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Vancomycin-Resistant *Aureobacterium* Species Cellulitis and Bacteremia in a Patient with Acute Myelogenous Leukemia

FREDERICK S. NOLTE,[1]* KATHRYN E. ARNOLD,[2] HEMELLA SWEAT,[1] ELLIOTT F. WINTON,[2] AND GUIDO FUNKE[3]

Departments of Pathology and Laboratory Medicine[1] and Medicine,[2] Emory University School of Medicine, Atlanta, Georgia, and Department of Medical Microbiology, University of Zürich, CH-8028 Zürich, Switzerland[3]

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A 39-year-old male with acute myelogenous leukemia and concomitant porphyria cutanea tarda was admitted to the hospital for consolidation chemotherapy of his leukemia. During his hospitalization, he developed cellulitis of the left hand and persistent bacteremia with a yellow-pigmented, nonfermenting coryneform bacterium that was identified as *Aureobacterium* sp. The portal of entry for the *Aureobacterium* infection was probably through the skin lesions due to porphyria cutanea tarda. The infection developed while the patient was receiving vancomycin prophylaxis, and the vancomycin MIC for the isolate was 32 μg/ml.

The genus *Aureobacterium* was first described by Collins et al. (3), who reclassified members of six taxa that were previously thought to belong to the genera *Microbacterium*, *Arthrobacter*, *Corynebacterium*, and *Curtobacterium* as *Aureobacterium* spp. This group of catalase-positive, yellow-pigmented, and irregularly shaped, gram-positive rods with oxidative metabolism have been isolated from a wide variety of environmental sources, including plants, milk, dairy products, soil, sewage, and insects (3, 4). Funke et al. (4) recently reported the first isolations of *Aureobacterium* spp. from clinical specimens. The previously described clinical isolates of *Aureobacterium* spp. have all been susceptible to vancomycin, with MICs ranging from <0.125 to 4 μg/ml.

In this report, we describe a case of cellulitis and fatal septicemia due to a *Aureobacterium* sp. in a patient with acute myelogenous leukemia and concomitant porphyria cutanea tarda (PCT). The isolate displayed both in vitro and in vivo resistance to vancomycin.

CASE REPORT

A 39-year-old white male with acute myelogenous leukemia was admitted to the hospital on 24 April 1995 for consolidation chemotherapy. Past medical history was significant for burns to the hands and feet secondary to a motor vehicle accident 20 years prior to admission. In addition, the patient had uncomplicated dental extractions in March 1995. The social history was significant for current alcohol and tobacco abuse and intravenous drug abuse in the remote past. His occupation was variously listed as odd jobs, floor buffer, and farm worker. The patient tested negative for antibody to human immunodeficiency virus type 1.

On admission to the hospital, the patient had no complaints and normal chest, cardiac, and abdominal examinations. Multiple cuts and crusted lesions on the hands from "hard work" trauma and scattered bullous lesions on the dorsum of the hands were noted. Chemotherapy with etoposide, mitoxantrone, and cytarabine was begun, and the patient was given oral norfloxacin, fluconazole, and acyclovir prophylactically per the leukemia protocol.

* Corresponding author. Mailing address: Clinical Laboratories, Emory University Hospital, Room F145, 1364 Clifton Rd., N.E. Atlanta, GA 30322. Phone: (404) 712-7297. Fax: (404) 712-5567. Electronic mail address: fnolte@emory.edu.

On hospital day 3, biopsies were taken from the right hand at the edge of the bullous lesions. The biopsies revealed subepidermal bullae with festooning of dermal papillae but no thickening of the vessel walls. There was a paucicellular inflammatory infiltrate consisting predominantly of eosinophils, and no organisms were seen. These findings were suggestive but not diagnostic of PCT. The diagnosis of PCT was supported by elevated urinary porphyrins, by immunofluorescent antibody studies of the biopsies, and by hypertrichosis at the temples and malar eminences.

The patient became neutropenic (absolute neutrophil count, $<500/mm^3$) secondary to chemotherapy on hospital day 10, and vancomycin (500 mg every 24 h) was added to the prophylactic antibiotic regimen. The patient remained neutropenic for the rest of his hospitalization.

