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CASE REPORTS

Implanted-Port-Catheter-Related Sepsis Caused by *Acidovorax avenae* and Methicillin-Sensitive *Staphylococcus aureus*▽

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***Acidovorax avenae* is a gram-negative rod in the family *Comamonadaceae* and a phytopathogen found in the environment. Human infections caused by members of the *Comamonadaceae* are extremely rare. We report a case of implanted-port-catheter-related sepsis caused by *Acidovorax avenae* and methicillin (meticillin)-sensitive *Staphylococcus aureus* (MSSA).**

CASE REPORT

A 27-year-old-white female with severe iron deficiency anemia underwent implantation of a central venous infusion port catheter 2 months previously for intravenous iron replacement therapy. The etiology of the anemia was thought to be secondary to multiple bowel surgeries for chronic abdominal pain. Six weeks after port placement, she developed fever (39.4°C) associated with shaking chills, nausea, vomiting, and diarrhea. She visited the emergency department, where two blood cultures were drawn, but refused hospital admission. She continued to tolerate worsening symptoms at home for the next 5 days. The two blood cultures previously drawn in the emergency department grew methicillin (meticillin)-sensitive *Staphylococcus aureus* (MSSA), and the patient was urged to return to the hospital. She agreed to the admission.

She was febrile to 40.3°C and tachycardic at 125 beats per minute and had a blood pressure of 100/60 mm Hg. Physical examination revealed a pale Caucasian female in moderate distress with a palpable subcutaneous device located in the right superior-anterior chest. There was no erythema, swelling, tenderness, or other pertinent physical examination findings. She had a normal white blood cell count of $9.1 \times 10^9/\mu l$ and a hemoglobin level of 7.7 g/dl. A diagnosis of sepsis was made. Antibiotics were started with daptomycin 500 mg intravenously once daily and cefazolin 1 g intravenously every 8 h. The port catheter was suspected as the source of sepsis, and surgical consultation was sought.

On hospital day 3, the patient underwent removal of the port catheter. At the time of port-catheter removal, purulent exudate was seen to exit from the accessed skin site. Preliminary culture results for this device revealed both gram-positive cocci (GPC) and gram-negative rods (GNRs). The patient remained febrile, and two blood cultures obtained later that day revealed solely GNRs. Gentamicin was added at this time to broaden coverage. Finally, on postoperative day 3, the patient defervesced. One subsequent blood culture documented sterility of the bloodstream. On postoperative day 7, a peripherally inserted central catheter was placed for further antibiotic therapy. The patient developed a mild erythematous rash thought to be secondary to beta-lactam allergy; therefore, antibiotic therapy was changed to vancomycin and gentamicin. The patient successfully completed 8 more days of treatment.

Blood cultures (Table 1) were obtained aseptically from different venipuncture sites by using BacT/Alert SA culture bottles (bioMérieux Inc., Durham, NC). After 17 h of incubation at 37°C, both blood cultures were positive and were then plated aerobically at 37°C in 5% CO_2 (MacConkey II, TSA II 5% sheep blood, and Chocolate II agar plates). Simultaneously, anaerobic cultures were plated on CDC anaerobe 5% sheep blood agar and CDC anaerobe laked sheep blood agar with kanamycin and vancomycin (BBL prepared culture media; Becton, Dickinson and Company, Sparks, MD) and incubated at 37°C in an anaerobic chamber.

The catheter tip was plated on chocolate, MacConkey II, and thioglycolate medium enriched with vitamin K_1 and hemin (BBL prepared culture media; Becton, Dickinson and Company, Sparks, MD) and incubated at 37°C in 5% CO_2. Phenotypic identification and susceptibility testing were performed with Vitek 2 compact gram-negative identification and AST-GN15 sensitivity cards (bioMérieux Inc., Durham, NC). An additional commercial diagnostic system, bioMérieux API 20E, was set up on all three isolates, according to the manufacturer's instructions. Susceptibility tests were performed by the gradient diffusion method (Etest; AB Biodisk North America, Inc., Piscataway, NJ).

