ORIGINAL ARTICLE 10.1002/2052-2975.31

Dermabacter hominis: a usually daptomycin-resistant gram-positive organism infrequently isolated from human clinical samples

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Abstract

During a 12-year period, *Dermabacter hominis* was isolated from 21 clinical samples belonging to 14 patients attending a tertiary hospital in León, Spain. Samples included blood cultures (14), peritoneal dialysis catheter exit sites (three), cutaneous abscesses (two), an infected vascular catheter (one) and a wound swab (one). Identification was made by API Coryne™ V2.0, Biolog™ GP2 and 16S rRNA gene amplification. Six febrile patients had positive blood cultures (one, two or three sets) and all of them were treated with teicoplanin (two patients), vancomycin, ampicillin plus gentamicin, amoxicillin/clavulanic acid and ciprofloxacin (one each). An additional patient with a single positive blood culture was not treated, the finding being considered non-significant. In the remaining seven patients the organism was isolated from a single specimen and three of them received antimicrobial treatment (ciprofloxacin, ceftriaxone plus vancomycin and amoxicillin/clavulanic acid). At least ten patients had several underlying diseases and conditions, and no direct mortality was observed in relation to the isolated organism. All isolates were susceptible to vancomycin, rifampin and linezolid. Resistance to other antibiotics varied: erythromycin (100%), clindamycin (78.5%), ciprofloxacin (21.4%) and gentamicin, quinupristin-dalfopristin, benzylpenicillin and imipenem 7.1% each. Thirteen isolates were highly resistant to daptomycin with MICs ranging from 8 to 48 (MIC_{90} = 32 mg/L); only one was daptomycin-sensitive (MIC = 0.19 mg/L).

Keywords: Antimicrobial susceptibility, clinical relevance, daptomycin resistance, *Dermabacter hominis*, identification, isolation
Original Submission: 6 October 2013; **Revised Submission:** 28 November 2013; **Accepted:** 29 November 2013
Article published online: 14 January 2014
New Microbe New Infect 2013; **1:** 35–40

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Introduction

Dermabacter hominis, formerly known as coryneform bacteria of Centers for Disease Control groups 3 and 5, is a facultative anaerobic, catalase-positive, non-motile, glucose, maltose and sucrose fermentative, irregular gram-positive bacillus. It hydrolyses aesculin and decarboxylates ornithine and lysine, and grows on nutrient and blood agar forming white, convex, creamy or dry colonies of 1–1.5 mm diameter at 48 h in an aerobic atmosphere, resembling coagulase-negative staphylococci [1–3]. It can be identified by conventional phenotype-based methods, including the API Coryne™ V2.0, and matrix assisted laser desorption ionization-time of flight mass spectrometry system [2,4,5]. A confirmatory test such as 16S rRNA gene sequencing is also recommended [2,4].

Dermabacter hominis is considered a common colonizer from human skin [1]. Operational taxonomic units with 99% sequence identity to the 16S rDNA gene of *D. hominis* have been identified in skin samples in the course of the Human Microbiome Project [6,7] and in human gastrointestinal specimens [8]. Furthermore, *D. hominis* has been isolated from a variety of clinical specimens, such as blood cultures,

abscesses, infected vascular grafts, bone, wound and eye infections, peritoneal dialysis and joint fluids [2,3,9–13].

Dermabacter hominis is usually susceptible to vancomycin, teicoplanin and linezolid with variable susceptibility to benzylpenicillin, ampicillin, cephalosporins, ciprofloxacin, clindamycin, erythromycin, gentamicin, tobramycin, amikacin, chloramphenicol, fusidic acid and rifampin [2,11,13–16]. Daptomycin, a lipopeptide antibiotic, is usually very active against most gram-positive organisms including members of the *Corynebacterium* genus and most diphtheroids [4,17–19]. However, very little information exists on daptomycin activity against *D. hominis* although a couple of communications to congresses suggest that this organism could be daptomycin-resistant (Cercenado E, Marín M, Gama B, Alcalá L, Bouza Santiago E. Daptomycin-resistant *Dermabacter hominis*: an emerging Gram-positive coryneform rod causing human infections. 23rd European Congress of Clinical Microbiology and Infectious Diseases, abstract 0451; Fernández-Natal I, Sáez-Nieto JA, Valdezate-Ramos S, *et al.*, Daptomycin-resistant coagulase-negative *Staphylococcus*? No, *Dermabacter hominis*. XVII Congress of the Spanish Society of Infectious Diseases and Clinical Microbiology, abstract 473).