On day 17, the patient became drowsy and developed a fever of 100.4°F (38°C). Aztreonam was added to the antibiotic coverage. A yellow-pigmented, diphtheroid-like, gram-positive rod, subsequently identified as *Aureobacterium* species, was isolated from one of two blood cultures drawn on this day. Initial growth was detected after 31.5 h of incubation. Broth microdilution MICs were determined with MicroScan (Dade International, West Sacramento, Calif.) panels supplemented with 5% lysed horse blood and were as follows: penicillin, 1 μg/ml; cephalothin, 16 μg/ml; ceftriaxone, 16 μg/ml; imipenem, 4 μg/ml; vancomycin, >16 μg/ml; chloramphenicol, >16 μg/ml; erythromycin, >4 μg/ml; clindamycin, >2 μg/ml; tetracycline, 4 μg/ml; rifampin, <1 mg/ml; trimethoprim-sulfamethoxazole, <2 (trimethoprim) and <38 (sulfamethoxazole) μg/ml; gentamicin, 6 μg/ml; amikacin, >32 μg/ml; and ciprofloxacin, >2 μg/ml. These results were available on day 20.

On day 18, the patient's temperature spiked to 101.8°F (38.8°C), and there were concerns about possible cellulitis of the left index finger and a Hickman catheter infection. Vancomycin was instilled into the catheter when it was not in use. Two more blood cultures drawn from the Hickman catheter on days 18 and 19 were found to contain the same gram-positive rod. The patient remained bacteremic with the gram-positive rod for the next 5 days (five additional positive blood cultures). In addition to the gram-positive rod, a coagulase-negative staphylococcus was isolated from blood cultures drawn on days 19 to 21, and a vancomycin-resistant *Enterococcus faecium* strain was isolated from cultures drawn on days 22 to 24.

The cellulitis of the left hand had worsened (Fig. 1), and

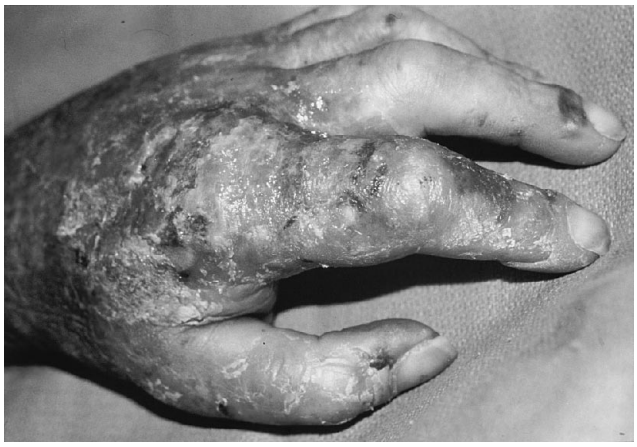

FIG. 1. Cellulitis of the left hand due to *Aureobacterium* sp.

amikacin and erythromycin were added to the antibiotic coverage on day 21. The next day, skin biopsies of the left index finger and the dorsum of the left hand were taken (biopsies that documented PCT were taken from the right hand). The biopsies revealed a massive replacement of the subcutaneous adipose tissue with irregularly shaped gram-positive bacilli. A gram-positive rod identical to the blood culture isolates was recovered from the biopsy specimens.

On day 22, the patient was mildly confused and appeared septic, with a temperature of 103.8°F (39.9°C) and a new II/VI systolic murmur. The Hickman catheter was removed, and leukocyte transfusions were ordered. After consultation with the Infectious Diseases team, erythromycin and aztreonam were discontinued and imipenem and rifampin were added to the antibiotic therapy.

The patient was transferred to the intensive care unit on day 24. The chest X-ray showed fluffy perihilar infiltrates, and the patient appeared cyanotic. The left hand was debrided and treated with local silver sulfadiazine and elevation. The patient developed a leukoagglutination reaction after the third leukocyte transfusion with cyanosis and dyspnea. He was intubated briefly and then extubated according to his wishes. The patient expired on hospital day 26. No autopsy was performed.

MATERIALS AND METHODS

Identification tests. Traditional biochemical tests were done as previously described (6). Enzyme activities were determined with the API ZYM system (api bioMerieux SA, Marcy l'Etoile, France). Oxidation of sugars was tested in cystine trypticase agar medium (Becton Dickinson, Sparks, Md.). Assimilation of carbohydrates was tested with the AUX medium in the API 50CH gallery (api bioMerieux).

