Gardnerella vaginalis bacteremia in a previously healthy man – Case report and characterization of the isolate

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Gardnerella vaginalis in women causes vaginitis or infections in other sites such as the urinary tract, but is an infrequent cause of bacteremia. Bacteremia in men is very rare, typically associated with immunocompromised states. Here we describe G. vaginalis bacteremia in a previously healthy man with renal calculi and urosepsis.

Case Report

A 41 year old male roofer with no prior medical problems presented with sudden onset of left flank pain. The pain was colicky in nature and not accompanied by fever, chills, urgency or dysuria. Physical examination at the time of presentation was unremarkable. A CT scan of the abdomen revealed a 6.5mm kidney stone in the mid pole of the kidney and a 3mm calculus at the left vesicoureteric junction. Obstructive uropathy and perinephric stranding was noted. Urine biochemistry revealed slight hemoglobinuria. The patient underwent ureteroscopy the following day, and as no infection was thought to be present, no antibiotics were given. The distal ureteric calculus was not seen and assumed to have passed spontaneously. Follow-up imaging demonstrated only the larger proximal stone. He was discharged from the hospital but returned two days later with worse flank pain. The CT scan was repeated and demonstrated a 4mm stone on the proximal left ureter with small fragments remaining in the mid pole of the kidney. Additional investigations revealed a leucocyte count of 16.0 x 10⁹ cells/L (normal range 4-11 x 10⁹) with a predominance of neutrophils (absolute count 12.6 x 10⁹ cells/L, normal count 2-5 x 10⁹). Creatinine was elevated at 148 µmol/L (normal range 70-110 µmol/L). He was re-admitted for repeat ureteroscopy. Prior to this procedure, the patient was febrile, with a temperature of 39.1°C and rigors. He appeared otherwise well
and his physical examination, including blood pressure was unremarkable. Ciprofloxacin 400mg IV q12h was empirically started for presumed urosepsis. His complete blood count was normal and cultures of urine and blood (two sets, with 20 ml from one site for anaerobe and aerobic culture, and 10ml from a second site for an aerobic bottle) were taken prior to initiating antimicrobial therapy. The quantitative urine culture revealed $6.5 \times 10^7$ CFU/L of a ciprofloxacin sensitive strain of *Escherichia coli*. On the fifth day of incubation, the aerobic blood culture from the first set were flagged as positive by the automated Bac/T Alert™ system. Subculture of the second blood culture set revealed the same organism. The hospital laboratory was unable to achieve a definitive identification of the blood culture isolate, so it was sent to a reference center.

The patient underwent repeat ureteroscopy with lithotripsy and extraction of the proximal stone. A ureteric stent was inserted and removed the week following. He was treated with a 10 day course of oral ciprofloxacin and had no recurrences or sequelae.

Initial Gram stain of the blood culture revealed pleomorphic, gram-negative coccobacilli. The blood culture isolate was plated to in-house prepared 5% sheep blood agar (base agar Oxoid Ltd. Ottawa ON, sheep blood supplied by Quad Five, Ryegate MT) and chocolate agar (Oxoid) in 5% CO₂, MacConkey agar (Oxoid) in aerobic incubation, and on brucella agar with vitamin K (Oxoid) for anaerobic incubation. After 48 hours of incubation, small grey colonies were observed on the chocolate agar with poor growth of grey, non-hemolytic colonies on sheep blood agar. Gram stain revealed similar gram- negative coccobacilli. Catalase and rapid oxidase were negative and so the isolate was referred out to the Canadian National Microbiology Laboratory as a suspected *Franciscella*.
F. tularensis. Rapid molecular-based testing indicated the isolate was not F. tularensis and further testing was undertaken, the strain being assigned NML Special Bacteriology identifier 060420. Repeat Gram staining suggested the organism was gram-positive to gram-variable short rods. Colonies were pinpoint (after 2d) to small (~1mm) translucent colonies (after 4d), with no hemolysis observed after growth on 5% sheep blood agar. The isolate did have a narrow zone of beta hemolysis after 4d on Vaginalis agar, which contains human red blood cells (PML MicrobiologicaI, Mississauga, ON). The isolate grew well at 37°C in 5% CO₂ and under strictly anaerobic conditions but no growth was observed in air at 25°C, 37°C or 42°C. Biochemical testing using carbohydrate (CHO) tube sugars, metabolic products of fermentation, cellular fatty acid (CFA) composition analysis and 16SrRNA gene sequencing were performed as previously described (3, 4). Acid was observed in CHO sugars containing galactose, glucose, glycogen, maltose sucrose and xylose. The strain produced lipase, and was negative for fermentation of fructose, glycerol, lactose, mannitol, mannose, raffinose, ribose, salicin and trehalose. Tests for utilization or hydrolysis of citrate, esculin, urea, nitrate reduction, indole, methyl red, Voges-Proskauer, gelatin and lecithinase production were all negative. An API Strep strip used as described by the manufacturer (Biomerieux, Montreal QC) generated a code of 2050001, which corresponds with a 99.8% confidence value of identification as G. vaginalis, including utilization of starch. These reactions are consistent with identification as G. vaginalis (6). The major metabolic product was acetic acid. CFA composition was consistent with those observed for G. vaginalis strains referred to the NML as well as for the type strain ATCC 14018, with CFA s C14:0, C16:0, 18:1ω9c and C18:0 predominating (3, 13).
Sequence analysis of a 1463 bp segment of the 16S ribosomal DNA of the organism demonstrated a 99.2% identity with *G. vaginalis* ATCC 14018T (GenBank accession no. M58744) and clustering only within GenBank’s 16S sequences for *G. vaginalis*. Nearly full 16S sequence for this isolate has been deposited as GenBank accession no. EF194095.