The aims of this study are to review clinical and epidemiological characteristics of patients with *D. hominis* isolated from diverse clinical samples. In addition, antimicrobial susceptibility to a variety of antimicrobials has been determined with special attention to daptomycin activity.

Material and Methods

Clinical samples

Isolates were recovered from 14 blood cultures (BacT/AlerT™, bioMérieux, Marcy-l'Etoile, France), three peritoneal dialysis catheter exit sites, two cutaneous abscesses, an infected vascular catheter and a wound swab. These samples were received in the clinical laboratory from January 2000 to December 2012 and belonged to 14 patients attended in a tertiary hospital in León, Spain.

Identification

Isolates were identified by using conventional phenotypic methods, API Coryne™ V2.0 (bioMérieux), and Biolog™ GP2 (Biolog, Inc., Hayward, CA, USA). In addition, identification was confirmed by 16S rRNA gene sequencing using a previously reported method [20].

Epidemiological and clinical data

Regarding age, sex, underlying diseases and conditions, antimicrobial treatment and outcome were retrospectively recorded by reviewing clinical charts.

Antimicrobial susceptibility

Antimicrobial susceptibility was determined by the Etest® method on Mueller–Hinton sheep blood agar plates, incubated at 37°C in aerobiosis for 24–48 h. The following Etest strips (bioMérieux) were used: benzylpenicillin, ampicillin, cefotaxime, imipenem, gentamicin, ciprofloxacin, moxifloxacin, tetracycline, tigecycline, rifampin, chloramphenicol, cotrimoxazole, erythromycin, clarithromycin, azithromycin, clindamycin, quinupristin-dalfopristin, linezolid and vancomycin. Daptomycin susceptibility was determined by using a calcium-supplemented MIC Test Strip (Liofilchem® s.r.l., Roseto degli Abruzzi, Italy). The MICs of 11 antibiotics were categorized as susceptible, intermediate and resistant following the CLSI-M45-A-2012 document for coryneform organisms [21]. Resistance to daptomycin was defined as MICs >1 mg/L. *Staphylococcus aureus* ATCC 29213 and *Enterococcus faecalis* ATCC 29212 served as controls. Phenotypic resistance to macrolide—lincosamide—streptogramin B antibiotics (MLS_B) was determined by a previously reported method [22].

Results

One isolate from each patient was characterized. All isolates were identified by API Coryne™ V2.0 with good to very good scores (>99.7% ID) with the following profiles: 4570165 (n = 5), 4570765 (n = 5), 4570325 (n = 2) and 4570365 (n = 2). Biolog™ GP2 identified all isolates with 85–100% of profiles corresponding to the taxon. The results of 16S rRNA gene sequences (fragments between 1360 and 1455 bp) were compared with sequences available in databases using BLAST, and they showed a homology of 99.3–99.9% with *D. hominis*.

Table 1 presents the main epidemiological and clinical data regarding patients, source and antimicrobial treatment. The age of the patients ranged from newborn to 79 years (mean, 54.0 years) with a male/female rate of 10/4. Twelve cases were considered to be hospital-related or healthcare-related and only two were community-acquired. At least ten patients had several underlying diseases and conditions (chronic renal failure, peritoneal dialysis, haemodialysis, human immunodeficiency virus infection, chronic hepatitis, preterm rupture of the membranes, lymphoma, lung cancer, cytotoxic treatment and neutropenia). Seven bacteraemic patients were diagnosed after one (two patients), two (three patients) and three (two patients) positive blood cultures. Five of these patients were treated with antibiotics that were proved to be active *in vitro* against the isolate: teicoplanin (two patients); vancomycin, amoxicillin/clavulanic acid and ampicillin plus gentamicin one patient each. One patient received ciprofloxacin, later proven