The GNR isolate was sent to the University of Washington Medical Center for 16S rRNA nucleic acid sequencing. Conclusive identification of the organism was based on comparing the nucleic acid sequence alignment using Basic Local Alignment Search Tool (BLAST) with databases at the National Center for Biotechnology Information (NCBI) and sequence-based phylogenic trees (bacterial sequencing database, University

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TABLE 1. Culture timeline during hospital course

Time	Culture type	Site[a]	No. of cultures with result/total no. of cultures, result	Time	Organism
5 days prior to admission	Blood	PV	2/2, +	10 h	MSSA
Day of admission	Blood	PV	2/2, +	10 h	MSSA
Hospital day 3 (operation)	Port catheter tip	SV	1/1, +	17 h, 41 h	4+ MSSA, 4+ *Cupriavidus pauculus*
Postoperative day 0	Blood	PV	2/2, +	17 h	*Cupriavidus pauculus*
Postoperative day 3	Blood	PV	1/1, −	5 days	No growth

[a] PV, peripheral vein; SV, subclavian vein.

of Washington Laboratory Medicine, Seattle, WA, 2007 [http://depts.washington.edu/molmicdx/mdx/tests/bctseq.shtml]).

The GNR culture plates showed small colonies, approximately 1 mm in diameter, under aerobic conditions. There was no growth anaerobically. Gram staining showed irregularly staining organisms with slightly tapered ends. The subcultures of both blood cultures had adequate growth on the sheep blood agar plate but only a slight haze on MacConkey and chocolate agar plates after 24 h. The catheter tip initially produced growth on both colistin-nalidixic acid agar and chocolate agar that was identified as *S. aureus*, which was consistent with the patient's blood cultures. After 48 h, there were pinpoint, dark pink colonies on MacConkey agar and medium-sized white colonies on chocolate agar.

The Vitek 2 compact system identified each isolate as *Cupriavidus pauculus* at the 98% confidence level. However, sensitivities were not reported due to the lack of correlation studies of MICs for this particular organism. The bacteria could not be definitively coded by the bioMérieux API 20E system. *Acidovorax* was not included in either compendium. Additional tests performed on the isolate included oxidase (positive), catalase (negative), nitrate (positive), and indole (negative). Etest antibiotic susceptibility testing for gentamicin yielded an MIC of 2.0 μg/ml. MICs determined using Sensititre from Trek Diagnostics in Microbiology, CLS, Saint Francis Hospital, Hartford, CT, are shown in Table 2. Gentamicin MIC was reported as intermediately sensitive at 8 μg/ml. Sequencing with 16S rRNA provided a 100% match over 485 nucleotides to an *Acidovorax avenae* type strain (ATCC 19860). Some of the closest genetic neighbors within the *Comamonadaceae* family include *Comamonas*, *Rubrivivax*, *Hydrogenophaga*, *Aquaspirillum*, *Polaromonas*, *Variovorax*, *Xylophilus*, and *Brachymonas* species (7), but they were less than 96.5% related to the isolate.

TABLE 2. MICs for *Acidovorax avenae*[a]

Antibiotic	MIC (μg/ml)	Interpretation[b]
Gentamicin	8	I
Tobramycin	≤4	S
Amikacin	≤8	S
Ampicillin	>32	R
Cefazolin	>32	R
Cefuroxime	>32	R
Ceftriaxone	64	R
Ceftazidime	4	S
Cefipime	32	R
Ampicillin-sulbactam	32/16	R
Ticarcillin-clavulanate	≤16/2	S
Pipericillin-tazobactam	≤2	S
Ertapenem	≤2	S
Meropenem	≤1	S
Ciprofloxacin	≤0.5	S
Trimethoprim-sulfamethoxazole	≤0.5/9.5	S
Tetracycline	≤1	S
Aztreonam	>32	R

[a] MICs were determined using Sensititre from Trek Diagnostics in Microbiology, CLS, Saint Francis Hospital, Hartford, CT.
[b] I, intermediate; S, susceptible; R, resistant.

Very few members of the *Comamonadaceae* family have been reported to cause infections in humans. However, most reports that exist are of cases due to *Comamonas acidovorans* or *Comamonas testosteroni*. Both organisms are known for producing ocular infections (11, 12, 15, 17, 22), endocarditis (4, 9), nosocomial pneumonia (6), bacteremia (8, 10, 19, 20), and central line-associated bloodstream infections (1, 2, 5, 13). There was also one report of bacteremia due to *Comamonas terrigena* in the literature (21).

