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# *Trueperella bernardiae* bloodstream infection following onco-gynaecologic surgery and literature review

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## SUMMARY

*Trueperella bernardiae* is a Gram-positive commensal bacillus of the human skin and oropharynx. It is known as an opportunistic human pathogen causing surgical wound, skin, and soft tissue, osteoarticular, and bloodstream infections (BSIs) with severe complications. We report a case of surgical wound related *T. bernardiae* BSI following onco-gynaecologic surgery together with a comprehensive literature review of *T. bernardiae* infections to alert clinicians about this emerging pathogen.

*Keywords*: *Trueperella bernardiae*, sepsis, onco-gynaecologic surgery, surgical wound infection, Gram-positive bacillus, MALDI-TOF MS.

## INTRODUCTION

Surgical wound infection is the most common health care–associated infection following surgery and may impact on morbidity and mortality, length of stay, and hospital costs [1, 2]. *Staphylococcus aureus*, coagulase-negative staphylococci, *Streptococcus* spp, *Enterococcus* spp, as well as Gram-negatives and anaerobic organisms, in the case of grossly contaminated wounds, are the most common pathogens isolated from infected surgical sites [3]. *Trueperella bernardiae* is a commensal of the human skin and oropharynx, coryneform, facultative anaerobic, catalase and oxidase negative, Gram-positive bacillus [4]. Despite human infections with *Trueperella* spp having a low prevalence, the addition to the Matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry database of the main spectrum for *T. bernardiae* made its pathogenicity increasingly documented in literature [5-23]. We report a case of *T. bernardiae* bloodstream infection (BSI) following onco-gynaecologic surgery together with a comprehensive literature review of *T. bernardiae* infections to help clinicians be aware about epidemiological, clinical, and microbiologic features of this emerging pathogen.

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## CASE REPORT

In May 2021, a 78-year-old woman with a history of hysterectomy for uterine myomas at the age of 38 and breast cancer treated with QUART six years earlier was admitted to the hospital for fever and abdominopelvic pain. Symptoms had started five days before the admission and had gradually become more severe. Two months before the admission she had been surgically

treated undergoing total vulvectomy with bilateral inguinofemoral lymphadenectomy due to the presence of a keratinizing squamous infiltrating carcinoma (pT1b) with no additional therapy. On physical examination the patient showed diastasis and purulent drainage from the inguinal surgical wound. Her body temperature was 37.4°C, pulse rate was 97 bpm, respiratory rate was 24/min, and blood pressure was 113/39 mmHg. Blood analysis showed neutrophilic leukocytosis (white blood cell count 13,000 per $mm^3$ [4,500-11,000]; neutrophils 85%) and increased inflammatory markers (C-reactive protein 276 mg/L [<0.5]; procalcitonin: 1.14 ng/mL [<0.5]). Abdominal-pelvic computer tomography revealed no alterations suggestive of infectious foci. Urine culture was negative. Polymicrobial flora was reported from the subculture of swab performed on the surgical wound. Four pairs of aerobic and anaerobic blood cultures (BCs) were drawn peripherally. Piperacillin/tazobactam (4.5 g every 8 h, i.v.) and metronidazole (500 mg every 8 h, i.v.) were started. Four BC vials became positive between 26 and 74 hours of incubation on the BACT/ALERT Virtuo (bioMérieux, Marcy l'Ètoile, France). Gram staining showed Gram-positive rods and non-hemolytic, whitish, rounded colonies grew on overnight subcultures on blood agar plates. MALDI-TOF mass spectrometry (Bruker DALTONIK GmbH, Bremen, Germany) provided identification of *T. bernardiae* (identification score of 2.20). Identification of the *T. bernardiae* isolate was confirmed by 16S rRNA gene sequencing. Three other BC vials became positive between 12 h and 20 h, and Gram-positive cocci and Gram-negative bacilli were observed at Gram staining. MALDI-TOF analysis identified *Enterococcus avium* and *Bacteroides fragilis* on overnight subcultures. *In vitro* susceptibility of *T. bernardiae*, *B. fragilis*, and *E. avium* was assessed with E-test® (bioMérieux, Marcy l'Étoile, France) and interpreted using the current EUCAST breakpoints (v.11 2021), specifically PK/PD (Non-species related), Gram-negative anaerobes, and *Enterococcus* spp. clinical breakpoints, respectively. *T. bernardiae* was susceptible to penicillin (MIC 0.064 µg/mL), amoxicillin-clavulanic acid (MIC 0.38 µg/mL), piperacillin/tazobactam (MIC 0.5 µg/mL), ertapenem (MIC 0.094 µg/mL), imipenem (MIC 0.094 µg/mL), meropenem (MIC 0.25 µg/mL), and non-interpretable due to insufficient evidence (IE) for clindamycin (MIC 0.047 µg/mL) and vancomycin (MIC 0.125 µg/mL). Both *B. fragilis* and *E. avium* were multi-susceptible. Following the results of susceptibility testing, piperacillin/tazobactam was stopped and clindamycin together with metronidazole was continued for 14 days. The surgical wound was cleaned and disinfected daily, kept without wound dressing, showing progressive improvement until purulent drainage stopped. Patient was discharged in good clinical condition, and she is still being followed up in the onco-gynecologic outpatient clinic of our center.