TABLE 1. Data on patients with *Dermabacter hominis* isolation

No.	Sex, age (years)	Source (*n*)	Underlying disease(s)	Diagnosis	Antimicrobial treatment
1	M, 43	Blood (2)[a]	HIV-infected, chronic hepatitis, lymphoma, cytotoxic drugs	Neutropenic fever	Teicoplanin
2	M, 54	Blood (1)[b]	No	Viral meningitis	No
3	M, 53	Blood (2)[a]	Lung cancer, cytotoxic drugs	Neutropenic fever	Teicoplanin
4	F, 79	Blood (3)[a]	Epilepsy	Bronchoaspiration, fever	Amoxicillin/clavulanic acid
5	M, 29	Blood (3)[a] Lymphoma	Pyelonephritis, fever	Ciprofloxacin	
6	M, newborn	Blood (1)[a]	Preterm rupture of the membranes	Chorioamnionitis, fever	Ampicillin + gentamicin
7	M, 65	Blood (2)[c]	Chronic renal insufficiency, haemodialysis	Fever	Vancomycin
8	F, 56	PDCES (1)[c]	Chronic renal insufficiency, peritoneal dialysis	Exit-site infection	Ciprofloxacin
9	F, 73	PDCES (1)[c]	Chronic renal insufficiency, peritoneal dialysis	Exit-site control	No
10	M, 66	PDCES (1)[c]	Chronic renal insufficiency, peritoneal dialysis	Exit-site infection, fever	No
11	M, 77	Vascular catheter (1)[c]	Chronic renal insufficiency, haemodialysis, amyloidosis	Fever	Ceftriaxone + vancomycin
12	M, 59	Abscess (1)[d]	Unknown	Cutaneous abscess	Unknown
13	M, 59	Wound swab (1)[a]	Chronic osteomyelitis	Unknown	Unknown
14	M, 44	Abscess (1)[d]	No	Cutaneous abscess	Amoxicillin/clavulanic acid

HIV, human immunodeficiency virus; PDCES, peritoneal dialysis catheter exit site.
Probably acquisition of the organism: [a]hospital; [b]hospital (probable contamination); [c]health care (dialysis); [d]community.

not to be active *in vitro* against the isolate and the remaining patient did not receive antibiotics.

In the seven remaining patients the organism was isolated in pure culture from a single clinical specimen. Exudates from cutaneous abscesses, vascular catheter and wound swab were Gram-stained and moderate numbers of polymorphonuclear leucocytes and coryneform organisms were seen. Three of the patients had positive peritoneal dialysis catheter exit site samples and one of them was treated with an antibiotic that was active *in vitro* against the isolate (ciprofloxacin), whereas the other two patients did not receive any antimicrobial treatment. One patient with a catheter infection and another one with a cutaneous abscess also received antibiotics active *in vitro* against the isolates (ceftriaxone plus vancomycin, and amoxicillin/clavulanic acid), the latter also requiring surgical drainage of the abscess. There was not enough clinical information regarding the other two patients. No mortality directly related with isolation of *D. hominis* was observed.

Table 2 presents the results of antimicrobial susceptibility of 14 *D. hominis* isolates to 21 antimicrobials. All isolates were susceptible to vancomycin, rifampin and linezolid. No resistance to tetracycline was detected although three isolates fell into the intermediate category. Eleven isolates were highly resistant to erythromycin and clindamycin (MICs >256 mg/L), and only one of them was resistant to quinupristin-dalfopristin. Low-level resistance to erythromycin (MICs 1.5–2 mg/L) was detected in three isolates, which were all susceptible to clindamycin and quinupristin-dalfopristin. Resistance to other antibiotics varied: ciprofloxacin (21.4%); gentamicin, quinupristin-dalfopristin, benzylpenicillin and imipenem 7.1% each. Thirteen isolates were highly resistant to daptomycin with MICs ranging from 8 to 48 (MIC_{90} = 32 mg/L) whereas only one was daptomycin-sensitive (MIC = 0.19 mg/L).

Although there are no defined susceptibility breakpoints for many of the other tested antibiotics, the low MIC values obtained in all isolates for teicoplanin (<0.19 mg/L), tigecycline (<0.5 mg/L), and in 11 isolates for ampicillin, cefotaxime and moxifloxacin (<1 mg/L) should be noted. The results for clarithromycin and azithromycin were similar to those of erythromycin. Seven isolates had chloramphenicol MICs <1 mg/L. On the other hand 12 isolates presented MICs >32 mg/L for cotrimoxazole.

