

Recurrent Intravascular-Catheter-Related Bacteremia Caused by *Delftia acidovorans* in a Hemodialysis Patient[∇]

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We report the first case of recurrent intravascular-catheter-related bacteremia in a pediatric hemodialysis patient caused by *Delftia acidovorans*, previously called *Comamonas acidovorans* or *Pseudomonas acidovorans*. The patient had a history of multiple infections of central vascular catheters with other organisms, requiring courses of antibiotics and catheter replacements. Previously reported cases of *D. acidovorans* infections are reviewed. The isolate appeared to become resistant to cephalosporins after antibiotic treatment, but resistance could not be confirmed with additional testing. *In vitro* susceptibility testing for cephalosporins is not reliable for this organism.

CASE REPORT

A 10-year-old girl with renal cortical necrosis and end-stage renal disease was receiving hemodialysis via a Quinton PermCath dual-lumen catheter for 5 years. Over this period, she had a history of 24 episodes of catheter-related infections, requiring multiple courses of antibiotics and catheter replacements. While receiving outpatient dialysis treatment on day 120 of the catheter, she developed a fever of 38°C and chills. There was no erythema, warmth, tenderness, or swelling at the exit site in the femoral area. A blood culture was obtained from the catheter which subsequently grew a Gram-negative rod identified as *Delftia acidovorans* by MicroScan WalkAway-40 BP combo panel type 34 (Siemens, Munich, Germany). The organism was susceptible to expanded-spectrum and broad-spectrum cephalosporins, aztreonam, carbapenems, piperacillin-tazobactam, ticarcillin-clavulanate, and quinolones but resistant to all aminoglycosides, penicillin, and narrow-spectrum cephalosporins and intermediately susceptible to ampicillin-sulbactam. A 14-day course of cefepime was given through the catheter with hemodialysis when microbial identification and susceptibility results were available. The patient remained afebrile. Blood cultures drawn from the catheter before starting antibiotic therapy, 3 days and 7 days after the end of therapy, were negative. The catheter was not removed.

Twenty-four days after cefepime was stopped, she became febrile again (38°C), with chills, after hemodialysis. Blood cultures were obtained from the catheter and peripheral vein. Vancomycin and cefepime were started, and she defervesced within 24 h. *Staphylococcus epidermidis* and *D. acidovorans* were identified from both specimens. The *D. acidovorans* isolate was initially not identifiable by MicroScan WalkAway (Sie-

mens, Munich, Germany). Additional testing was done with Vitek and API 20 NE version 6.0 (bioMérieux, Marcy l'Etoile, France). The Vitek reported *D. acidovorans* with 53% probability, and the API 20 NE version 6.0 reported *D. acidovorans* as a significant taxon with an unacceptable profile. Finally, it was further characterized with long-chain-fatty-acid analysis by gas chromatography using the MIDI 62 system (Microbial Identification Systems, Newark, DE). The susceptibilities of the second *D. acidovorans* isolate by MicroScan were now reported as resistant to cefotaxime, ceftriaxone, cefepime, aztreonam, and piperacillin-tazobactam but susceptible to ceftazidime, amoxicillin-clavulanate, ticarcillin-clavulanate, and trimethoprim-sulfamethoxazole. Treatment was changed to ceftazidime and given along with vancomycin. Blood cultures became negative after 3 days of the antibiotics. The patient remained afebrile. The antibiotics were continued to complete a 21-day course. Her catheter became malpositioned and required replacement at the end of the treatment. Blood cultures remained negative for 18 days after removal of the catheter.

Because of the changes in the antimicrobial susceptibility profiles, the second isolate was screened for genes encoding CTX-M extended-spectrum β -lactamases using multiplex PCR with previously identified primers and PCR conditions (20). No CTX-M enzymes were detected. *In vitro* susceptibilities of the second isolate were retested by MicroScan, Etest, and broth macrodilution, which revealed inconsistencies of the cephalosporin susceptibilities (Table 1). Evaluation for the presence of β -lactamases with penicillin, cefazolin, and ceftriaxone hydrolysis measurement by spectrophotometric assay was performed (13). Maximal hydrolysis rates using penicillin, cefazolin, and ceftriaxone substrate were 0.05, 0.04, and 0 $\mu\text{mol/mg}$ of protein/min, respectively.

