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Actinobaculum Bacteremia: a Report of 12 Cases[▽]

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Actinobaculum **species are anaerobic Gram-positive rods that have previously been associated with urinary tract infection (UTI) in the elderly. We report 12 patients with** ***Actinobaculum*** **bacteremia. Only 40% of blood cultures were clinically considered significant by the treating physicians, but most patients were treated for UTI, suggesting a possible urinary source of bacteremia. Clinicians should be aware of the pathogenic potential of** ***Actinobaculum*** **spp.**

Actinobaculum is a recently described genus, of which *Actinobaculum suis* is the type species (7). *A. suis* is a pathogen in swine, being the most common cause of urinary tract infection (UTI) in these animals (15). Three other species, *A. schaalii*, *A. massiliense*, and *A. urinale*, have been associated with human infection. Recent reports have identified *A. schaalii* as a cause of UTI in the elderly. However, standard methods for urine culture are inadequate for isolation and identification of *Actinobaculum* species in urine, so *Actinobaculum* UTI may be diagnosed only when accompanied by bacteremia (6, 7, 10). There appears to be little awareness among clinicians regarding the pathogenic role of *Actinobaculum* spp. Therefore, we describe the clinical characteristics of 12 patients from whom *Actinobaculum* spp. were isolated from blood (Table 1).

(This study was presented in part at the 111th General Meeting of the American Society for Microbiology, New Orleans, LA, 21 to 24 May 2011.)

Between November 2004 and May 2010, we identified 12 patients with a positive blood culture for *Actinobaculum* spp. at Mayo Clinic, Rochester, MN. Blood cultures were performed using sets of two Bactec Plus Aerobic/F bottles and one Bactec Lytic Anaerobic/F bottle incubated on the Bactec 9240 system (Becton Dickinson BioSciences, Sparks, MD). *Actinobaculum* spp. grew only in the anaerobic bottles, which were subcultured to blood agar and CDC anaerobic blood agar plates and incubated in an anaerobic chamber (Coy anaerobic glove box; Ann Arbor, MI) at 35°C. All isolates were identified using 16S rRNA gene sequencing using the following primers: 5′-TGGAGAGTTTGATCCTGGCTCAG-3′ and 5′-TACCGCGGCTGCTGGCAC-3′. DNA was prepared for PCR using PrepMan Ultra (Applied Biosystems, Foster City, CA) and subsequently amplified and sequenced using the BigDye Terminator method. The generated sequences were compared to the National Center for Biotechnology Information (NCBI) GenBank database. Antimicrobial susceptibility testing was performed under anaerobic conditions using the Etest (bioMérieux, Marcy l'Étoile, France) according to the manufacturer's instructions.

For nine patients, growth in blood culture bottles was observed in 2 days; for two patients, growth was observed in 1 day; and for one patient, growth was observed in 3 days. The sequences generated were between 464 and 486 bp. Out of 12 isolates, nine showed 100% identity to *A. schaalii*, one showed 95% identity to *A. schaalii* (GenBank accession no. EF151128.1), one showed 99.7% identity to *A. urinale* (GenBank accession no. NR_028978.1), and one showed 100% identity to *A. massiliense* (GenBank accession no. AF487679.1). The next closest match to all sequences (88 to 90% sequence identity) was *Arcanobacterium abortisuis* (GenBank accession no. AB305159.1). The isolate with 95% identity to *A. schaalii* was reported as *Actinobaculum* species. All were susceptible to penicillin (MIC, <0.5 μg/ml) and resistant to metronidazole (MIC, >256 μg/ml). Ten were susceptible to clindamycin (MIC, <0.5 μg/ml), and two were clindamycin resistant (cases 2 and 8; MIC, >256 μg/ml).

All patients were older than 65 years, with a mean age of 73 years. Men constituted 66% of patients, and the majority (10/12) had underlying urogenital pathology (benign prostatic hyperplasia, prostate cancer, urinary retention, urethral stricture, or urologic instrumentation).

