Jpn. J. Infect. Dis., 70, 682–684, 2017

Short Communication

Two Rare Cases of Wound Infections Caused by *Trueperella bernardiae*

Fernando Cobo[1]*, Javier Rodríguez-Granger[1], Antonio Sampedro[1], José Gutiérrez-Fernández[2], and José María Navarro-Marí[1]

[1]*Department of Microbiology, University Hospital Virgen de las Nieves, Instituto Biosanitario de Granada; and* [2]*Department of Microbiology, School of Medicine, University of Granada, Granada, Spain*

SUMMARY: *Trueperella bernardiae (T.bernardiae)* is a gram-positive curved rod that is considered an uncommon pathogen involved in few infections. The true incidence of infections with this bacterium, and the clinical implications, remain unknown. We report 2 cases of wound infections in 2 patients who underwent different surgical procedures, although in the second case the microorganism was isolated in mixed culture. Culture of wound secretions resulted in isolation of *T. bernardiae*. Treatment was performed and resolution of the infections was documented.

Trueperella bernardiae (T. bernardiae) was originally classified within the provisionally named CDC fermentative coryneform group 2 (1), transferred to the genus *Arcanobacterium* (2), and finally reclassified into the genus *Trueperella* (3). *T. bernardiae* was initially isolated from a variety of clinical sources (1), but the first isolation in pure culture was reported by Ieven et al. in 1996 (4). To our knowledge, only 8 additional cases of human infection in pure culture have been reported in the medical literature, which consist of urinary tract infection (5), joint infection (6-8), skin and wound infection (9, 10), blood infection (11), and infection of both kidney and pleura (12).

We were recently confronted with 2 cases of wound infection caused by *T. bernardiae* in 2 patients after different surgical procedures, one of them in pure culture.

A 69-year-old woman underwent an anterior rectal resection in 2000, owing to rectal carcinoma. In 2001, the patient was treated with abdominoperineal amputation and eventroplasty; in 2006, a terminal colostomy was performed. Otherwise, her clinical history was unremarkable. After 2006, the patient experienced several episodes of pericolostomy eventration, and in April 2017, a medial laparotomy was performed to relocate the colostomy.

On the seventh postoperative day, the patient had fever (38.0ºC), pain, and drainage of purulent material through the surgical wound. A complete blood count, chemical profile, and urinalysis were all normal except for a C-reactive protein (CRP) level of 218 mg/L (normal value 0.02–5 mg/L) and white cell blood count (WBC) of 12,270/mm^3 (70% neutrophils). Treatment with metronidazole (500 mg / 8 h / 7 days) and ciprofloxacin (500 mg /12 h / 7 days) was started. An aspirate of purulent exudate was sent to the microbiology laboratory for culture. The sample was inoculated in blood agar (either aerobic or anaerobic) (BD™ Columbia Agar with 5% Sheep Blood; Becton Dickinson, NJ, USA), chocolate agar (BD™ Chocolate Agar; Becton Dickinson), and thioglycollate broth (BD™ Fluid Thioglycollate Medium; Becton Dickinson). All media were incubated at 37ºC. Gram staining of the exudate revealed no microorganisms. On the third day of incubation, growth of gram-positive bacilli in pure culture was observed in all plates. The observed colonies were nonhemolytic, rounded, creamy, and whitish (Fig. 1). Mass spectrometry (Bruker Biotyper; Billerica, MA, USA) was used to identify the strain as *T. bernardiae* (score 2.13), which was confirmed by 16S rRNA gene sequencing. The minimum inhibitory concentration (MIC) of the bacteria to different antibiotics was determined by the Etest method (bioMérieux, Marcy l'Étoile, France). As no specific clinical breakpoints have been established for *T. bernardiae*, we used the EUCAST PK/PD (non-species related) clinical breakpoints. The isolate was susceptible to penicillin G (MIC 0.094 µg/mL), linezolid (MIC 0.38 µg/mL), amoxicillin/clavulanate (MIC 0.047 µg/mL), and resistant to ciprofloxacin (MIC 1.5 µg/mL). Vancomycin, clindamycin, daptomycin, erythromycin, and gentamicin were not evaluated because no PK/PD clinical breakpoints have been defined for them.