Discussion

Dermabacter hominis is the only recognized species of the *Dermabacter* genus and it can be easily identified by phenotypic conventional methods, including the API Coryne™ V2.0 system [2,4] and matrix-assisted laser desorption/ionization–time of flight mass spectrometry [5]. Our data, together with the published information [2,10–13], indicate that the predominant API Coryne™ profiles for *D. hominis* are 4570365, 4570765 and 4570165. Identification of *D. hominis* by using the Biolog™ system proved to be useful and reliable. As widely demonstrated for other organisms, including members of the *Corynebacterium* genus and coryneforms [2,4,20], the study of the 16S rRNA gene sequence confirmed phenotypic identification.

We have isolated *D. hominis* from a variety of clinical samples including 14 blood cultures belonging to seven patients. Among the seven bacteraemic patients, five were immunosuppressed and one had a lung infection secondary to bronchoaspiration, and all were treated with antibiotics. The remaining patient who had a single positive blood culture did not receive antimicrobial treatment because the culture was not considered clinically relevant.

TABLE 2. Antimicrobial susceptibility of 14 *Dermabacter hominis* isolates (MICs in mg/L)

	Isolate													
Antibiotic	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Benzylpenicillin	0.064	0.064	0.125	0.094	1.5	0.125	0.25	0.5	0.5	2	6	2	0.19	0.094
Ampicillin	0.064	0.25	0.5	0.5	2	0.38	2	1	0.75	0.5	6	0.5	0.25	0.125
Cefotaxime	0.047	0.064	0.094	0.064	3	0.19	0.064	0.125	0.25	3	4	0.094	0.125	0.047
Imipenem	0.25	0.5	0.75	0.5	>32	0.5	0.38	0.75	0.75	2	2	0.38	0.75	0.38
Gentamicin	0.5	0.75	0.75	0.75	>256	1	4	1	1.5	2	3	0.75	1	0.38
Ciprofloxacin	0.75	0.5	1	0.75	>32	1.5	1	1.5	2	>32	>32	0.75	1.5	0.5
Moxifloxacin	0.064	0.094	0.125	0.094	>32	0.125	0.125	0.19	0.19	4	12	0.094	0.12	0.094
Tetracycline	0.125	0.25	0.5	0.25	4	0.38	6	1.5	0.75	6	8	0.19	1	0.5
Tigecycline	0.125	0.094	0.125	0.125	0.19	0.094	0.38	0.19	0.25	0.19	0.5	0.064	0.19	0.094
Rifampin	0.006	0.006	0.004	0.006	0.006	0.003	0.004	0.006	0.006	0.006	0.006	0.006	0.006	0.004
Chloramphenicol	1	1.5	0.32	1.5	12	1.5	1	2	12	16	1	1	2	24
Cotrimoxazole	>32	>32	>32	>32	>32	>32	0.25	>32	>32	>32	>32	>32	>32	0.25
Erythromycin	>256	>256	>256	>256	>256	2	>256	>256	1.5	>256	>256	>256	1.5	>256
Clarithromycin	>256	>256	>256	>256	>256	1.5	>256	>256	2	>256	>256	>256	2	>256
Azithromycin	>256	>256	>256	>256	>256	3	>256	>256	3	>256	>256	>256	3	>256
Clindamycin	>256	>256	>256	>256	>256	0.064	>256	>256	0.125	>256	>256	>256	0.094	>256
Quinupristin-dalfopristin	0.75	0.75	0.38	0.5	>32	0.25	1	0.38	0.38	1.5	2	0.5	0.38	1
Linezolid	0.5	1	0.75	0.75	0.25	0.38	0.38	1.5	1	0.75	0.38	0.75	0.75	0.75
Vancomycin	0.38	0.38	0.38	0.38	0.75	0.38	0.38	0.5	0.38	0.38	0.5	0.38	0.38	0.38
Teicoplanin	0.19	0.125	0.19	0.19	0.125	0.064	0.094	0.19	0.064	0.125	0.125	0.19	0.047	0.125
Daptomycin	16	16	24	16	16	8	32	32	8	32	48	16	32	0.19

In the seven remaining patients, the organism was isolated from a single clinical specimen. Three of these patients received antibiotics that were active *in vitro* against the isolate, plus surgical drainage in the case of a cutaneous abscess. Although the clinical information is not complete for all patients, the data obtained support that *D. hominis* can be an opportunistic microorganism usually associated with very low mortality, in agreement with what has been previously reported [2,3,9–12]. Nevertheless, a fatal septicaemia in an immunosuppressed patient has been reported [13].