## DISCUSSION

Identification of Gram-positive rods in blood cultures should always alert about the possibility of blood sample contamination, as they are mostly skin commensal bacteria with low pathogenic potential. In this report, we presented a microbiologically well documented case of *T. bernardiae* BSI in which the surgical wound was the plausible route of infection and we also highlighted how the introduction of MALDI-TOF mass spectrometry analysis provided both rapid bacterial identification and clinical contextualization of this emerging organism.

The rising and pathogenic role in immunocompromised patients of microorganisms previously considered to be contaminants is supported, in our case, by the fact that *T. bernardiae* isolates were identified from several blood culture vials drawn from different sites, the plausible route of infection, and patient's clinical history. However, since *T. bernardiae* is often reported to be identified, as in our case, in polymicrobial infections, it is difficult to establish its real pathogenicity and contribution to the clinical setting, especially when patient improvement following broad-spectrum antimicrobial treatment is observed.

Since the virulence of *T. bernardiae* is still unclear, and its occurrence is overall rare, a comprehensive literature review of *T. bernardiae* infections was performed. We conducted a literature search in Pubmed, with the keywords "*Trueperella bernardiae*" OR "*Arcanobacterium bernardiae*", which resulted in 27 articles. The more relevant articles were analyzed and epidemiological and clinical features of all recently diagnosed cases of *T. bernardiae* were provided in the Table 1 [6-23]. We highlight that *T. bernardiae* infection has

been mostly identified in immunocompromised hosts, with no apparent age or gender predilection, often diagnosed in polymicrobial cultures, and presenting a good prognosis. *T. bernardiae* was deemed to cause skin and soft tissue including two cases of breast abscess, osteoarticular, BSIs with severe complications, and two cases of brain abscess following otitis media are also reported [6-23]. Of note, among soft tissue and osteoarticular infections, there are various cases related with arthroplasty and, as in our case, surgical wound.

Identification of Gram-positive bacilli is quite difficult using conventional laboratory methods,

**Table 1** - Epidemiological and clinical features of Trueperella bernardiae infections recently reported in the literature.

