

## *Gardnerella vaginalis* Bacteremia in Male Patients: A Case Series and Review of the Literature

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*Gardnerella vaginalis* colonization and invasive disease of the genitourinary tract in women has been well described. In men, this organism uncommonly causes infection, and bacteremia is rare. We describe 2 cases of *G vaginalis* bacteremia in men and present a review of the literature.

Our 2 patients each had underlying comorbid conditions that predispose to serious bacterial infection. One presented with symptoms of urinary tract infection, the other presented with sepsis. Urine, cultured under usual aerobic conditions, was negative in both cases, but blood cultures after prolonged incubation yielded *G vaginalis*. Treatment with antibiotics was successful in both cases. Our review of the medical literature revealed 12 previously reported cases of *G vaginalis* bacteremia in men. Almost all infections in men have originated in the genitourinary tract. Three patients had no reported history of or evidence for disease of the urinary tract, one each with endocarditis, empyema, and odontogenic abscess.

Isolation and identification of *G vaginalis* is often delayed. Selection and duration of treatment have ranged widely in previously reported cases, likely due to the absence of reports on antibiotic susceptibility of *G vaginalis* and a lack of guidance regarding effective treatment.

**Keywords.** bacteremia; *Gardnerella vaginalis*; male.

*Gardnerella vaginalis* is a known colonizer of the female genitourinary tract and can cause serious morbidity as a pathogen, especially after gynecologic procedures or obstetric complications [1, 2]. However, *G vaginalis* is an uncommon cause of infection in men, and, in men, bacteremia with this organism is rare. We now describe 2 cases of *G vaginalis* bacteremia in male patients.

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Our review of the English literature disclosed only 12 previous cases of bacteremia in men due to this organism. In the present study, we review the clinical and laboratory features of these 14 cases.

### CASE 1

A 52-year-old man with poorly controlled type 2 diabetes and a history of nephrolithiasis presented to the emergency department for 1 month of dysuria. He also reported hematuria, left-sided flank pain, sandy urine sediment, and a gritty sensation while voiding. He had previously required a left percutaneous nephrostomy and ureteral stent placement for obstructive nephrolithiasis and had received extracorporeal shock wave lithotripsy more than 2 years before presentation.

On presentation he was febrile and tachycardic with left costovertebral angle tenderness. His white blood cell (WBC) count was  $14.5 \times 10^9$  cells/L, creatinine 1.22 mg/dL, and blood glucose 293 mg/dL. Urinalysis revealed glucosuria, hematuria and pyuria. Urine and blood cultures were collected. Computed tomography of the abdomen and pelvis with contrast revealed left perinephric fat stranding, mild hydronephrosis, and a small calculus of the proximal left ureter.

He was treated empirically with ceftriaxone and then piperacillin-tazobactam. A left percutaneous nephrostomy was placed on the second day of hospitalization, followed by rapid clinical improvement. Aerobic culture of the urine from admission yielded  $<10\ 000$  colony-forming units/mL mixed Gram-positive flora. On hospital day 3, 2 blood cultures from admission yielded Gram-positive rods in anaerobic bottles. The organism was identified as *G vaginalis* by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF). He was treated with 500 mg of ciprofloxacin orally twice daily for 7 total days, based on a search of the available literature at the time, and the patient clinically recovered. No procedure was done to treat for renal stones. He was readmitted to the hospital with recurrent symptoms 1 month later; urine and blood culture then revealed *Escherichia coli* without isolation of *G vaginalis*.

### CASE 2

A 61-year-old man with alcohol use disorder, gout, and G6PD deficiency presented to the emergency room with altered mental status. On presentation he was hypothermic, but otherwise he had stable vital signs. His hemoglobin was 8.7 grams/dL and WBC count was  $17.8 \times 10^9$  cells/L. His serum creatinine was 1.74 mg/dL. A workup for hemolysis was unremarkable. Serum lactate was 15.7 mM/L, and his anion gap was 32 mEq/L.

