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Bacteremia caused by the novel species *Mycobacterium canariasense*

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Several rapidly growing mycobacteria (RGM) species have been described as etiologic agents of bacteremia in cancer patients with long-term central devices [1–5]. We report here a series of cases of bacteremia caused by the novel species of RGM named *M. canariasense* that were identified through a retrospective review of all cases in which at least one blood culture was positive for *M. canariasense* at a tertiary care hospital.

Blood cultures performed using Bactec Vial–Aerobic Cultures (Becton–Dickinson Microbiology Systems, Sparks, MD, USA) were incubated for a maximum of 15 days. Species assignment was done according to phenotypic and genotypic characteristics [6]. The agar disk elution method [7] was used to determine the susceptibility of the isolates to amikacin, tobramycin, imipenem, doxycycline, cefoxitin, and ciprofloxacin, and the *E* test (AB Biodisk, Solna, Sweden) [1] was used to test susceptibility to clarithromycin.

The medical records of all patients from whom *M. canariasense* was isolated were examined, and clinical and microbiological data were obtained from their medical

charts. A clinically significant case of bacteremia was defined when the following criteria were met: (a) presence of clinical symptoms such as fever (oral temperature of $>38^{\circ}\text{C}$), chills or hypotension of acute onset at the time the blood specimens were taken; and (b) absence of another infectious cause that could explain the clinical symptoms. Definite catheter-related bacteremia was defined using the following criteria outlined previously by Raad et al. [2]: (a) clinical (or autopsy) and microbiological data disclosed no source of bacteremia other than the catheter; and (b) the same *Mycobacterium* species was recovered from the catheter tip (i.e., >15 cfu/catheter segment was recovered using the roll-plate semiquantitative culture technique). Probable catheter-related bacteremia was diagnosed if only the first criterion was fulfilled, and relapse was diagnosed when the same *Mycobacterium* species was isolated and clinical symptoms recurred after the end of therapy.

To analyze concordance between the clinical classifications made according to the above criteria and the outcome of the clinical evaluation performed by the patient's doctor (as reflected in the clinical chart), the Kappa index was measured; $K>0.75$ was considered excellent.

The review identified 17 cases in which *M. canariasense* was isolated from blood between January 2000 and September 2002; in ten of these cases more than one blood culture was positive. Blood specimens were obtained via the indwelling catheters in all cases in which the drawing procedure was specified. Mycobacteria grew after the standard incubation period of 5 days in the blood culture bottles of 11 patients, and they were not isolated from any clinical specimens other than the blood or the catheter tip. All strains showed susceptibility to all antibiotics tested.

M. canariasense was considered the etiologic agent of bacteremia in 12 of the 17 cases. The main characteristics of the patients are shown in Table 1. Eleven patients had received chemotherapy previously, eight had received transfusions, six were neutropenic, three had undergone bone marrow transplantation, three had received steroid therapy, and two had received parenteral nutrition. None of the patients had clinical evidence of tissue invasion. All 12

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Table 1 Characteristics of patients with clinically significant blood isolates of *M. canariasense*

Case	Age (year)/sex	Underlying disease	Central catheter	Antimycobacterial treatment	Antibiotic therapy (duration in days)	Catheter removal	Catheter tip culture	Outcome
1	43/M	Multiple myeloma	Port-A-Cath	No	CAZ+VAN+AMK (10)	Yes	ND	Favorable
2	40/F	Leukemia	Hickman	No	CAZ+VAN+AMK (5)	Yes	Negative	Favorable
3	58/M	Leukemia	Hickman	Yes	CLR-AMK+FOX-AMK+IMP (21)	Yes	ND	Favorable
4	59/M	Multiple myeloma	Hickman	Yes	AMK+IMP (12)	Yes	ND	Favorable
5	57/F	Leukemia	Hickman	Yes	IMP (10)	Yes	Negative	Favorable
6	40/M	Leukemia	Hickman	Yes	CLR+CIP (15)	No ^a	<i>M. canariasense</i>	Relapse
7	59/F	Leukemia	Hickman	No	CEF+TEI (8)	Yes	Negative	Favorable
8	49/F	Lymphoma	Port-A-Cath	No	CAZ+AMK (5)	No	–	Favorable
9	50/F	Leukemia	Hickman	Yes	CIP+AMK (10)	Yes	ND	Favorable
10	37/M	Leukemia	Hickman	Yes	CIP+AMK (10)	Yes	ND	Favorable
11	63/F	Lymphoma	Hickman	Yes	CIP+AMK (13)	No	–	Death
12	48/F	Solid tumor	Port-A-Cath	Yes	CLR (14)	No	–	Relapse

M male, *F* female, *CAZ* ceftazidime, *VAN* vancomycin, *AMK* amikacin, *CLR* clarithromycin, *FOX* cefoxitin, *IMP* imipenem, *CIP* ciprofloxacin, *CEF* ceftriaxone, *TEI* teicoplanin

^aCatheter was removed after relapse of the infection with a subsequent favorable outcome

patients had received parenteral antibiotic therapy for 5–21 days and the catheter was additionally removed from eight of them. In two patients whose catheters remained in place, the infection relapsed several months later, and the central device was finally removed from one of the two. In four cases, the catheter tips were cultured. Definite catheter-related bacteremia was found in one case and another patient had signs of infection at the catheter insertion site.

