Propionimicrobium lymphophilum and *Actinotignum schaalii* bacteraemia: a case report

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Abstract

Propionimicrobium lymphophilum is an anaerobic Gram-positive bacillus that exists in human skin and urinary tract. The pathogenicity is, however, not well known. Only two cases of urinary tract infection have been described recently. In the case presented here, the bacterium was isolated, concomitant with *Actinotignum schaalii,* from blood culture of a patient with fever and difficulty of urination. The bacteria were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and 16S rRNA sequencing. The case was successfully treated with ampicillin/sulbactam.

Keywords: *Actinotignum schaalii*, bacteraemia, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, *Propionimicrobium lymphophilum*, 16S rRNA sequencing
Original Submission: 17 December 2016; **Revised Submission:** 25 March 2017; **Accepted:** 28 March 2017
Article published online: 4 April 2017

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Introduction

Propionimicrobium lymphophilum was originally described as a member of the *Corynebacterium*. However, because it growths under anaerobic condition and produces propionic acid, this bacteria was classified as *Propionibacterium* and then was reclassified in 2002 as a single species in the genus *Propionimicrobium* [1]. This organism colonizes in the human skin and genital tract [2–4].

Actinotignum schaalii is a facultative anaerobic Gram-positive bacillus and originally was described as a member of *Actinobaculum* in 1997 [5]. As of 2015, the genus *Actinobaculum* was divided into *Actinotignum* and *Actinobaculum* [6]. *A. schaalii* is currently considered to be an emerging uropathogen because it has been associated with urinary tract infections (UTIs) in many cases [7–10]. In contrast to that of *A. schaalii,* the pathogenicity of *P. lymphophilum* remains poorly defined. A single case report was published of nonbacteraemic UTI of the anaerobe [11].

Here we report the first case of *P. lymphophilum* bacteraemia with *A. schaalii.* The organisms were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and 16S rRNA sequencing, and the case was successfully treated with ampicillin/sulbactam.

Case Report

An 80-year-old man visited our emergency department complaining of fever, chills and general fatigue after several days with difficulty urinating. The patient regularly visited the outpatient clinic for postsurgical follow-up of colon cancer with pulmonary metastasis. He also had bladder dysfunction due to diabetes mellitus neuropathy.

At admission, he had no significant physical signs, but his vital signs were as follows: body temperature, 38.9°C; blood pressure, 164/74 mm Hg; pulse rate, 95/min; and respiratory rate, 24/min. Laboratory data were as follows: white blood cell count, 9300/μL (neutrophil 71.9%); serum creatinine, 1.79 mg/dL; and C-reactive protein, 7.01 mg/dL. Urinary analysis revealed 3+ leukocyte esterase and positivity for nitrites. Abdominal computed tomography revealed bilateral hydronephrosis and bilateral dilatation of the ureters. The presence of fluid around the seminal gland and thickening of the urinary bladder were also observed.

Insertion of a urinary catheter resulted in the discharge of more than 1000 mL of turbid urine. The patient was clinically diagnosed with postrenal pyelonephritis by urinary stasis due to neurogenic bladder. After the collection of two sets of blood culture bottles with aseptic procedure and one urine specimen for culturing, ceftriaxone therapy was initiated (day 0). On day 2, the urine culture detected only α-streptococci on sheep's blood/chocolate agar (Eiken Chemicals, Tokyo, Japan), incubated at 37°C in 5% CO_2. Although it was inoculated for subculture on sheep's blood/chocolate agar again, no colony