**Table 1. Cases of *Gardnerella vaginalis* Bacteremia in Men**

Reference	Source of Bacteremia	Age	Comorbidities	Case Presentation/Clinical Course	Urinalysis/Urine Culture	Time to Blood Culture Growth	Treatment, Outcome
Bastida Vilá [12]	Urinary tract infection	78	Alcohol use disorder	Prostatic hypertrophy, recurrent urinary tract infections. Fever, chills, hematuria	Urinalysis with hematuria and 7 WBC/pf, no growth after 48 hours	7 days	Cefonicid for 10 days, clinical resolution.
Babics [13]	Urinary tract infection	36	None stated	Recurrent UTIs. Presented with fever and dysuria. Relapsed. Blood and urine cultures positive at readmission.	Urinalysis negative, Gram-negative coccobacilli seen, no growth. <i>G vaginalis</i> on readmission	5 days	Ciprofloxacin 14 days. Relapsed. Azithromycin + ceftriaxone, for 14 days, clinical resolution.
Bhatia [14]	Traumatic urinary catheter insertion	51	AIDS (off ART)	Presented with cryptococcal meningitis, developed urinary retention. Three attempts to place a urinary catheter followed by fever.	Urinalysis negative, urine culture not done	7 days	Ceftriaxone initially then metronidazole orally for 2 weeks, clinical resolution.
Wilson [15]	Urethral stricture	19	None stated	Urethral stricture. Fevers and chills; admitted to ICU for septic shock.	Urinalysis with pyuria, Gram-positive bacilli; no growth on culture	48 hours	Cefuroxime and gentamicin. Dilatation of urethral stricture. Clinical resolution.
Harper [16]	s/p TURP	60	None stated	s/p TURP developed rigors after removal of indwelling urinary catheter on postoperative day 3.	Urinalysis with scant RBCs and WBCs, <i>G vaginalis</i> on culture	24 hours	Gentamicin. Clinical outcome not stated.
Patrick [17]	s/p TURP	57	None stated	s/p TURP developed fever.	Urinalysis with 20 WBCs/hpf, no growth	7 days	Co-trimoxazole 2 tabs twice daily (no duration listed). Clinical resolution.
Alfrail [18]	Nephrolithiasis	77	CAD s/p CABG, colon cancer s/p hemicolectomy	Altered mental status and urinary frequency; found to have a renal calculus. No surgical intervention.	Urinalysis with numerous WBCs, no growth	Not stated	Ceftriaxone, then metronidazole to complete a 10-day course. Clinical resolution.
Lagacé-Wiens [11]	Pyelonephritis with nephrolithiasis	41	None stated	Admitted for flank pain, nephrolithiasis, and discharged without antibiotics. Returned 2 days later with worsened symptoms. Ureteral stent placed.	>10 <sup>7</sup> <i>Escherichia coli</i> per mL (at readmission)	5 days	Ciprofloxacin. Clinical resolution.
Pritchard [19]	Pyelonephritis with nephrolithiasis	36	Diabetes, HTN	Initial admission for flank pain, nephrolithiasis, and discharged without antibiotics; Returned with abdominal pain, fever, and worsening flank pain. Nephrostomy tube placed.	Urinalysis with 51 WBC/hpf, >10 <sup>5</sup> <i>G vaginalis</i> per mL (at readmission)	72 hours	Vancomycin, gentamicin, completed metronidazole for 14 days. Clinical resolution.
Denoyel [20]	Prostatic adenoma	65	None stated	Prostatic adenoma. Urinary frequency, urgency, fevers for 15 days. Urinary retention due to prostatic adenoma.	Urinalysis negative, no growth	NA	Amoxicillin and gentamicin. Unclear duration.
Yoon [6]	Endocarditis	39	Diabetes	Weight loss, malaise for 4 months. Vegetations on mitral valve with septic emboli to the kidney and brain. Underwent valvuloplasty, cultures and histology of the valve were unrevealing	No growth	At least 72 hours	Ceftriaxone and gentamicin, then metronidazole, ceftriaxone, erythromycin PO. Unclear clinical outcome.

**Table 1. Continued**

Reference	Source of Bacteremia	Age	Comorbidities	Case Presentation/Clinical Course	Urinalysis/Urine Culture	Time to Blood Culture Growth	Treatment, Outcome
Legrand [21]	Pneumonia, lung empyema, lung abscess	41	Alcohol use disorder	Fever and altered mental status. Found to have pneumonia, lung abscess, and empyema. Multiple bronchoscopic washings showed "contaminating oral flora" but eventually <i>G vaginalis</i> was isolated. Empyema culture with <i>Streptococcus milleri</i> , <i>Bacteroides oralis</i> , <i>Neisseria sicca</i> , and <i>G vaginalis</i>	Not reported	48 hours	Ceftazidime, penicillin, minocycline and metronidazole, clindamycin and ampicillin + minocycline, chloramphenicol (injected to pleural space). Expired after major fistulization between the abscess and the pleural space.
Current Report	Unknown	61	HTN, alcohol use disorder, gout, G6PD deficiency	Presented with altered mental status; found to have odontogenic sinusitis and a possible periodontal abscess, which was drained.	No urinalysis reported, No growth on urine culture	96 hours	Amoxicillin-clavulanic acid (14 days). Clinical resolution
Current Report	Nephrolithiasis	56	DM	Nephrolithiasis. Presented with hematuria and left flank pain, required percutaneous nephrostomy and ureteral stent placement for obstructive nephrolithiasis.	Urinalysis with pyuria, mixed Gram-positive flora (<10 000 CFU/mL), reported as suggestive of contamination	48 hours	Ciprofloxacin (7 days). Recurrent symptoms 1 month later, however, with different organisms

Abbreviations: AIDS, acquired immunodeficiency syndrome; ART, antiretroviral therapy; CABG, coronary artery bypass graft; CAD, coronary artery disease; CFU, colony-forming unit; DM, diabetes; HLD, hyperlipidemia; hpf, high-powered field; HTN, hypertension; ICU, intensive care unit; IV, intravenous; lpf, lower-powered field; NA, not applicable; NAFLD, nonalcoholic fatty liver disease; OSA, obstructive sleep apnea; PO, by mouth; RBC, red blood cells; S.p, status post; TURP, transurethral resection of the prostate; UTI, urinary tract infection; WBC, white blood cells.