D. acidovorans was formerly called *Comamonas acidovorans* or *Pseudomonas acidovorans*. Prior to 1987, a variety of now independent genera, including *Burkholderia*, *Stenotrophomonas*, *Ralstonia*, *Comamonas*, *Delftia*, *Acidovorax*, and others,

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TABLE 1. MicroScan and Etest MICs for isolates of *D. acidovorans* from the patient

Antibiotic(s)	MIC (µg/ml) of isolate:				Broth macrodilution
	1 (MicroScan)	2		Etest	
		MicroScan	Repeat MicroScan		
Amikacin	>32	>32	>32	32	
Ampicillin-sulbactam	16/8	>16/8	>16/8		
Aztreonam	<8	>16	16	1.5	
Cefazolin	>16	>16	>16		
Cefepime	<8	>16	>16	1.5	
Cefotaxime	<2	>32	32	0.38	
Ceftazidime	<1	8	4	0.25	
Ceftriaxone	<8	>32	>32		8
Ciprofloxacin	<1	<1	<1	0.064	
Cefotaxime-clavulanate	<0.5	<0.5	<0.5		
Ceftazidime-clavulanate	<0.25	<0.25	<0.25		
Gentamicin	>8	>8	>8	>256	
Imipenem	<4	<4	<4	0.19	
Levofloxacin	<2	<2	<2	0.064	
Meropenem	<4	<4	<4	0.094	
Piperacillin-tazobactam	<16	>64	<16	<0.016	
Ticarcillin-clavulanate	<16	<16	<16		
Trimethoprim-sulfamethoxazole	<2/38	<2/38	<2/38	0.125	

were all identified within the broad genus *Pseudomonas*. As a collective, they are all generally aerobic, oxidase-positive, Gram-negative bacilli that grow on MacConkey's agar. This broad genus was rearranged based on rRNA homology studies. *D. acidovorans* belongs to the family *Comamonadaceae* based on 16S rRNA gene sequence analysis. *Comamonas acidovorans* was found phylogenetically distant from the type species of *Comamonas*, *Comamonas terrigena*, and was removed from the genus *Comamonas* and renamed *Delftia acidovorans* (6, 19).

Microscopically, *D. acidovorans* is characterized by straight to slightly curved Gram-negative bacilli, which occur single or in pairs. Strains are motile by means of polar or bipolar tufts of one to six flagella, with the distinctive feature of having a long wavelength (3.0 µm between the tops of adjacent waves). The organism is strictly aerobic; growth occurs at 30°C to 37°C, and 8% of the strains grow at 42°C. It grows well on media containing organic acids, amino acids, peptone, and carbohydrates but not glucose; 29% of the strains grow in the presence of 6.0% NaCl. Endospores are not produced. Only 26% of the strains produce a fluorescent pigment, while 44% may produce a soluble yellow to tan color. *D. acidovorans* is oxidase and catalase positive and nonfermentative. No acid production occurs in oxidative fermentative glucose medium. It is acetamide positive, reduces nitrate to nitrite, reduces nitrate without gas formation, and oxidizes fructose and mannitol, which is a key characteristic of the species. The organism does not hydrolyze starch, esculin, gelatin, or urea, and arginine dihydrolase is negative. There is negative acid production in lactose, xylose, sucrose, and maltose, and no production of hydrogen sulfide in Kligler iron agar, but 57% of the strains are positive with lead acetate paper. The organism is also negative for beta-galactosidase activity and DNase and indole production, but most strains have an orange indole reaction (6, 19). All *D. acidovorans* isolates are resistant to 10-µg colistin disks and 300-U polymyxin B disks, while the related species *Comamonas testosteroni* and *C. terrigena* are susceptible (9). The following

tests are suggested for identification of nonfermenters: alkaline phosphatase, benzyl-arginine arylamidase, pyrrolidonyl arylamidase, and 10-µg colistin disks (9).