Acidovorax avenae is a non-lactose-fermenting, oxidase-positive, aerobic, nonpigmented GNR (14, 16). These organisms are found in soil and water and are also recognized as plant pathogens. This bacterium infects a wide range of plants, including corn, rice, watermelon, pumpkins, and orchids. It often manifests as a seedling disease with brown stripes forming on the plant sheaths (18). The medical literature contains a case of *A. avenae* bloodstream infection involving a peripheral venous catheter as the potential source of entry (18). The individual was on long-term steroid therapy for sarcoidosis and was treated with 7 days of ciprofloxacin. A second case describes *A. avenae* bacteremia in a neutropenic patient with non-Hodgkin's lymphoma. However, information on antibiotic therapy was not provided (23).

Our patient appeared to suffer sepsis caused by two different organisms, *A. avenae* and MSSA. We were surprised by the finding of *A. avenae* and its apparent pathogenicity. Initial blood cultures did not demonstrate any GNRs, and therapy was targeted only at MSSA with daptomycin and cefazolin. As the patient remained febrile despite this therapy, follow-up blood cultures were collected. These showed eradication of MSSA with the new finding of a GNR. We believe that both organisms were responsible for the patient's sepsis because of failure to improve on targeted MSSA treatment alone.

We surmise that MSSA overgrew *A. avenae* initially because of a higher growth rate, as *A. avenae* was found only when MSSA was eradicated. To test this hypothesis, we performed blood culture and comparative growth studies. We used the original *A. avenae* isolate and also *S. aureus* ATCC 29213,

TABLE 3. Comparative growth studies for *Acidovorax avenae*

Time (h) and agar	Growth at temp:	
	27°C	37°C
24		
MacConkey	None	None
Chocolate	None	Slow
BAP	None	None
48		
MacConkey	None	Pinpoint
Chocolate	Good	Good
BAP	Good	Good
72		
MacConkey	None	Good
Chocolate		
BAP		

which had a sensitivity pattern similar to that of the patient's strain.

Blood culture bottles were spiked with pure cultures of either *A. avenae*, MSSA, or a 50/50 mixture of the two organisms. Six milliliters of 0.45% saline in a suspension at a McFarland standard of 0.60 was used. The MSSA and the combined *A. avenae*-MSSA bottles turned positive at 5 h 13 min (both Gram stains showed GPC). The *A. avenae* bottle turned positive at 9 h 27 min (Gram stain showed GNRs). The combined *A. avenae*-MSSA bottle was reincubated and Gram stained after 20 h. This demonstrated both GPC and GNRs.

Comparative growth studies were performed at 27 and 37°C (Table 3). Three different media were used to plate *A. avenae* including MacConkey, chocolate, and blood agar plates. The organism demonstrated better growth at 37°C, and yet growth rates were still much lower than those of MSSA (data not shown). These findings support our assertion that *Acidovorax avenae* was initially missed because of the MSSA overgrowth.

The antibiogram for *A. avenae* supports this selection hypothesis. Culture of the port catheter demonstrated MSSA and *A. avenae*, suggesting that both organisms were relevant. Since there were no CLSI breakpoints for *A. avenae*, breakpoints were taken from MIC interpretive standards for other non-*Enterobacteriaceae* for the Etest and Sensititre methods (3). There was an obvious discrepancy between the Etest and Sensititre gentamicin MICs, which were 2 and 8 μg/ml, respectively. Repeat Etest performance confirmed the lower MIC. Fortunately, the addition of gentamicin led to a clinical improvement and the patient defervesced. The remainder of the hospital course was uneventful, and device removal coupled with 14 days of antibiotic treatment led to a successful clinical outcome.

Acidovorax infections in humans are rare. There is little information regarding clinical epidemiology, pathogenicity, or approach to treatment. One reported case of *Acidovorax* infection utilized ciprofloxacin for successful treatment (18). Treatment in the other case was not specified. To our knowledge, this is the third documented case of *A. avenae*-related bacteremia.

In this case, gentamicin proved effective. Antibiotic sensitivity testing of the GNR isolate by Etest provided rapid clinically useful information. This simple test allowed direct visualization of the effect of gentamicin on the organism's growth. We advocate at a minimum this type of testing in lieu of more advanced tests, particularly if the patient's course is not improving.

Our hospital laboratory initially missed the etiologic diagnosis of this GNR infection. The isolation of unusual bacteria on automated bacterial identification systems should raise suspicions about accuracy. Sequencing of 16S RNA with BLAST analysis yielded the identity of the causative organism—*Acidovorax avenae*—in this case. When clinical conditions mandate, we advocate a thorough diagnostic approach.

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