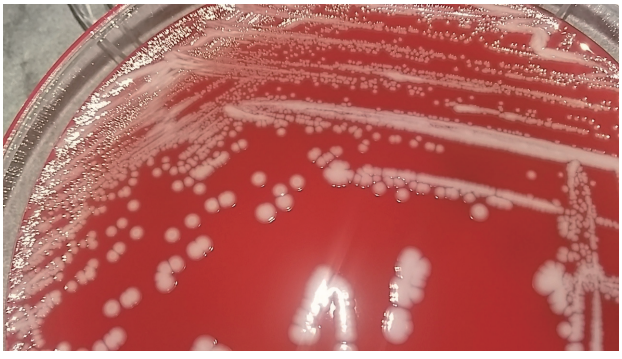

Fig. 1. (Color online) Aspect of colonies of *Trueperella bernardiae*. The colonies were non-hemolytic, rounded, creamy and whitish.

Received May 16, 2017. Accepted July 18, 2017.
J-STAGE Advance Publication September 11, 2017.
DOI: 10.78883/yoken.JJID.2017.221

*Corresponding author: Mailing address: Department of Microbiology, Hospital Virgen de las Nieves,Avda Fuerzas Armadas 2, Granada 18014, Spain. Tel: +34 958020364, Fax: +34 958241245, E-mail: fernando.cobo.sspa@juntadeandalucia.es

Blood cultures taken on admission were negative. Treatment was changed and amoxicillin-clavulanate (500 mg /8 h) was administered for 7 days. At 1 month follow-up, the patient remained well.

Our second case was a 70-year-old woman that came to the Emergency Department in April 2017 due to fever, pain, and infection signs in an inguinal granuloma. The patient underwent major abdominal surgery in 2012 owing to unilateral ovarian cancer. She was also treated with coadjuvant chemotherapy based on Carbo/Taxol (paclitaxel and carboplatin). In May 2014, the patient was found to have inguinal ganglionar metastasis and was treated with Caelyx, Carbo/Taxol, and topotecan. In January 2016, she underwent removal of the inguinal adenopathies. After that time, the patient presented with an ulcerated inguinal granuloma with chronic purulent secretion. A complete blood count, chemical profile, and urinalysis were all normal except for a C-reactive protein (CRP) level of 18 mg/L. Treatment with metronidazole (500 mg / 8 h / 7 days) was started without improvement. An aspirate of purulent exudate was sent to the microbiology laboratory for culture, and the sample was processed as in the first case. Gram staining of the exudate exhibited gram-positive and gram-negative bacilli. On the first day of incubation, growth of predominantly gram-positive bacilli along with gram-negative bacilli was observed in all plates. The aspect of the colonies was similar to the first case. Using the same mass spectrometry method, the bacteria were identified as *T. bernardiae* (score 2.08) and *Escherichia coli* (score 2.26), respectively. *Trueperella* was also confirmed by 16S rRNA gene sequencing. Following the same procedure as in the first case to test for antimicrobial susceptibility, the isolate was found to be susceptible to penicillin G (MIC 0.064 μg/mL), linezolid (MIC 0.75 μg/mL), amoxicillin/clavulanate (MIC 0.047 μg/mL) and resistant to ciprofloxacin (MIC 2 μg/mL). Treatment with amoxicillin/clavulanate (500 mg / 8 h) was administered for 7 days and improvement was observed.