The patient was treated with vancomycin and ceftipime empirically. Admission blood cultures demonstrated *Gardnerella vaginalis* in the anaerobic bottle of 1 of 2 cultures, reported 96 hours after their collection. No urinalysis was reported; however, urine culture remained negative. The patient was treated with ampicillin-sulbactam and switched to amoxicillin-clavulanate on discharge to complete a 14-day course with clinical resolution.

## DISCUSSION

In 1955, Gardner and Dukes [2, 3] first described *G vaginalis*, initially named *Haemophilus vaginalis*, which was linked to bacterial vaginosis in women. The bacterium was briefly reclassified as *Corynebacterium vaginale* before being renamed *G vaginalis* [4]. *Gardnerella vaginalis* is a facultative anaerobic Gram-positive pleomorphic rod, which is also described as Gram variable due to poor staining of the thin peptidoglycan cell wall [1, 3]. It grows slowly and requires a complex medium for growth; thus, isolation and identification are often delayed [2]. Early case reports suggested that the organism yields identifiable colonies on chocolate agar after 24–72 hours of incubation at 37°C under 10% CO<sub>2</sub> [5, 6].

A regular inhabitant of the female reproductive tract, *G vaginalis* has also been isolated from men; urethral colonization was reported in 4.5% of men whose female partners were found to carry the organism [7]. Kinghorn et al [8] reported a prevalence of 7.2% in men who presented to their genitourinary department of medicine with new urethral complaints. When compared with men who had sex with men, heterosexual men were shown to have a higher prevalence of urethral colonization (14.5% vs 4.5%) [9].

The proposed virulence factors of *G vaginalis* in bacterial vaginosis include exotoxin secretion (vaginolysin), vaginal mucus degradation by enzymes, and biofilm formation [10]. Other likely mechanisms of virulence include production of hemolysin and sialidase, which result in local tissue damage and evasion of mucosal immunity [11]. It remains uncertain whether these same virulence factors play a role in causing disease in males.

*Gardnerella vaginalis* bacteremia in men is a rare phenomenon, but almost all infections have originated in the genitourinary tract (Table 1) [11–20]. Three cases occurred in men who had no recognized urinary tract disease [6, 21]. Our Case 2 did not report a urinalysis but urine culture was negative. The cases of *G vaginalis* bacteremia described by Yoon et al [6] and Legrand et al [21] implicate endocarditis and an empyema as the sources of bacteremia. Legrand et al [21] did not report any urinalysis or urine culture, so it is unclear whether there was a potential urinary tract infection, and Yoon et al [6] reported that urine culture did not exhibit growth. Another severe case, described by Wilson et al [15], found a urethral stricture as a

predisposing factor. All 3 cases had identification of the causative organism within 48 to 72 hours of collection of blood cultures, and all received combination antibiotic therapy. The usual methods for routine culture are not likely to isolate this fastidious organism, which leads to a prolonged time to identification. Of those reports that included duration of time between collection of blood cultures and speciation, it ranged from 48 hours to 7 days. Many laboratories relied on automated microbial identification systems for identification, whereas others had to send the isolates out to reference laboratories for further identification. Our institutional laboratory utilized the MALDI-TOF Biotyper from Bruker Daltonik GmbH, which is capable of phylogenetically differentiating the diverse groups of *Gardnerella* [22].

Of the 10 cases with a urinary tract as the probable source of bacteremia, 4 showed significant pyuria on urinalysis [15, 17–19], 2 had only scant WBCs [12, 16], 3 had unremarkable urinalyses [13, 14, 20], and 1 with no reported urinalysis [11]. It is interesting to note that only 3 cases demonstrated *G vaginalis* on urine culture [13, 16, 19].

To date, there are no susceptibility data available for *Gardnerella vaginalis* from either the Clinical and Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing, and there are no guidelines on the treatment of *Gardnerella vaginalis* infections in males. Reported minimum inhibitory concentrations from infections in men show that susceptibility to antibiotics is strain-dependent.

## CONCLUSIONS

Bacteremic infection in men due to *G vaginalis* is rare; our 2 cases bring the total reported in the English medical literature to 14. Abnormalities of the urinary tract appeared to be an obvious or likely source in most cases. A source in 3 cases, including our Case 2, is unknown, and only 1 described a urine culture but no urinalysis. *Gardnerella vaginalis* grows slowly in anaerobic blood culture bottles or under 10% CO<sub>2</sub> on chocolate agar plates, so it is not surprising that isolation from urine is only rarely reported. Selection and duration of treatment have ranged widely, likely due to the lack of information on susceptibility to antibiotics or guidance regarding effective treatment.

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