This organism is a common water and soil saprophyte and has wide geographic distribution (6). *D. acidovorans* appears to be an organism of limited virulence that has usually been considered nonpathogenic when isolated from clinical specimens. However, it has been reported to be a pathogen under certain circumstances. Weinstein et al. described an outbreak of *D. acidovorans* bacteremia associated with contaminated pressure-monitoring devices (18). Unfortunately, clinical and epidemiologic information was not provided in association with this outbreak. Horowitz et al. reported a case of *D. acidovorans* endocarditis in an intravenous drug user with alcoholic liver disease (7). The illness occurred soon after the patient was treated for 4 weeks with ampicillin for viridans streptococcal endocarditis. Several cases of ocular infections have been reported, including keratitis, blepharitis, and conjunctivitis in immunocompromised corneas, contact lens wearers, or otherwise healthy patients (1, 11, 12, 17). *D. acidovorans* has further been reported to cause acute suppurative otitis externa and pneumonia in a patient with AIDS (5, 16). Chun et al. reported *D. acidovorans* chronic empyema in an immunocompetent patient (3).

We identified four previous reports of vascular catheter-related *D. acidovorans* bacteremia (2, 4, 8, 10). All four patients were immunocompromised with underlying malignancies or AIDS. All responded to antimicrobial treatment, but eventually removal of the central venous catheter was required for three patients, with the exception of the case described by Ender et al. (4).

The *D. acidovorans* bacteremia in our patient was likely secondary to an intravascular catheter. Although the girl did not meet the strict criteria for catheter-related sepsis (14), the catheter was probably the origin of the bacteremia based on the clinical presentation and the exclusion of other sources.

TABLE 2. Summary of antibiotic susceptibilities of *D. acidovorans* reported in the literature

Antibiotic(s)	MIC ($\mu\text{g/ml}$) from reference:			Susceptibility ^a from reference:					
	7	8	8	2	3	4	10	12	17
Amikacin	>8	>32	>32	S	R	R	R		
Ampicillin	>16			R				R	R
Aztreonam	16	4	>16	S		S			
Cefazolin	>16			R					R
Cefuroxime	>16								
Cefepime		≤ 2	>16		S	S			
Cefotaxime	<4			S	S	S		S	
Ceftazidime	<8	2	8		S	S	S		
Ceftriaxone	<8			S		S		S	
Ciprofloxacin	<1	≤ 0.5	≤ 0.5	S	I	S			
Gentamicin	>8	>8	>8	R	R	R	R	R	R
Imipenem					S		S		
Levofloxacin		≤ 0.5	≤ 0.5						
Meropenem		≤ 1	≤ 1	S					
Piperacillin-tazobactam	16	≤ 8	>64		S	S	S		
Trimethoprim-sulfamethoxazole	<2	$\leq 2/38$	$\leq 2/38$	S	S				

^a S, susceptible; I, intermediate; R, resistant.

The catheter was not removed immediately, and differential quantitative blood cultures were not obtained. However, the patient had the same organism isolated from the hemodialysis catheter and a peripheral blood sample. She had no other source of infection based on clinical assessment. Therefore, the infection likely represented a recurrent vascular-catheter-related bacteremia.

Information about susceptibility of this organism is limited. Case reports revealed that all were resistant to gentamicin, and some were resistant to all aminoglycosides. They are generally susceptible to broad-spectrum cephalosporins, piperacillin, aztreonam, carbapenems, quinolones, and trimethoprim-sulfamethoxazole (1, 2, 3, 4, 7, 8, 10, 12, 17) (Table 2). *D. acidovorans* has been reported to have β -lactamase in two resistant laboratory mutant strains and inducible β -lactamase production in one resistant clinical strain (15). Kawamura et al. reported recurrent bacteremia in an 11-year-old girl with metastatic neuroblastoma during sustained neutropenia after peripheral blood transplant, where the isolate developed resistance to broad-spectrum penicillins and cephalosporins during antibiotic treatment (8).

The second isolate from our case also appeared to have developed resistance to broad-spectrum cephalosporins by MicroScan after antibiotic treatment. With the previous reports of inducible β -lactamase production and a pattern of resistance after the antibiotic therapy, a PCR for genes encoding CTX-M extended-spectrum β -lactamases was performed but was negative. We subsequently performed β -lactamase hydrolysis testing using penicillin, cefazolin, and ceftriaxone as a substrate to evaluate β -lactamase activity. The very slow hydrolysis rates of penicillin and cefazolin were in the range of error measurement from spectrophotometry, suggesting no β -lactamase activity in the second isolate. Susceptibility testing by Etest and broth macrodilution demonstrated inconsistent results for cephalosporins.

In conclusion, we report a case of recurrent intravascular-catheter-related infection caused by *D. acidovorans*. Antibiotic susceptibility testing for cephalosporins using MicroScan appears to be unreliable for this organism.

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