http://dx.doi.org/10.1016/j.nmni.2017.03.004

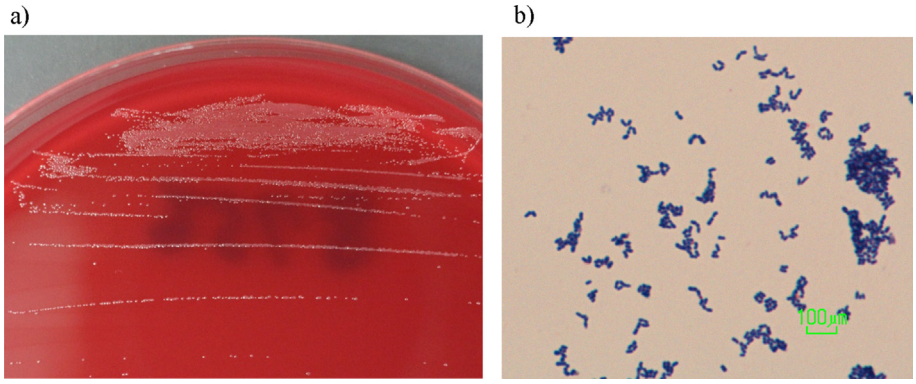

FIG. 1. Morphology of *Propionimicrobium lymphophilum*. (a) Appearance of colonies was small, grey and tiny after 72 hours' growth on *Brucella* agar medium under anaerobic conditions. (b) Gram staining of (a) revealed the presence of short Gram-positive bacilli with coccoid form.

growth was observed. The α-streptococci could not be isolated and identified. No anaerobic culture was performed in routine analysis.

Two anaerobic bottles of two sets of blood cultures (BacT/ALERT; SYSMEX bioMérieux, Tokyo, Japan) collected on day 0 yielded one each of two Gram-positive bacilli on day 4 and day 5. After a further 72 hours under anaerobic conditions, streaks of both of the isolates grew as small grey-colored, smooth colonies on *Brucella* agar (Figs 1 and 2). Both anaerobes were identified as *Actinomyces meyeri* by VITEK2 ANC identification card (SYSMEX bioMérieux). However, MALDI-TOF MS (using the MALDI Biotyper; Bruker Daltonics, Bremen, Germany) identified one of the anaerobes as *Actinotignum schaalii* and the other as *Propionimicrobium lymphophilum*.

16S rRNA sequencing was also performed [12] and identified these bacteria as *A. schaalii* and *P. lymphophilum,* respectively. Specifically, comparison to sequences in the BLAST database (http://www.ncbi.nlm.nih.gov/BLAST) revealed that the case isolates showed 99% homology with GenBank accession numbers HQ992948 and HM135521 respectively. Antimicrobial susceptibility testing was performed anaerobically by Etest (SYSMEX bioMérieux) on *Brucella* HK agar plates (Kyokuto Pharm Ind, Tokyo, Japan). The minimum inhibitory concentration (MIC) results are shown in Table 1.

The antibiotic therapy was changed on day 9 to ampicillin/sulbactam. Two sets of blood culture bottles were collected at the time of changeover in antimicrobial agent; both of these blood cultures were sterile. On day 12, abdominal computed tomography revealed improvement of bilateral pyelonephritis, and magnetic resonance imaging indicated the presence of prostate cancer and invasion of the seminal vesicles. A biopsy of the prostate was performed, and the presence of prostate cancer was pathologically confirmed. Therefore, we suspected that *P. lymphophilum* and *A. schaalii* might cause bacteraemia through UTI with invasive prostate cancer and neurogenic bladder. Recurrence of bacteraemia by these anaerobes was not observed after completion of 32 days of antimicrobial therapy.

Discussion

We describe here a case of bacteraemia due to *P. lymphophilum* and *A. schaalii. A. schaalii* has already been recognized as an emerging human uropathogen [7–10]. Increased risk of