Concordance between the results of clinical evaluations according to the criteria mentioned above and those made by each patient's doctor was excellent ($K=0.87$).

Regarding the outcome of the infections, one patient died and the rest, including those who relapsed, recovered. The patient who died had become afebrile with antibiotic therapy and death was attributed to her underlying disease: an autopsy was not done. When the first episodes of bacteremia were analyzed, we found that the disease did not resolve more frequently in patients treated with antimycobacterial therapy guided by the susceptibility test results than in those who received empiric antibiotic treatment; however, removal of the catheter did predict a better outcome of the infection ($p<0.05$).

RGM are environmental organisms that can behave as contaminants as well as pathogens; consequently, we used clinical and microbiological criteria to define the significance of the blood isolates, and *M. canariasense* was considered to be the cause of most of the febrile syndromes. Due to the retrospective character of the review, we were unable to determine if a common source of infection existed. Blood vials did not undergo any manipulation in the laboratory

before they became positive and there was no temporal clustering of isolates. Since mycobacteria grew within the standard incubation time period in only six of the 17 cases, we recommend an extended incubation period of 10 days for blood vials and, as indicated previously by Raad et al. [2], for catheter tips from hematology patients.

Just one case was diagnosed as definite catheter-related bacteremia. However, we consider the catheter to be the most probable source of infection in the other cases as well for the following reasons: (a) all patients had a central catheter in place at the time of the infection; (b) no other source of bacteremia was found; (c) catheter removal predicted a better outcome of infection; and (d) lack of inflammation around the catheter (seen in only one case) does not preclude infection of the catheter [3].

Appropriate treatment consists of antibiotic therapy and catheter removal. A regimen consisting of amikacin plus cefoxitin is the initial choice for intravenous therapy [2, 8], but the optimal duration is unknown. Two of our patients became afebrile (one with additional catheter removal) despite receiving a short course of antibiotics, which supports the previously reported finding of Graham et al. [9]. Antimycobacterial therapy guided by in vitro susceptibility results [8] did not improve the outcome in our cases, probably because the prescribed empiric therapy included, in the majority of cases, amikacin and vancomycin, which have been reported as useful drugs to treat RGM infections [5, 10]. Failure to remove the catheter can lead to relapse of the infection, as occurred in two of our patients. The outcome of catheter-related mycobacteremia has been reported to be

favorable, even in patients whose infection relapsed but who later recovered after catheter removal [2]; this is supported by the cases in our series. These cases demonstrate that *M. canariasense* should be considered as a new potential cause of catheter-related bacteremia in patients with cancer.

References

1. Brown-Elliott BA, Wallace RJ Jr (2002) Clinical and taxonomic status of pathogenic nonpigmented or late-pigmenting rapidly growing mycobacteria. *Clin Microbiol Rev* 15:716–746
2. Raad II, Vartivarian S, Khan A, Bodey GP (1991) Catheter-related infections caused by the *Mycobacterium fortuitum* complex: 15 cases and review. *Rev Infect Dis* 13:1120–1125
3. Hoy JF, Rolston KVI, Hopfer RL, Bodey GP (1987) *Mycobacterium fortuitum* bacteremia in patients with cancer and long-term venous catheters. *Am J Med* 83:213–217
4. Roy V, Weisdorf D (1997) Mycobacterial infections following bone marrow transplantation: a 20-year retrospective review. *Bone Marrow Transplant* 19:467–470
5. McWhinney PHM, Yates M, Prentice HG, Thrussell M, Gillespie SH, Kibbler CC (1992) Infection caused by *Mycobacterium chelonae*: a diagnostic and therapeutic problem in the neutropenic patient. *Clin Infect Dis* 14:1208–1212
6. Jimenez MS, Campos-Herrero MI, Garcia D, Luquin M, Herrera L, Garcia MJ (2004) *Mycobacterium canariasense* sp. nov. *Int J Syst Evol Microbiol* 54:1729–1734
7. Brown BA, Swenson JM, Wallace Jr RJ (1992) Agar disk elution test for rapidly growing mycobacteria. In: Isenberg HD (ed), *Clinical microbiology procedures handbook*. American Society of Microbiology, Washington, District of Columbia, pp 5.10.1–5.10.11
8. Wallace RJ Jr, Swenson JM, Silcox VA, Bullen MG (1985) Treatment of non-pulmonary infections due to *Mycobacterium fortuitum* and *Mycobacterium chelonae* on the basis of in vitro susceptibilities. *J Infect Dis* 152:500–514
9. Graham JC, Tweddle DA, Jenkins DR, Pollitt C, Pedler SJ (1998) Non-tuberculous mycobacterial infection in children with cancer. *Eur J Clin Microbiol Infect Dis* 17:394–397
10. Jadeja L, Bolivar R, Wallace RJ Jr, Silcox VA, Bodey GP (1983) Bacteremia caused by a previously unidentified species of rapidly growing *Mycobacterium* successfully treated with vancomycin. *Ann Intern Med* 99:475–476