Urinary tract infection caused by *Actinobaculum schaalii*: a urosepsis pathogen that should not be underestimated

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Introduction: *Actinobaculum schaalii* is a Gram-positive facultative anaerobic coccoid rod bacterium that grows slowly in culture. This bacterium was classified as a new genus in 1997 but is often overlooked or considered a contaminant because of both its resemblance to the normal bacterial flora on skin and mucosa and the overgrowth of other bacteria. During the past decade, *A. schaalii* has emerged as a more common urinary tract pathogen than previously thought.

Case presentation: Here, we describe the case of a patient with an untreated *A. schaalii* urinary tract infection that turned into urosepsis.

Conclusion: This case shows that the invasive potential of this bacterium should not always be underestimated.

Keywords: *Actinobaculum schaalii*; emerging uropathogen; penicillin; urosepsis.

Case report

An overweight 62-year-old man had been diagnosed with locally advanced prostate cancer with a Gleason score of 4+3 5 years ago and received combined radiation and hormone therapy after initial treatment. His initial prostate-specific antigen (PSA) level was 63 ng ml⁻¹. An increase in PSA levels was discovered during follow-up (from 0 to 12 ng ml⁻¹), indicating recurrence of the disease, which required maximum androgen blockade therapy. The disease also progressed locally, with the gradual onset of obstructive renal failure initially requiring internal ureteral stents. In December 2013, the patient was hospitalized in the urology department of the University Hospital of Tours owing to severe renal failure requiring haemodialysis. His C-reactive protein level was 66 mg l⁻¹ and his creatinine level 369 µmol l⁻¹, indicating severe kidney damage due to post-renal blockage. Urinary drainage was required, and a percutaneous right nephrostomy tube was inserted into his kidney to drain his urine. Collected urine was purulent and was therefore sent to the laboratory for cytobacteriological examination. Analysis of a urine sample from the nephrostomy tube showed high counts of leukocytes (>10,000 mm⁻³) and erythrocytes (>10,000 mm⁻³).

Urine was plated on a ChromID CPS3 plate according to standard procedures (BioMérieux), but no growth was observed after 18 h at 37 °C. Gram-staining of the urine sample, kept at 4 °C and stained the second day, revealed the presence of Gram-positive rods. Owing to the presence of these Gram-positive bacilli on direct examination and in the absence of growth on ChromID CPS3 medium, the urine was plated again on chocolate agar at 37 °C under 5% CO₂ and on sheep blood agar under anaerobic conditions at 37 °C. Small colonies, corresponding to 10³ c.f.u. ml⁻¹, were observed on both plates after 48 h of incubation; however, the colonies grew better on sheep blood agar than on chocolate agar. The growing Gram-positive rods were catalase-negative and could not be identified by the API Coryne System or the Vitek ANC System (BioMérieux). Matrix-assisted laser desorption/
ionization time-of-flight MS (MALDI-TOF-MS) on a Vitek-MS instrument (BioMérieux) also failed to identify the strain. The bacterium was finally identified by 16S rRNA gene sequencing. A 633 bp sequence was obtained and sequence homology search on the BIBI database (http://pbil.univ-lyon1.fr/bibi) found 98 % identity with A. schaalii strain FJ960443. The antibiotic susceptibility of the bacterium was assessed in vitro by the disc-diffusion method on Columbia blood agar under anaerobic conditions. Consistent with the CA-SFM (Antibiogram Committee of the French Society for Microbiology) criteria for Streptococcus spp., the strain was highly susceptible to all beta-lactams tested, including penicillin. It was also susceptible to tetracycline, linezolid, rifampicin, vancomycin and clindamycin. The isolate was resistant to trimethoprim–sulfa-methoxazole and ciprofloxacin. The patient was not treated because he was asymptomatic (no clinical signs of infection or biological inflammatory syndrome).

The patient was admitted again to the urology department for the replacement of his nephrostomy tube 52 days later. Two hours after surgery, the patient developed fever with a peak of 39.4 °C. Blood and urine cultures were performed and the patient received 1 g ceftriaxone. The patient became apyretic and after 48 h of monitoring in the hospital, he was discharged without antibiotics. Urinalysis detected 10³ c.f.u. Enterobacter cloacae (ml urine)⁻¹. The E. cloacae was WT, susceptible to ceftriaxone. Despite careful examination, no colonies other than those of E. cloacae were observed on plates. Culture of E. cloacae does not allow the detection of other bacteria. However, a Gram-positive rod was isolated from the anaerobic bottle of a blood culture incubated for 48 h in the BACTEC 9240 culture system (Becton Dickinson). After 48 h, subcultures on horse blood agar plates incubated under aerobic conditions were negative, but those on sheep blood agar under anaerobic conditions were positive, and contained small non-haemolytic colonies (less than 1 mm in diameter) of rod-shaped Gram-positive bacilli. The bacterium could not be identified by classical biochemical methods. Therefore, the species was identified by 16S rRNA gene sequencing of the colonies. BLAST analysis of the 623 bp nucleotide amplicon showed 98 % identity with A. schaalii type strain. This isolate showed the same profile of antibiotic susceptibility as the first isolate. The patient was treated orally with amoxicillin for 14 days.