Cellular fatty acid profiles were determined with the MIDI system (Microbial ID, Inc., Newark, Del.). Peptidoglycan analysis was done, as previously described, with thin-layer chromatographic techniques (8).

Antibiotic susceptibility testing. Reference broth microdilution MICs for the isolate were determined at the Centers for Disease Control and Prevention, Atlanta, Ga., with cation-supplemented Mueller-Hinton broth with 5% lysed horse blood. The isolate was analyzed for the *vanA*, *vanB*, and *vanC* resistance genes by PCR as previously described (1).

RESULTS

The isolate was catalase positive, oxidase negative, nonmotile, and did not reduce nitrate. It hydrolyzed esculin, gelatin, and casein but not urea. The isolate possessed valine arylamidase, cystine arylamidase, and α-fucosidase enzymatic activities. It oxidized glucose and maltose but not sucrose, mannitol, and xylose after 48 h and assimilated D-arabinose and L-fucose but not β-methylxyloside after 120 h.

Anteisoheptadecanoic acid ($C_{17:0ai}$) (44% of total cellular fatty acids [CFA]), anteisopentadecanoic acid ($C_{15:0ai}$) (26% of total CFA), and isohexadecanoic acid ($C_{16:0i}$) (21% of total CFA) were the predominant cellular fatty acids. Ornithine was detected as the diamino acid of the peptidoglycan. The pattern of the partial peptidoglycan hydrolysate, in particular the presence of both L- and D-ornithine, has only been described for *Aureobacterium* spp. (5, 9).

The biochemical characteristics, CFA profile, and peptidoglycan analysis identified the isolate as *Aureobacterium* sp. The key characteristics differentiating the yellow-pigmented coryneform bacteria and those of our isolate are given in Table 1. The isolate could not be identified to the species level since it did not fit any of the biochemical profiles for the 13 described *Aureobacterium* species (4, 9).

The reference MICs were as follows: penicillin, 4.0 μg/ml; ampicillin, 2.0 μg/ml; vancomycin, 32.0 μg/ml; teicoplanin, 0.5 μg/ml; tetracycline, 16.0 μg/ml; ciprofloxacin, 4.0 μg/ml; erythromycin, 4.0 μg/ml; clindamycin, 8.0 μg/ml; imipenem, 4.0 μg/ml; and trimethoprim-sulfamethoxazole 1.0 (trimethoprim) and 19.0 (sulfamethoxazole) μg/ml. It did not contain *vanA*, *vanB*, or *vanC* resistance genes.

DISCUSSION

Funke et al. (4) first reported the isolation of *Aureobacterium* spp. from clinical specimens. They found that 7 of 11 isolates referred to their laboratory with initial identification of "*Corynebacterium aquaticum*" were, in fact, *Aureobacterium* spp. The sources included blood, cerebrospinal fluid, wound drainage, peritoneal fluid, abscess, and soft tissue. This is the first well-documented case report of an *Aureobacterium* infection.

The group of catalase-positive, yellow-pigmented, irregularly shaped, gram-positive rods that may be isolated from clinical specimens include *Microbacterium*, *Oerskovia*, *Cellulomonas*, *Brevibacterium*, "*Corynebacterium aquaticum*," and *Aureobacterium* isolates (2). The latter three genera contain strains with only oxidative metabolism. Our isolate was placed in the genus *Aureobacterium* by traditional biochemical tests and chemotaxonomic methods (4).

A major limitation of identification of yellow-pigmented, gram-positive rods is that most species descriptions are based on very few strains. The biochemical profile of our isolate did not fit those of any of the 13 presently established *Aureobacterium* spp. (4, 9). Although it is likely that our isolate represents a new *Aureobacterium* species, quantitative DNA-DNA hybridization studies or 16S rRNA gene sequence analysis would be required to resolve this issue. These studies are in progress and will be the subject of a later report.