Antimicrobial susceptibilities were determined by microbroth dilution using Sensititre® GPN3F panels and cation adjusted Mueller Hinton broth with lysed horse blood (2-5% v/v) by Trek Diagnostics Inc (Nova Century Scientific Inc, Burlington ON) using manufacturer’s instructions and following CLSI guidelines for *Streptococcus* spp. other than *S. pneumoniae* (8). Minimum inhibitory concentrations (ug/ml) observed were: erythromycin ≤0.25, quinupristin/dalfopristin ≤0.12, vancomycin ≤1.0, ampicillin 0.5, rifampin ≤0.5, clindamycin ≤0.12, daptomycin 0.5, tetracycline ≤2.0, levofloxacin 1.0, linezolid ≤0.5, penicillin 0.5, gentamicin ≤2.0, ciprofloxacin 1.0, trimethoprim/sulfamethoxazole, ≤1/19, ceftriaxone ≤8.0, and gatifloxacin ≤1.0, consistent with previous findings (6).

*Gardnerella vaginalis* is typically associated with bacterial vaginosis (6). It has also been reported as a pathogen in women following delivery or pelvic surgery, potentially leading to preterm rupture of membranes, chorioamnionitis, post-partum fever and bacteremia and in neonates (1, 11, 14). However, in one study, 7-11% of men had *G. vaginalis* as part of their urogenital or anorectal flora, leading to the possibility of urinary tract colonization and infection (9). In this instance, the patient had a sexual partner but status regarding colonization or infection by this agent was not known. Rarely, *G. vaginalis*
bacteremia has been described in men, usually in men with identifiable risk factors including immunosuppression, anatomical genitourinary abnormalities or alcoholism (2, 5, 10, 12, 15). Here we present the first published case of G. vaginalis bacteremia in a previously healthy man with urolithiasis. Although the patient’s urine culture grew a potential uropathogen, it was present in <10^8 cfu/L and was not identified in any of the blood cultures obtained despite the patient not receiving antimicrobials at the time of culture. Furthermore, due to lack of onsite microbiology facilities, 15 hours elapsed from the time of specimen collection to its arrival at the microbiology laboratory, and for part of that period, refrigeration for storage of the urine was not available. Therefore, the isolation of E. coli from the urine specimen may have represented overgrowth of a contaminant. Lastly, since two sets and three bottles of blood cultures were positive for G. vaginalis but neither were positive for E. coli, it is unlikely that this organism was playing a role in his urosepsis.

Treatment of G. vaginalis infections outside the female genital tract has not been studied. Previous case reports have documented successful therapy with β-lactams, tetracyclines, cephalosporins, clindamycin, chloramphenicol and metronidazole alone or in combination (2, 5, 10, 12, 15). Cases of severe sepsis have been treated with combination therapy (5, 12, 15). In our case, the removal of the stone and a short course of ciprofloxacin therapy were curative.

Virulence factors of G. vaginalis are not well characterized. The bacterium produces a hemolysin and a sialidase which play a role in evading mucosal immunity and result in local tissue damage (7). Techoic acid in the cell wall may produce a systemic
inflammatory response after invasion, but the factors that allow the organism to cause systemic infection are not known. However, a recent report of *G. vaginalis* bacteremia with multifocal abscess formation in an alcoholic but otherwise immunocompetent patient suggests the organism has some capacity to evade the immune response (5).

In conclusion, we report the first case of urolithiasis complicated by *G. vaginalis* bacteremia in an otherwise well male patient. The patient was successfully treated with stone extraction and a short course of ciprofloxacin without adverse sequelae. This case illustrates that *G. vaginalis* may be an occasional cause of significant systemic disease in both men and women and that the original smear, being read as a gram-negative coccobacillus, caused some delay in diagnosis and correct identification of the pathogen.