Table 1. Main findings in 16 patients with infection caused by *Trueperella bernardiae*

Patient (year of publication) Author	Age (years)/ sex	Localization of infection	Clinical manifestation	Microbiological diagnosis	Treatment	Outcome
1(1996)[1] Ieven M	69/M	Urinary tract	Fever	Urine, perirenal abscess and necrotic tissue cultures Blood culture (+)	Amoxicillin-clavulanate Drainage and excision	Cure
2(1998)[1] Adderson EE	19/F	Hip	Pain, fever, deteriorating renal function	Synovial fluid culture	Vancomycin + cefotaxime Clindamycin	Cure
3(1998)[1] Lepargneur JP	75/M	Urinary tract	Pain, fever	Urine culture	Netilmicin + cefixime Amoxicillin	Cure
4(2009) Bemer P	63/M	Knee	Wound drainage	IoS	Clindamycin + fusidic acid	Cure
5(2009)[1] Loïez C	78/M	Hip prosthesis	Haematoma, pain	IoS	Linezolid + cefotaxime Rifampicin + ofloxacin	Cure
6(2010)[1] Sirijatuphat R	60/M	Kidney Pleura	Fever, dysuria, pain, weight loss	Perinephric drainage culture	Ceftazidime Ceftriaxone + clindamycin	Cure
7(2010) Clarke TM	62/F	Skin abscess	Abdominal pain, redness of the skin, fever, mass on the skin	Abscess and tissue cultures	Vancomycin + aztreonam Piperacillin-tazobactam	Cure
8(2011)[1] Weitzel T	72/F	Blood	Fever, chills, anorexia, prostration	Blood cultures (+)	Ceftriaxone + metronidazole Amoxicillin + clavulanate	Cure
9(2013) Otto MP	78/F	Wound	Fever, leg and sacrum ulcers	Ulcer culture Blood cultures (+)	Ceftriaxone + ciprofloxacin + metronidazole Amoxicillin + clavulanate	Cure
10(2015) Parha E	68/F	Brain	Confusion, vomiting, slurry speech, incontinence	Abscess culture	Gentamicin + teicoplanin + metronidazole + ceftriaxone Amoxicillin + metronidazole + ceftazidime Ceftriaxone	NR
11(2015) Schneider UV	45/M	Skin ulcers	Foot ulcers, fever	Ulcer tissue culture	Piperacillin-tazobactam + ciprofloxacin + gentamicin Amoxicillin	Cure
12(2016)[1] Rattes ALR	24/F	Wound	Fever, pain, secretion	Umbilical secretion culture	Piperacillin-tazobactam + vancomycin Amoxicillin + clavulanate	Cure
13(2016)[1] Gilarranz R	73/F	Knee prosthesis	Leg pain	Synovial fluid Blood cultures (+)	Ciprofloxacin	Cure
14(2016)[1] VanGorder B	77/F	Skin	Indurated lesion, pain, drainage	Drainage abscess culture	Trimethoprim/ sulfamethoxazole	Cure
15(PR/2017)[1] Cobo F	69/F	Wound	Wound drainage, fever	Wound secretion culture	Amoxicillin + clavulanate	Cure
16(PR/2017) Cobo F	70/F	Inguinal granuloma	Wound drainage, fever	Wound secretion culture	Metronidazole Amoxicillin + clavulanate	Cure

M, male; F, female; NR, not reported; CRP, C-reactive protein; IoS, intraoperative specimens.
[1]: Cases with *T. bernardiae* found in pure culture.

T. bernardiae is a gram-positive bacillus that forms part of the normal microbiota of human skin and the oropharynx. Few cases of infection due to this microorganism in pure culture have been reported until now (4-12), and 5 additional cases have been reported as causing mixed infections (Table 1). The true incidence of infections with this bacterium is unknown because when isolated in clinical samples, these coryneform bacteria are not identified. For that reason, today its occurrence is uncommon and the pathogenicity and clinical implications of *T. bernardiae* have not yet been clearly established, especially when infections are polymicrobial and also contain other kinds of microorganisms.

The diagnosis of *T. bernardiae* infection is mainly based on culture of an adequate sample obtained from the site of infection, although final identification may be difficult because it could be confused with other microorganisms such as other coryneform bacteria, gram-positive bacilli, or streptococci (13). Regarding identification, the use of new mass spectrometry technologies may greatly assist in the final identification, as in our case. Use of MALDI-TOF has represented a breakthrough in the identification of these kinds of microorganisms owing to its speed and accuracy (14).