This is also the first report of a vancomycin-resistant *Aureobacterium* sp. The cellulitis and bacteremia developed in the face of vancomycin prophylaxis, and the MIC of vancomycin for the isolate was 32 μg/ml. Although the genetic basis of vancomycin resistance is not known, the isolate did not possess *vanA*, *vanB*, or *vanC* resistance genes. Decreased susceptibility to vancomycin has been reported for other gram-positive rods, including *Lactobacillus* spp., *Erysipelothrix rhusiopathiae*, and "*C. aquaticum*" (4, 7). Since vancomycin resistance does not appear to be inherent to *Aureobacterium* spp., it is likely that resistance was induced in or acquired by our strain.

The probable portal of entry of the *Aureobacterium* isolate in our patient was through the multiple bullous skin lesions on his hands, which were due to PCT. PCT is characterized by mechanical fragility and blistering of light-exposed skin. Trivial trauma to the skin leads to formation of vesicles that rupture and form open sores. Most patients with PCT have a history of

TABLE 1. Characteristics differentiating yellow-pigmented coryneform bacteria and characteristics of the strain reported

Characteristic	Result for:							
	Aureobacterium sp.	"*Corynebacterium aquaticum*"	*Brevibacterium* sp.	*Microbacterium* sp.	*Cellulomonas* sp.	*Oerskovia* sp.	*Exiguobacterium* sp.	Our strain
Cell wall diamino acid[a]	Orn	DAB	*m*-DAP	Lys	Orn	Lys	Lys	Orn
Major CFA[b]	15:0*ai* 17:0*ai* 16:0*i*	17:0*ai* 15:0*ai* 16:0*i*	15:0*ai* 17:0*ai* 15:0*i*	15:0*ai* 17:0*ai* 16:0*i*	15:0*ai* 16:0	15:0*ai* 15:0*i* 17:0*ai*	17:0*i* 15:0*i* 16:0	17:0*ai* 15:0*ai* 16:0*i*
Motility	V[c]	+	−	V	V	+	+	−
Nitrate reduction	V	V	V	V	+	+	V	−
Hydrolysis of:								
Urea	V	−	−	−	−	−	−	−
Esculin	V	V	−	+	+	+	+	+
Gelatin	+	−	+	V	+	+	V	+
Casein	V	−	+	V	−	+	+	+
Type of metabolism[d]	O	O	O	F	F	F	F	O
Acid from:								
Glucose	+	+	V	+	+	+	+	+
Maltose	+	V	V	+	+	+	+	+
Sucrose	V	V	V	+	+	+	+	−
Mannitol	V	+	−	+	V	−	+	−
Xylose	V	+	−	V	+	+	−	−
Other (unique)			Odor		Cellulase	Agar penetration		

[a] DAB, diaminobutyric acid; *m*-DAP, *meso*-diaminopimelic acid.
[b] *ai*, anteiso; *i*, iso.
[c] V, variable; +, positive; −, negative.
[d] O, oxidative; F, fermentative.

ethanol abuse and/or chronic liver disease with associated iron overload. The patient had clinical evidence of cellulitis of the left hand, irregularly shaped, gram-positive rods seen in the biopsy, and *Aureobacterium* cells isolated from the necrotic tissue. Because the positive blood cultures coincided with the development of the cellulitis and persisted after removal of the Hickman catheter, it is likely that the skin rather than the catheter was the portal of entry. We did not attempt to identify an environmental source of *Aureobacterium* infection for our patient. The patient's prolonged neutropenia and the antibiotic resistance of the *Aureobacterium* isolate help explain the progression of the cellulitis and the persistence of the bacteremia.

This case report demonstrates that *Aureobacterium* spp. can be significant and difficult to treat opportunistic pathogens. Although it is anticipated that *Aureobacterium* spp. will be encountered infrequently in clinical laboratories, they should be considered whenever yellow-pigmented, coryneform bacteria are isolated from clinical specimens.

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ADDENDUM IN PROOF

Saweljew et al. (P. Saweljew, J. Kunkel, A. Feddersen, M. Baumert, J. Baumert, J. Baehr, W. Ludwig, S. Bhakdi, and M. Husmann, J. Clin. Microbiol. **34:**1540–1541, 1996) recently reported a case of fatal systemic infection with an *Aureobacterium* sp. in a 75-year-old man with severe arteriosclerosis. The organism was isolated from postmortem samples taken from the meninges, kidneys, liver, and spleen and from an antemortem blood culture. The isolate was identified as an *Aureobacterium* sp. by 16S rRNA gene analysis.

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