Staphylococcus pettenkoferi bacteremia: A case report and review of the literature

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AA Hashi, JA Delport, S Elsayed, MS Silverman. *Staphylococcus pettenkoferi* bacteremia: A case report and review of the literature. Can J Infect Dis Med Microbiol 2015;26(6):319-322.

Staphylococcus pettenkoferi is a relatively recently described coagulase-negative staphylococci species first described in 2002. Since then, nine additional cases of infection caused by this species have been reported in various countries around the world, including Germany, Belgium, France, South Korea, Italy, Brazil and Mexico. The present report describes a case of *S pettenkoferi* peripheral line-associated bacteremia. To our knowledge, the present report is the first description of human infection caused by *S pettenkoferi* in Canada. The present report also provides an overview of the laboratory detection of uncommon coagulase-negative staphylococci.

Key Words: *Bacteremia; Coagulase negative; MALDI-ToF;* Staphylococcus pettenkoferi

La bactériémie à *Staphylococcus pettenkoferi* : rapport de cas et analyse bibliographique

Le *Staphylococcus pettenkoferi* est une espèce de staphylocoque à coagulase négative qui a été décrit pour la première fois en 2002. Depuis, neuf autres cas d'infections causées par cette espèce ont été signalés dans divers pays du monde, y compris l'Allemagne, la Belgique, la France, la Corée du Sud, l'Italie, le Brésil et le Mexique. Le présent rapport décrit un cas de bactériémie à *S pettenkoferi* associée à un cathéter périphérique. En autant que les auteurs le sachent, il s'agit du premier rapport d'infection humaine à *S pettenkoferi* au Canada, qui donne également un aperçu de la détection en laboratoire de staphylocoques à coagulase négative rares.

CASE PRESENTATION

A 75-year-old woman presented to the emergency department after experiencing an unwitnessed fall at home. She had been experiencing symptoms consistent with vertigo for a few days before presentation. Her medical history was significant for hypertension, type 2 diabetes mellitus, psoriasis, dyslipidemia, a seizure disorder and right knee arthroplasty. Collateral history revealed that she had been assessed one week before for a planned total left knee arthroplasty, which had subsequently been postponed after the patient had been found to have a truncal rash that had been present for two weeks.

Her physical examination was significant for a petechial maculopapular rash on her chest, arms and legs, as well as a positive Dix-Hallpike test. Vitals signs were within normal parameters and she was afebrile. Initial laboratory investigations (electrolytes, urea, creatinine, glucose) were unremarkable. She had a hemoglobin level of 138 g/L, white blood cell count of 9.0×10^9 cells/L and a platelet count of 176×10^9/L. While in the emergency department, a peripheral intravenous (IV) catheter was placed at the dorsum of her left hand for administration of fluids.

The patient was admitted for further assessment and evaluation. Twelve hours later, she became febrile, but was otherwise asymptomatic. Two blood samples were drawn from separate venipuncture sites and sent for culture. Both sets of blood cultures were positive for Gram-positive cocci in clusters. She was then administered empirical IV vancomycin (1 g every 12 h).

Staphylococcus pettenkoferi was isolated in both blood cultures using a 3 h short-incubation matrix-assisted laser desorption/ionization time-of-flight (MALDI-ToF) identification protocol. It was approximately 36 h from the time of blood culture draws until preliminary results demonstrated coagulase-negative staphylococci, and 51 h for the final culture result of *S pettenkoferi*. The positive blood cultures were subcultured onto a Columbia blood-agar plate (Oxoid, Thermo Fisher Scientific Inc, USA) and incubated at 35°C in 5% CO_2 for 3 h. Identification of the isolates was performed using the Microflex LT with FlexControl version 3.4 software (Bruker Corporation, USA) for the automatic acquisition of mass spectra in the linear positive mode within a range of 2 kDa to 20 kDa. Automated analysis of the raw spectral data was performed using the MALDI BioTyper automation version 3.1 software (Bruker Corporation, USA).

The isolate was identified as *S pettenkoferi* (score 1.904); the top four choices were all strains of *S pettenkoferi*. *Staphylococcus parauberis* (score 1.250) was considered to be the next most likely identification.