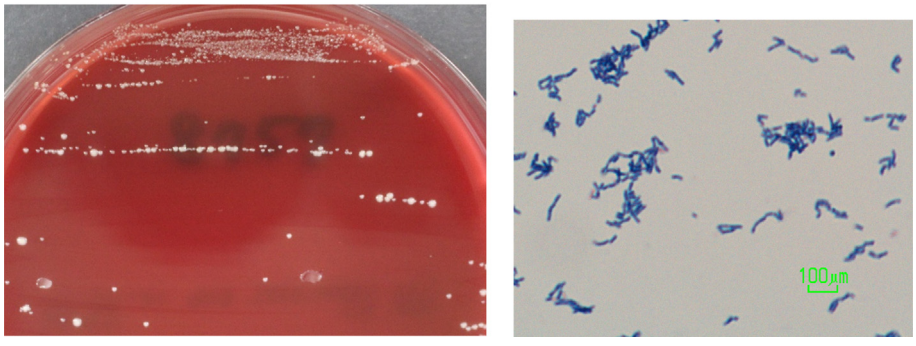

FIG. 2. Morphology of *Actinotignum schaalii*. (a) Appearance of colonies was small, light yellow to grey-colored and smooth after 72 hours' growth on *Brucella* agar medium under anaerobic conditions. (b) Gram staining of (a) revealed the presence of Gram-positive slightly curved rods that seemed to be longer than *P. lymphophilum*.

TABLE 1. Antimicrobial susceptibility of *Propionimicrobium lymphophilum* and *Actinotignum schaalii*

Antimicrobial	Minimum inhibitory concentrations (mg/L)	
	A. schaalii	*P. lymphophilum*
Ampicillin	<0.016	<0.016
Cefotaxime	0.012	0.064
Cefepime	0.016	0.25
Cefoxitin	0.016	0.19
Meropenem	0.008	<0.002
Vancomycin	0.094	0.064
Clindamycin	<0.016	0.032
Clarithromycin	<0.016	<0.016
Minocycline	0.023	<0.016
Levofloxacin	1	0.5
Metronidazole	>256	>256

Minimum inhibitory concentrations were determined by Etest on *Brucella* HK agar plates.

A. schaalii infection has been reported for the elderly, especially those with diseases of the genitourinary region, and for newborns using diapers [10,13]. The present case was considered as high risk for *A. schaalii* infection because the patient was elder with prostate cancer.

P. lymphophilum has been reported as a possible urogenital pathogen based on metagenomic analysis using 16S rRNA sequencing [4]. Two cases have been reported of non-bacteraemic UTI associated with *P. lymphophilum* [11]. In this case, *P. lymphophilum* caused bacteraemia from the patient with UTI. Further cases are needed to clear the clinical characteristics and risk factors for *P. lymphophilum* infection.

MALDI-TOF MS has been reported to provide more accurate identification of bacteria, even anaerobes, compared to phenotypic methods based on biochemical reactions (e.g. VITEK2) [14]. Indeed, in the present work, *A. schaalii* and *P. lymphophilum* were misidentified as *A. meyeri* by the VITEK2 system. Although the reference standard for bacterial identification is 16S rRNA sequencing, such sequencing is not routinely used in clinical microbial laboratories. MALDI-TOF MS was useful for the rapid correct identification of these anaerobic bacilli in this case.

A. schaalii is susceptible to penicillin, cephalosporin and carbapenem [10,13] but has high MICs of sulfamethoxazole/trimethoprim and fluoroquinolones, which are antibiotics often used to treat UTIs. In the present case, *P. lymphophilum* showed low MICs of β-lactam antibiotics and a high MIC of levofloxacin. Clinical breakpoints of antimicrobial susceptibility against *P. lymphophilum* or *A. schaalii* are not provided. In the present case, anaerobic polymicrobial bacteraemia was diagnosed; given that β-lactam antibiotics are the preferred therapy for *A. schaalii,* treatment with ampicillin/sulbactam was selected.

We report here the first case and successful treatment of bacteraemia due to *P. lymphophilum* and *A. schaalii*. MALDI-TOF MS was useful for the rapid correct identification of these anaerobic bacilli.

MALDI-TOF MS spectrum accession number

The MALDI-TOF MS spectrum of the *Propionimicrobium lymphophilum* isolate (*Propionimicrobium lymphophilum* 8756) and the *Actinotignum schaalii* isolate (*Actinotignum schaalii* 8757) are available online (http://mediterranee-infection.com/article.php?laref=256&titre=urms-database).

Nucleotide sequence accession number

The 16S rRNA gene sequences were deposited in DDBJ/EMBL/GenBank databases under the accession numbers LC222741 for *Propionimicrobium lymphophilum* and LC222742 for *Actinotignum schaalii.*

Ethics statement

Written informed consent for publication of the clinical details was obtained from the patient.

Conflict of Interest

None declared.

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