Only 40% of blood cultures (5/12) were considered clinically significant by the treating physicians. This included four complicated UTIs and a case of UTI with perineal necrotizing cellulitis. For seven patients, the treating physicians considered the blood cultures not clinically significant. Six of these had UTIs (cases 3, 6, 7, 9, 10, and 12), and one had acute cholecystitis (case 4). Five patients (cases 3, 6, 9, 10, and 12) whose positive blood cultures were considered clinically nonsignificant but who were treated for UTI had negative or mixed-flora urine cultures. Four of these five (cases 6, 9, 10, and 12) had urine Gram stains performed, three of which showed many Gram-positive bacilli (cases 9, 10, and 12) and one of which was negative (case 6).

All patients received quinolones as initial antimicrobial therapy. In five patients, quinolones were changed to an antimicrobial regimen directed against *Actinobaculum* spp. In three patients, quinolones were prescribed to treat UTI. Two patients had clinical resolution of UTI symptoms after treatment, and one had clinical improvement while on treatment with no follow-up data available. One patient was initially treated with ciprofloxacin and changed to trimethoprim-sulfamethoxazole

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TABLE 1. Characteristic of patients with positive blood cultures for *Actinobaculum* species[a]

Patient	Age (yr)/gender	Diagnosis	Comorbidity(-ies)	No. of urine leukocytes/HPF	Urine Gram stain result	Urine culture result	Blood culture (no. of positive sets)[b]	Clinical significance (assessed by treating physicians)	Treatment (duration in days)
1	70/Male	UTI	BPH, prostate CA	100	GPB	–	*A. schaalii* (2)	Yes	Ciprofloxacin (3), pip-taz (2), amoxicillin-clavulanate (7)
2	89/Male	Urosepsis and pneumonia	Dementia, BPH	10	GPB, GPC	*Aerococcus urinae*	*Aerococcus urinae* (3), *A. schaalii* (2)	Yes	Pip-taz (14), amoxicillin-clavulanate (14)
3	70/Male	Urosepsis	BPH, CKD, diabetes	41–50	Not done	–	*A. urinale* (1)	No	Vancomycin plus cefepime (2), levofloxacin (7)
4	91/Male	Acute cholecystitis	Dementia	0	–	–	*A. schaalii* (1)	No	No antibiotics
5	90/Male	Complicated UTI and prostatitis	Dementia, BPH	51–100	GPC, GPB	Yeast	*A. schaalii* (2), *Candida glabrata* (1)	Yes	Penicillin G (5), cefpodoxime (42)
6	84/Male	Pneumonia and UTI	Dementia, recurrent hematuria	51–100	–	–	*A. schaalii* (1)	No	Levofloxacin plus metronidazole (14)
7	77/Male	Urosepsis	Dementia, Parkinson disease, urinary retention	51–100	GNB, GPB	*Escherichia coli*, *Enterococcus* sp.	*A. massiliense* (1), *Escherichia coli* (2)	No	Ciprofloxacin (4), TMP-SMX (17)
8	65/Female	Urosepsis s/p ureteral stents	Neurogenic bladder with cystectomy/ileal conduit/ureter stent	51–100	Not done	–	*A. schaalii* (2)	Yes	Ciprofloxacin (2), pip-taz (4), amoxicillin-clavulanate (14)
9	67/Female	UTI	Urethral stricture, rheumatoid arthritis	Not done	GPB	–	*A. schaalii* (1)	No	Ciprofloxacin (7)
10	81/Female	UTI	Lung CA	4–10	GPB	Mixed	CNS (1), *Actinobaculum* sp. (1)	No	Ceftriaxone (4), cephalexin (2)
11	77/Male	Perineal necrotizing cellulitis	Prostate CA, cystoprostatectomy, and artificial urethral sphincter	4–10	GPB	–	*A. schaalii* (2)	Yes	Vancomycin plus metronidazole (21)
12	94/Female	UTI	CKD, Evan syndrome, resection of bladder CA	41–50	GPB, GNB	–	*A. schaalii* (1)	No	Ciprofloxacin (7)

[a] Abbreviations: HPF, high-power field; UTI, urinary tract infection; BPH, benign prostatic hyperplasia; CKD, chronic kidney disease; CA, cancer; pip-taz, piperacillin-tazobactam; −, no growth; GPB, Gram-positive bacilli; GNB, Gram-negative bacilli; GPC, Gram-positive cocci; CNS, coagulase-negative *Staphylococcus* species; TMP-SMX, trimethoprim-sulfamethoxazole.