TABLE 1
Susceptibilities for isolated *Staphylococcus pettenkoferi* performed using AST-GP67 cards on the Vitek 2* system

	S pettenkoferi	
Drug	**VMICINT**	**VMICDIL, mg/L**
Clindamycin	Susceptible	≤0.25
Erythromycin	Susceptible	0.5
Oxacillin/cloxacillin	Susceptible	2
Trimethoprim/sulfamethaoxazole	Susceptible	≤10
Vancomycin	Susceptible	1

**BioMerieux, France. VMICDIL Vitek mean inhibitory dilution interpretation; VMICINT Vitek mean inhibitory concentration interpretation*

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TABLE 2
Patient demographics, mode of diagnosis and treatment

Study	Age, years/ sex	Comorbidities	Presentation	Culture	Biochemistry/diagnosis	Treatment	Outcome
Trülzsch et al (1), 2002; Germany (strain B3117 [index strain])	25/unknown	Extrapulmonary TB	Fever of unknown origin, weight loss; found to have TB	Blood culture	Biochemistry: API/ID32 Staph* initially suggested *Kocuria rosea* or *Staphylococcus capitis*. Diagnosis: confirmed using 16S rRNA gene sequencing followed by genomic DNA preparation and pulsed-field gel electrophoresis.	Rifampin, pyrazinamide, ethambutol. Specific treatment of *S pettenkoferi* not mentioned.	Successful (recovered)
Loïez et al (3), 2007; France	63/male	Diabetes, chronic diabetic foot infection	Osteomyelitis displayed in x-ray findings following worsening pain, redness and wound exudate	Bone biopsy (4 of 6 specimens produced bacteria)	Biochemistry: API/ID32 Staph initially suggested *K rosea* and *Micrococcus lylae*; a second API/ID32 Staph strip using a larger inoculum and incubation period suggested *S capitis* or *Staphylococcus auricularis*. Diagnosis: confirmed using MicroSeq 500† DNA sequencing of 16S rRNA genes with subsequent homology search on NCBI GenBank compared with entry strain B3117 from 2002.	Transtarsal amputation, then pristinamycin ×14 weeks	Successful (recovered)
Trülzsch et al (2), 2007; Germany (strain K6999)	Unknown	Unknown	Unknown	Blood culture	Biochemistry: API/ID32 Staph initially suggested *S capitis* or *S auricularis*. Diagnosis: confirmed using 16S rRNA gene sequencing (one base pair difference), partial *rpoB* gene sequencing (99.8% similarity), 100% DNA–DNA hybridization and RiboPrint‡ analysis (nearly identical) compared with strain B3117 from 2002.	Unknown	Unknown
Trülzsch et al (2), 2007; Belgium (isolate 229)	Unknown	Unknown	Unknown	Blood culture	Biochemistry: API/ID32 Staph initially suggested *S capitis* or *S auricularis*. Diagnosis: Confirmed using 16S rRNA gene sequencing (identical), partial *rpoB* gene sequencing (99.8% similarity) and RiboPrint analysis (nearly identical) compared with strain B3117 from 2002.	Unknown	Unknown
Trülzsch et al (2), 2007; Belgium (isolate 230)	Unknown	Unknown	Unknown	Blood culture	Biochemistry: API/ID32 Staph initially suggested *S capitis* or *S auricularis*. Diagnosis: confirmed using 16S rRNA gene sequencing (identical), partial *rpoB* gene sequencing (99.8% similarity) and RiboPrint analysis (nearly identical) compared with strain B3117 from 2002.	Unknown	Unknown
Song et al (4), 2009; South Korea	76/male	Recurrent pulmonary TB	Admitted for recurrent pulmonary TB. Developed Stevens-Johnson syndrome. Became febrile while being treated for both; found to have bloodstream infection	Blood cultures from different lumens of a central line	Biochemistry: MicroScan WalkAway Pos Combo Panel§ suggested *Staphylococcus hominis* (92%) or *S auricularis* (99%); VITEK 2 Gram Positive Identification system suggested *S auricularis* (70%), *S capitis* (50%), or *Staphylococcus wrneri* (50%); API/ID32 Staph V4 1 Kit suggested *S capitis* (61.5%) or *Kocuria varians*/*K rosea* (27.8%). Gene sequencing: gene sequencing of 16S rRNA using the MicroSeq Microbial Identification System¶ and a consensus sequence of 495 base pairs suggested *Staphylococcus caprae* (99.36%), *Staphylococcus hyicus* (96.94%), or *Staphylococcus cohnii* (97.08%). Diagnosis: using a larger sequence of 1533 base pairs and sending the data to GenBank suggested *S pettenkoferi*. Phylogenetic tree confirmed isolate to be most consistent with *S pettenkoferi*.	Vancomycin 2 g IV every 24 h ×1 week	Successful (negative blood cultures; patient then treated for TB)
d'Azevedo et al (5), 2010; Brazil	56/unknown	Unknown	Unknown	Blood cultures	Biochemistry: VITEK 2* identification system suggested *K varians*. Diagnosis: confirmed using DNA sequencing of 16S rRNA and *sodA* genes with subsequent homology search on GenBank matching *S pettenkoferi*.	Unknown	Unknown