The antimicrobial susceptibility of *D. hominis* is variable but it has always been uniformly susceptible to vancomycin and linezolid [2,11,13–16], which is also confirmed in the present study. We have not found resistance to rifampin and tetracycline, and the rate of benzylpenicillin, imipenem, quinupristin-dalfopristin resistance was very low (7.1%). Moderate resistance was found for ciprofloxacin (21.4%). The high rate of erythromycin and clindamycin resistance as well as the results with quinupristin-dalfopristin suggests that resistance to MLS_B antibiotics is mainly constitutive, probably due to the presence of the *erm* gene in 78.5% of our isolates.

The very recently established draft genome sequence of isolate no. 5 (our unpublished data) led to the detection of the corynebacterial *erm(X)* gene in this strain, explaining the resistance against antimicrobials of the MLS class [23]. The genome of isolate no. 5 also contains the *cmx* transporter gene for chloramphenicol resistance, the *strAB* tandem genes for streptomycin resistance [23] and the *sul1* gene encoding a dihydropteroate synthase that can confer resistance to a broad spectrum of sulphonamides [24]. The *gyrA* gene contains the deduced sequence motif FAIYD in the quinolone-resistance-determining region, which might be associated with ciprofloxacin, moxifloxacin and levofloxacin resistance [25].

The high rate of daptomycin-resistance is remarkable and it contrasts with the wide and powerful activity of this drug against most gram-positive organisms, including *S. aureus*, enterococci, members of the *Corynebacterium* species and coryneforms [4,16–19]. Although daptomycin's mechanism of action has not been fully elucidated, it seems to act by insertion into the bacterial cell membrane in a calcium-dependent manner, resulting in rapid membrane depolarization [26]. The addition of ionized calcium is highly recommended for *in vitro* testing of daptomycin, as the MICs are much lower when a concentration similar to the one found in human serum is incorporated [17,18]. All except one of our *D. hominis* isolates presented high daptomycin MICs in spite of having been tested in calcium-supplemented conditions. This emphasizes the relevance of our findings. Our report confirms what had been communicated to congresses on daptomycin resistance in this organism but it also presents what we believe is the first report of a daptomycin-susceptible *D. hominis* strain.

Acquired resistance to daptomycin in gram-positive organisms is rare but it is being increasingly reported in relation to the use of this drug [27–29]. However, resistance to daptomycin in *D. hominis* is very common and it seems to be unrelated to the use of this antibiotic. The whole-genome sequencing of an isogenic, clinical and laboratory-derived *S. aureus* strain, which had been exposed to daptomycin, has been performed and found a point mutation in genes coding for membrane phospholipids [26]. On the other hand, electron microscopy and lipid membrane studies have shown that daptomycin non-susceptible *S. aureus* strains had a thicker cell

wall and an increase in membrane lysyl-phosphatidylglycerol [27]. In enterococci, mutations in genes encoding a putative membrane protein and a GdpD-family protein are necessary and sufficient for the development of resistance to daptomycin during the treatment of vancomycin-resistant strains [28]. In daptomycin non-susceptible isolates of *Enterococcus faecium*, a higher net surface charge and an increased septum formation have been found compared with susceptible isolates [29].

Enzymatic inactivation of daptomycin, as recently shown in some actinomycetes, could also be responsible for resistance owing to ring hydrolysis, which leads to drug linearization, and deacylation of the lipid tail [30]. Comparative genomics and lipid membrane studies of *D. hominis* could allow new insights into the mechanisms that convey resistance to daptomycin in this organism.

Funding

Research Project GRS 698/A/11. Gerencia Regional de Salud. Junta de Castilla y León, Spain.

Conflict of Interest

The authors declare no conflicts.

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