| *Study* | *Gender/ Age* | *Clinical setting* | *Other organism coisolated* | *Treatment* | *Outcome* |
|---|---|---|---|---|---|
| Otto *et al.*, 2013, France | F/78 | Infected sacral ulcer and bacteremia in obese patient | *B. fragilis*, *Enterococcus avium* | Ceftriaxone + ciprofloxacin + metronidazole, then amoxicillin/clavulanic acid (ten days) | Cure |
| Schneider *et al.*, 2015, Denmark | M/45 | Bacteraemia in diabetic foot gangrene | *Peptostreptococcus* | Amoxicillin (14 days) | Cure |
| Gilarranz *et al.*, 2016, Spain | F/73 | Knee hematoma in patient with total knee replacement | NA | Ciprofloxacin (14 days) | Cure |
| Rattes *et al.*, 2016, Brazil | F/24 | Periumbilical cellulitis after laparoscopic cholecystectomy | NA | Piperacillin/tazobactam + vancomycin (six days), then amoxicillin/clavulanic acid (seven days) | Cure |
| Cobo *et al.*, 2017, Spain | F/69 | Laparotomy due to pericolostomy eventration | NA | Metronidazole + ciprofloxacin, then amoxicillin/clavulanic acid (seven days) | Cure |
| | F/70 | Ulcerated inguinal granuloma in patient with metastatic ovarian cancer | E. coli | Metronidazole (seven days), then amoxicillin/clavulanic acid (seven days) | Cure |
| Gowe *et al.*, 2018, USA | M/57 | Olecranon bursitis | NA | Ceftriaxone + vancomycin (three days), then doxycycline (14 days) | Cure |
| Lawrence *et al.*, 2018, UK | M/32 | Bacteremia in patient with Still disease | *Fusobacterium gonidiaformans* | NA | NA |
| | M/50 | Bacteremia in patient with metastatic cervical cancer | *Escherichia coli* | NA | NA |
| | M/50 | Septic thrombophlebitis in injection drug user | *Fusobacterium gonidiaformans*, *Actinomyces funkei* | NA | NA |
| | M/43 | Diabetic foot infection | *Enterobacter cloacae*, *Citrobacter koseri*, *Corynebacterium spp.* | NA | NA |
| | F/32 | Breast abscess | None | NA | NA |
| | F/42 | Ileal conduit | *Enterococcus faecalis* | NA | NA |
| | M/56 | Diabetic foot infection | None | NA | NA |
| | M/45 | Septic thrombophlebitis in injection drug user | *Peptoniphilus harei* | Cefuroxime + metronidazole (14 days), then amoxicillin/ clavulanic acid (four weeks) | Cure |

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| *Study* | *Gender/ Age* | *Clinical setting* | *Other organism coisolated* | *Treatment* | *Outcome* |
|---|---|---|---|---|---|
| Calatrava *et al.*, 2019, Spain | F/39 | Breast abscess | *Actinotignum sanguinis* | Cloxacillin, then amoxicillin/ clavulanic acid (ten days) | Cure |
| Pan *et al.*, 2019, USA | M/5 | Brain abscess following otitis media | *Actinomyces europaeus*, Corynebacterium amycolatum, Corynebacterium aurimucosum | Vancomycin + cefepime + metronidazole (six weeks), then amoxicillin for (six months) | Cure |
| Roh *et al.*, 2019, Korea | F/83 | Bacteremia in patient with diabetes mellitus and cerebrovascular disease | *S. aureus* | Doxycycline (six days), then meropenem + teicoplanin | Cure |
| Tang *et al.*, 2021, USA | M/71 | Hip arthroplasty with hematoma on surgical scar | NA | Doxycycline (seven days), then ceftriaxone (six weeks) | Cure |
| Casale *et al.*, 2021, Italy | F/78 | Bacteraemia following onco-gynaecologic surgery | *B. fragilis*, *Enterococcus avium* | Piperacillin-tazobactam + metronidazole, then clindamycin (14 days) | Cure |

while implementation of MALDI-TOF mass spectrometry has greatly assisted in the final diagnosis. Concerning *T. bernardiae*, MALDI-TOF mass spectrometry analysis showed to provide rapid and reliable identification at species level helping to elucidate the pathogenic role of this rarely isolated microorganism [5]. A treatment of choice for *T. bernardiae* infection has not been established yet, because of the small amount of data available and the lack of clinical breakpoints for this bacterium. Drug resistance in *T. bernardiae* still seems not to represent a relevant clinical issue, since *T. bernardiae* has been reported to be multi-susceptible to the antibiotics tested with few exceptions regarding ciprofloxacin, gentamicin, and penicillin [6, 7, 17, 22].

In conclusion, we report a case of *T. bernardiae* BSI following onco-gynaecologic surgery with the surgical wound as the bacteraemia's port of entry. Rapid bacterial identification with MALDI-TOF mass spectrometry analysis and envisaging possible routes of infection could help clinicians to set the clinical value of Gram-positive rods observed in blood cultures obtained from patients suffering surgical wound infections.

**Ethical approval**

This study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient.

**Disclosure statement**

No competing interests exist.

**Funding information**

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