Met NTM infection criteria
1 ^{a,b}	52/M	65	Yes	None	Blood Tracheal aspirate	<i>M. abscessus</i>	3	Multifocal airspace consolidation with ground glass opacities	Yes
2	52/M	25	Yes	Tobacco and ETOH use	Sputum	<i>M. simiae</i> MAC	1	Mild pulmonary edema, right pleural effusion	No
3	48/M	25	No	COPD, ETOH abuse, Cirrhosis, Tobacco use	Sputum	<i>M. fortuitum</i>	1	Bibasilar atelectasis	No
4	29/M	5	No	Heroin use, HBV, HCV	Sputum	<i>M. simiae</i> MAC	1	No abnormalities	No
5	18/M	30	No	Marijuana, Tobacco use	Sputum	<i>M. simiae</i>	1	No abnormalities	No
6	56/F	10	No	DM2, MTB (treated), COPD, Tobacco use	BAL Sputum	<i>M. simiae</i> MAC	1	Fibrotic process, scarring, cavitation, atelectasis,	No
7	79/M	24	No	Unknown	Sputum	<i>M. goodii</i> MAC	1	Increased interstitial markings	No
8*	29/M	78	Yes	None	Gastric aspirate	MAC	1	No abnormalities	No

TBSA total body surface area burn; BAL bronchoalveolar lavage; COPD chronic obstructive pulmonary disease; NTM nontuberculous mycobacterium; MAC *Mycobacterium avium* complex; ETOH alcohol; DM2 diabetes mellitus type II; HBV hepatitis B virus; HCV hepatitis C virus; MTB *Mycobacterium tuberculosis*

^a Combat related injury
^b Current case

liquids including water and sterile solutions [13]. Environmental contamination has also been associated with a small cluster of NTM where the origin of the organism was attributed to dust generated from building construction [12]. Although our patient did have multiple risk factors for a nosocomial source, it is unlikely that a contaminant outbreak occurred at our facility as no other cases were identified either before or after our patient was hospitalized.

Although severely burned patients may be at increased risk for NTM infection because of their injury, these infections were not common in thermal burn patients in our facility. Limitations of the study include the lack of routine screening for mycobacterial infections. However, traditional culture and histological techniques should have enabled us to detect either outbreaks with NTM or ongoing infections. Overall, infections caused by NTM appear to be rare in burn patients and routine screening or testing for mycobacteria is not required. However, infections with NTM should remain in the differential diagnosis for patients failing to clinically improve despite appropriate identification and treatment of typical bacterial and fungal pathogens associated with burns.

REFERENCES

- Keen III EF, Robinson BJ, Hospenthal DR, Aldous WK, Wolf SE, Chung KK, et al. Incidence and bacteriology of burn infections at a military burn center. *Burns* 2010;36:461-8.
- Keen III EF, Robinson BJ, Hospenthal DR, Aldous WK, Wolf SE, Chung KK, et al. Prevalence of multidrug resistant organisms recovered at a military burn center. *Burns* 2010. doi: 10.1016/j.burns.2009.10.013.
- Horvath EE, Vaughan GM, Chung KK, Hospenthal DR, Wade CE, Holcomb JB, et al. Fungal wound infection (not colonization) is independently associated with mortality in burn patients. *Ann Surg* 2007;245:978-85.
- D'Avignon LC, Hogan BK, Murray CK, Loo FL, Hospenthal DR, Cancio LC, et al. Contribution of bacterial and viral infections to attributable mortality in patients with severe burns: an autopsy series. *Burns* 2010. doi: 10.1016/j.burns.2009.11.007.
- Griffith DE, Aksmit T, Brown Elliot BA, Catanzaro A, Daley C, Gordin F, et al. Diagnosis, treatment and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med* 2007;175:367-416.
- Regules JA, Glasser JS, Wolf SE, Hospenthal DR, Murray CK. Endocarditis in burn patients: clinical and diagnostic considerations. *Burns* 2008;34:610-6.
- Wallace Jr RJ, Brown BA, Onyi GO. Skin, soft tissue and bone infections due to *Mycobacterium chelonae*: importance of prior corticosteroid therapy, frequency of disseminated infections and resistance to oral antimicrobials other than clarithromycin. *J Infect Dis* 1992;166:405-12.
- Ward MS, Lam KV, Cannell PK, Herrmann ARP. Mycobacterial central venous catheter tunnel infection: a difficult problem. *Bone Marrow Transpl* 1999;24:325-9.
- Siu YP, Leung KT, Tong MKH, Lee MKF. *Mycobacterium chelonae* exit site infection in a patient on peritoneal dialysis. *Clin Nephrol* 2005;63:321-4.
- Rho M, Bia F, Brewster U. Nontuberculous mycobacterial peritonitis in peritoneal dialysis patients. *Semin Dial* 2007;20:271-6.

-
- [11] Galil K, Turner R, Glatter K, Bariam T. Disseminated *Mycobacterium chelonae* infection resulting in endocarditis. Clin Infect Dis 1996;23:1322-3.
- [12] McCracken D, Flanagan P, Hill D, Hosein I. Cluster of cases of *Mycobacterium chelonae* bacteremia. Eur J Clin Microbiol Infect Dis 2000;19:43-6.
- [13] Bolan G, Reingold AL, Carson LA, Silcox VA, Woodley CA, Hayes PS, et al. Infections with *Mycobacterium chelonae* in patients receiving dialysis and using processed hemodialyzers. J Infect Dis 1985;152:1013-9.