[b] A blood culture set consisted of two aerobic bottles and an anaerobic bottle.

with good clinical response, despite a positive urine culture for *Enterococcus* sp.

Actinobaculum spp. are nonsporulating, nonmotile, Gram-positive rods related to the *Arcanobacterium* and *Actinomyces* species. *Actinobaculum* spp. are anaerobes or facultative anaerobes that can grow on blood agar at 37°C in 5% CO_2 (7). Four species are currently described, *A. schaalii*, *A. massiliense*, *A. urinale*, and *A. suis*, the last being the type strain.

A. suis has been isolated from sows with cystitis (14). Interestingly, multiple case reports have associated *A. schaalii* with UTI in humans (6–8, 11). Despite the description of this bacterium as a cause of UTI, its isolation from urine is not routine in most clinical laboratories because it requires an anaerobic or CO_2 environment and prolonged incubation ($\geq$48 h) to grow (9). In addition, there are no standard methods for its identification, so molecular techniques are typically needed. Our laboratory does not routinely isolate *A. schaalii* from urine. Although seven blood cultures were clinically considered of questionable significance because only one set of blood cultures (of several performed) was positive, six of these patients were diagnosed and treated for UTIs, raising the possibility that many were actually significant bacteremias, associated with *Actinobaculum* UTI.

In a recent study of patients with *Actinobaculum* infection, all patients with positive urine cultures had pyuria, negative nitrates, and Gram-positive bacilli on urine Gram stain (2). The authors suggest that in patients with these findings and underlying urogenital pathology, *Actinobaculum* spp. should be screened for in the urine by prolonged incubation in 5% CO_2. Nielsen et al. showed that *A. schaalii* is isolated from the urine of 0.6% of the elderly with UTI (9). Using a real-time PCR, Bank et al. detected *A. schaalii* in 22% of 155 urine specimens of elderly patients (1). *A. schaalii* was also, however, detected in asymptomatic patients (up to 13%) by PCR, so (as with other uropathogens) its detection has to be correlated with clinical symptoms (1).

A. massiliense and *A. urinale* have been recently described in association with UTI (5) and septicemia in patients with chronic kidney disease (4), respectively. Besides UTI, other infections have been reported with *Actinobaculum* spp., including skin and soft tissue infection and vertebral osteomyelitis (6, 13). We present herein a case of perineal necrotizing cellulitis caused by *A. schaalii* in a 77-year-old man (case 11). Multiple tissue cultures and two sets of blood cultures grew *A. schaalii*. *A. schaalii* has been reported as a cause of Fournier's gangrene (12).

A. schaalii has been reported as being susceptible to penicillin and resistant to ciprofloxacin and trimethoprim-sulfamethoxazole, both of which are antibiotics commonly used in the treatment of UTIs (2, 10). All of our isolates (including the *A. urinale* and *A. massiliense* isolates) were penicillin susceptible. Ciprofloxacin was not tested. Three patients with *A. schaalii* and one with *A. urinale* were treated with a fluoroquinolone with good response. Patient 8 received ciprofloxacin prophylaxis prior to ureteral stent exchange and developed *A. schaalii* sepsis postoperatively. Of note, 5 months before the procedure, a urinalysis had shown many Gram-positive bacilli and cocci. Although quinolone susceptibility was not reported on this isolate, failure of prophylaxis may have related to lack of activity against *A. schaalii*. A recent study reporting *in vitro* susceptibility testing in 48 isolates of *A. schaalii* showed that all were resistant to ciprofloxacin but that 90 and 96% were susceptible to levofloxacin and moxifloxacin, respectively (3).

In this series, most patients with positive blood cultures for *Actinobaculum* spp. had concomitant UTIs, which we suspect (but cannot prove) were the likely source of the bacteremia. However, in the majority, the bloodstream isolate was considered by the treating clinician to be of questionable significance, possibly due to lack of knowledge of the recently recognized significance of *Actinobaculum* spp. New laboratory methods and techniques are needed for identification of *Actinobaculum* spp. in the urine to institute appropriate early antimicrobial therapy and prevent complications, including bacteremia.

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