**Discussion**

*A. schaalii* is a Gram-positive coccoid rod that can cause UTIs in humans and occasionally septic complications (Beguelin et al., 2011; Cattoir, 2012; Gomez et al., 2011; Reinhard et al., 2005; Tavassoli et al., 2012). *A. schaalii* is common among elderly people with suspected UTI and may be clinically significant, when found alone or together with other bacteria, in children and in patients treated for kidney stones and those with underlying urological conditions (Andersen et al., 2012; Bank et al., 2010, 2011; Nielsen et al., 2010; Vasquez et al., 2013; Zimmerman et al., 2012). This bacterium is easily overlooked in cultures because it grows slowly and requires carbon dioxide (Lawson et al., 1997). Thus, if urine samples are cultured in ambient air or if there is growth of conventional species, this bacterium can go undetected. *A. schaalii* is an emerging pathogen, and has been increasingly associated with UTIs in the past decade (Cattoir, 2012). The detection of this Gram-positive rod in clinical isolates indicates that it is not an innocent bystander and can cause infection (Tschudin-Sutter et al., 2011). Olsen et al. (2013) found that *A. schaalii* is a commensal bacterium found in urine and on the skin and vaginal mucosa in the human urogenital area. Other studies support these findings and show that the elderly are at greatest risk of being colonized with *A. schaalii*, and that *A. schaalii* is also a potential pathogen in patients with kidney stones undergoing extracorporeal shock wave lithotripsy (Olsen et al., 2013; Tschudin-Sutter et al., 2011). These studies did not find *A. schaalii* in faeces.

Our patient can be classified as an individual at high risk of *A. schaalii* infection. Colonization of the nephrostomy tube by *A. schaalii* during the first episode of bacteruria, associated with local immunosuppression, could have promoted infection. Moreover, this first UTI was considered simple colonization and was therefore not treated, which in turn may have led to sepsis with the same bacterium. This case illustrates well the pathogenicity of this bacterium. The recommended antibiotics are beta-lactam-based (Nielsen et al., 2010; Reinhard et al., 2005; Sturm et al., 2006). The optimal duration of antibiotic therapy is unknown, but previous failures in 1-week-long treatment suggest that treatment should last at least 2 weeks (Nielsen et al., 2010; Reinhard et al., 2005). Indeed, 2 weeks of antibiotic therapy appears to be the minimum requirement to avoid recurrences and the spread of the bacterium to secondary sites. Thus, this case, in addition to previous reports (Tschudin-Sutter et al., 2011; Sandlund et al., 2014; Sturm et al., 2006; Zimmermann et al., 2012), demonstrates that *A. schaalii* should be considered a true opportunistic uropathogen with potential to spread and cause severe infections. In the paper by Tschudin-Sutter et al., 2011, the authors observed 27 patients with an isolate of *A. schaalii* in clinical samples. Among these patients, *A. schaalii* was implicated in an invasive infection in 81.5 % and the bacterium was detected in blood cultures in 10 cases and only half of them were associated with urinary tract infections. The majority of the remaining patients had underlying intra-abdominal infections and one patient suffered from spondylodiscitis (Tschudin-Sutter et al., 2011). In other studies, *A. schaalii* has mainly been considered as a pathogen in a UTI context and in cases of treatment failure (Gomez et al., 2011; Beguelin et al., 2011; Sandlund et al., 2014). Therefore, screening patients with underlying urological conditions for this pathogen may be useful in order to enable early implementation of antibiotic therapy to prevent invasive infections.

Another important issue involves the susceptibility profile of the bacterium. *A. schaalii* is susceptible to penicillin,
third-generation cephalosporins, aminoglycosides, and nitrofurantoin, but is usually resistant to ciprofloxacin and trimethoprim–sulfamethoxazole, which are widely used for treatment or prophylaxis in urology (Andersen et al., 2011; Cattoir et al., 2010; Cattoir, 2012; Larios et al., 2010; Nielsen et al., 2010; Reinhard et al., 2005; Sturm et al., 2006). A study by Andersen et al. (2011) suggests that pivmecillinam is an effective alternative to other beta-lactams for the treatment of A. schaalii UTIs. Pivmecillinam has several advantages: urinary pathogens are highly susceptible to this antibiotic and very high urinary concentrations can be achieved owing to its active excretion in urine.

Most clinicians are not aware of this potential uropathogen. Thus, clinicians must be encouraged to work closely with biologists. Urologists should notify the laboratory if they suspect urinary infection with an unusual organism such as A. schaalii, based on risk factors and urologic history of the patient. Accordingly, conventional laboratory methods must be updated to isolate A. schaalii from biological specimens. In addition, laboratories should also consider A. schaalii as a possible cause of UTI in culture-negative urine specimens, especially if Gram-positive cocci rods and/or leukocytes are present on the Gram stain. Barberis et al. (2014) proposed a simple approach involving a vancomycin disc, Mann, Rogosa and Sharpe (MRS) growth broth (Difco, BD, Franklin Lakes, USA) and a sodium polyanethol sulfonate disc for the preliminary identification of A. schaalii. This approach may help laboratories that are unable to perform molecular techniques for identification.

In conclusion, although A. schaalii is a rare cause of UTIs, our case illustrates the potential invasiveness of this pathogen, and shows that it should be taken into consideration, particularly for patients presenting underlying urological conditions. The development of MALDITOF-MS is likely to lead to more accurate diagnosis and will improve our understanding of the epidemiology of A. schaalii infections (McKew et al., 2013). The eradication of this pathogen, especially in patients with catheters, will probably require several weeks of treatment and further studies are needed to define optimal regimens.

References