The treatment of choice for *T. bernardiae* infections has not yet been established due to both the scarcity of data and absence of clinical breakpoints for this bacterium. Some studies have shown that *T. bernardiae* is susceptible to all antimicrobial drugs tested, except for ciprofloxacin (4, 15). However, other studies show resistance to clindamycin and erythromycin (9), norfloxacin and fosfomycin (13), metronidazole (6), pefloxacin (5), and penicillin G (7). However, the lack of standardization and absence of clinical breakpoints for antimicrobial studies of *T. bernardiae* prevent any conclusion being drawn about antimicrobial susceptibility, thereby necessitating further studies. Meanwhile, patient monitoring through susceptibility testing is advisable.

Conflict of interest None to declare.

REFERENCES

1. Na'Was TE, Hollis DG, Moss CW, et al. Comparison of biochemical, morphologic, and chemical characteristics of centers for disease control fermentative coryneform groups 1, 2, and A-4. J Clin Microbiol. 1987;25:1354-8.
2. Ramos CP, Foster G, Collins MD. Phylogenetic analysis of the genus *Actinomyces* based on 16S rRNA gene sequences: description of *Arcanobacterium phocae* sp. nov., *Arcanobacterium bernardiae* comb. nov., and *Arcanobacterium pyogenes* comb. nov. Int J Syst Bacteriol. 1997;47:46-53.
3. Yassin AF, Hupfer H, Siering C, et al. Comparative chemotaxonomic and philogenetic studies on the genus *Arcanobacterium* Collins et al. 1982 emend. Lehnen et al. 2006: proposal for *Trueperella* gen. nov. and emended description of the genus *Arcanobacterium*. Int J Syst Evol Microbiol. 2011;61:1265-74.
4. Ieven M, Verhoeven J, Gentens P, et al. Severe infection due to *Actinomyces bernardiae*: case report. Clin Infect Dis. 1996;22:157-8.
5. Lepargneur JP, Heller R, Soulié R, et al. Urinary tract infection due to *Arcanobacterium bernardiae* in a patient with a urinary tract diversion. Eur J Clin Microbiol Infect Dis. 1998;17:399-401.
6. Adderson EE, Croft A, Leonard R, et al. Septic arthritis due to *Arcanobacterium bernardiae* in an immunocompromised patient. Clin Infect Dis. 1998;27:211-2.
7. Loïez C, Tavani F, Wallet F, et al. An unusual case of prosthetic joint infection due to *Arcanobacterium bernardiae*. J Med Microbiol. 2009;58:842-3.
8. Gilarranz R, Chamizo F, Horcajada I, et al. Prosthetic joint infection caused by *Trueperella bernardiae*. J Infect Chemother. 2016;22:642-4.
9. Rattes ALR, Araujo MR, Federico MP, et al. *Trueperella bernardiae*: first report of wound infection post-laparoscopic surgery. Clin Case Rep. 2016;4:812-5.
10. VanGorder BRF, Ahmed SS, Rwling RA, et al. *Trueperella bernardiae* abscess infection: a case report. Clin Microbiol Newsletter. 2016;38:100-1.
11. Weitzel T, Braun S, Porte L. *Arcanobacterium bernardiae* bacteremia in a patient with deep soft tissue infection. Surg Infect. 2011;12:83-4.
12. Sirijatuphat R, Angkasekwinai N. Perinephric abscess and empyema thoracis due to *Arcanobacterium bernardiae*. J Infect Dis Antimicrob Agents. 2010;27:103-8.
13. Otto MP, Foucher B, Lions C, et al. [Trueperella bernardiae soft tissue infection and bacteremia]. Med Mal Infect. 2013;43:487-9. French.
14. Hijazin M, Alber J, Lämmler C, et al. Identification of *Trueperella (Arcanobacterium) bernardiae* by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry analysis and by species-specific PCR. J Med Microbiol. 2012;61:457-459.
15. Funke G, Ramos CP, Fernández-Garayzabal JF, et al. Description of human-derived Centers for Disease Control coryneform group 2 bacteria as *Actinomyces bernardiae* sp. nov. Int J Syst Bacteriol. 1995;45:57-60.