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TABLE 2 – CONTINUED

Study	Age, sex	Comorbidities	Presentation	Culture	Biochemistry/diagnosis	Treatment	Outcome
Mammina et al (6), 2011; Italy	49/male	Post-traumatic hydrocephalus	Surgical treatment of hydrocephalus. Underwent placement of ventriculoperitoneal drain, replaced by external ventricular drain 10 days later due to occlusion of internal device. External drain became infected. Treated, but developed shock 10 days later	Blood cultures (source of sepsis suspected of being bloodstream)	Biochemistry: VITEK 2 suggested *S capitis*; API/ID32 Staph suggested *S capitis*. Diagnosis: confirmed using DNA sequencing of 16S rRNA genes with homology search on GenBank (100% similarity to strains B3117 and A6664).	Daptocycin 8 mg/kg and Pip-Tazo 4.5 g × 4 doses, then daptomycin alone	Unsuccessful (died)
Morfin-Otero, et al (7), 2012; Mexico	Newborn/male	Premature (33 weeks)	Fever	Blood cultures (1 of 3)	Biochemistry: API/ID 32 Staph suggested *K varians*; Sensititre did not identify isolate. Diagnosis: confirmed using DNA sequencing of 16S rRNA, *sodA* and *tuf* genes with subsequent homology search on GenBank matching *S pettenkoferi*.	Ampicillin ×4 days, amikacin ×4 days, then ampicillin ×10 days	Successful (recovered)
Morfin-Otero, et al (7), 2012; Mexico	45/male	AIDS, herpes zoster, hepatitis C	Cerebral toxoplasmosis	Blood cultures (2 of 2)	Biochemistry: API/ID32 Staph suggested *K varians*; Sensititre suggested *Staphylococcus cohnii epidermidis*. Diagnosis: confirmed using DNA sequencing of 16S rRNA, *sodA* and *tuf* genes with subsequent homology search on GenBank matching *S pettenkoferi*.	Clindamycin ×8 days, trimethoprim/sulfamethoxazole ×8 days, azithromycin ×8 days, amphotericin B ×8 days	Unsuccessful (died)

**BioMerieux, France; †Applied Biosystems, USA; ‡DuPont, USA; §Beckman Coulter, USA; ¶Life Technologies, USA. IV Intravenous; NCBI National Center for Biotechnology Information; rRNA Ribosomal RNA; TB Tuberculosis*

A score >1.700 and a differential spread of 0.654 (being greater than the recommended 0.200 spread) helped secure the identification of this organism to genus and species.

The isolate was catalase positive, with a Gram-stain consistent with a *Staphylococcus* species, differentiating it from the next available genus identification of *Streptococcus*. As part of the routine processing of positive blood cultures with Gram stain suggestive of staphylococci species, polymerase chain reaction was performed for detection of methicillin resistance and to differentiate the strain from *Staphylococcus aureus*. Neither the *nuc* nor *mecA* genes were detected, therefore, confirming that this was a coagulase-negative methicillin-susceptible staphylococcal strain.

Susceptibility testing was performed using AST-GP67 cards on the Vitek 2 (BioMerieux, France) microbial identification system. The isolate had a minimum inhibitory concentration of 2 mg/L for oxacillin indicating that it was susceptible. Susceptibilities are listed in Table 1.

The patient developed erythema and mild tenderness at the site of her peripheral intravenous catheter, and was diagnosed with catheter-associated bacteremia. The IV catheter was removed and her antibiotic therapy was changed to 2 g IV cloxacillin every 6 h, after having received two days of IV vancomycin. A transthoracic echocardiogram demonstrated no evidence of valvular heart disease or vegetations. Consideration was initially given to conducting a skin biopsy to better delineate the cause of the patient's rash; however, the rash resolved spontaneously. Her vertigo improved with the use of particle repositioning manoeuvres. The patient was given a prescription to complete a seven-day course of 500 mg oral cloxacillin every 6 h for six days because she had completed one day of IV cloxacillin in hospital. She was then discharged home. Repeat blood cultures taken five days after completion of antibiotic therapy were negative.

DISCUSSION

S pettenkoferi is a coagulase-negative *Staphylococcus*. *S pettenkoferi* was first described by Trülzsch et al (1) in 2002. While the authors initially reported two cases of infection with this organism (strains B3117 and A6664), subsequent investigations revealed that only one of the isolates (B3117) was *S pettenkoferi* (2); that strain was recovered from a blood culture sample in a patient with extra pulmonary tuberculosis. Since then, nine cases have been documented in the literature (Table 2). Trülzsch et al (2) described three more isolates of *S pettenkoferi* in Germany and Belgium (strain K699, isolate 229 and isolate 230) all from blood cultures, and all displaying 100% DNA-DNA homology with strain B3117 from their 2002 study. Also in 2007, the first case of *S pettenkoferi* osteomyelitis was described by Loïez et al (3) in France in a 63-year old diabetic man using bone biopsy cultures. Song et al (4) described the first case of *S pettenkoferi* in Asia in 2008 from central line blood cultures in a 76-year old man in South Korea with tuberculosis and Stevens-Johnson syndrome who developed bacteremia. The first South American case of *S pettenkoferi* was described by d'Azevedo et al (5) using blood cultures from a patient in Brazil. Other cases have also been reported including one case in Italy (6) using blood cultures and two cases in Mexico (an adult with HIV and a premature infant) using blood cultures, which were the first reported cases in North America (7).

To our knowledge, this is the first case of *S pettenkoferi* reported in Canada. While our patient did have a history of a maculopapular rash, the rash was deemed unlikely to be related to her infection, particularly because it preceded her IV catheter insertion. We were unable to perform convalescent serology for infectious causes of rash because the patient was subsequently lost to follow-up.

It is known that coagulase-negative staphylococci are associated with infections of indwelling and implanted devices (8). This is possibly consistent with the present patient's presentation, although a peripheral IV site was believed to be involved in her case. With regard to antibiotic choice, different agents have been used (see Table 2). To the best of our knowledge, our patient was the first to be treated successfully with cloxacillin, albeit having previously received a short course of vancomycin (Table 1).

We suspect that *S pettenkoferi* is significantly more commonly encountered than the above reports would suggest. Laboratory identification can be challenging because biochemical tests may result in misidentification of *S pettenkoferi* as *Staphylococcus hominis*, *Staphylococcus auricularis*, *Staphylococcus capitis* and *Kocuria varians* (Table 2). In several situations, the correct identity of the bacterium was not made until molecular tests, such as 16S ribosomal RNA (rRNA) gene sequencing were performed. Notwithstanding, while genetic sequencing of 16S rRNA has been the most commonly used method to confirm the diagnosis of *S pettenkoferi*, strain A6664, one of the two originally described *S pettenkoferi* isolates, has a slightly different *rpoB* gene sequence and does not have 100% DNA-DNA homology with the other strains described in 2007 by Trülzsch et al (2) compared to strain B31117. This suggests that it is a different species altogether and, therefore, 16S rRNA gene sequencing may not be sufficiently robust to definitively diagnose the presence of *S pettenkoferi*.

A limitation of our study is the lack of sequencing data because the isolate is no longer available. Nevertheless, we believe that in the present case the species diagnosis is confirmed. Our laboratory uses MALDI-ToF mass spectrometry. MALDI-ToF has been used to correctly identify other coagulase-negative staphylococci that have been under-reported in the past, such as *Staphylococcus lugdunensis* (9). The use of MALDI-ToF may result in increased reports of *S pettenkoferi* infection. In studies performed at our institution, the Bruker MALDI-ToF correctly identified 485 of 485 coagulase-negative staphylococci to the species level. Included in these were 117 isolates of *S capitis* and *S hominis* species that were all identified correctly by the MALDI-ToF with none being identified as *S pettenkoferi* (10,11).

DISCLOSURES: The authors have no financial relationships or conflicts of interest to declare.

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