Prosthetic joint infection by *Bordetella holmesii*: Case report and a review of the literature

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Abstract

Introduction: *Bordetella holmesii* is a Gram-negative coccobacillus involved in different infections mostly described in case reports. Prosthetic joint infections in relation to this pathogen are rare. Here, we present the third case of *B. holmesii* in a patient without anatomical or functional spleen dysfunction.

Case report: The patient was a 62-year-old female with a total knee prosthesis implanted in 1997 that required multiple replacements of the femoral component due to aseptic loosening in the past years. The patient was admitted to our hospital for an elective replacement surgery due to new radiological signs of loosening. *B. holmesii* was isolated from synovial fluid obtained during surgery. The identification was performed by matrix-assisted laser desorption ionization–time of flight mass spectrometry and confirmed by 16S rRNA gene amplification and sequencing. Antibiotic treatment was started but 14 days after surgery the patient presented pain and joint effusion. An arthrocentesis was performed and synovial fluid culture was positive again for *B. holmesii*. Surgical debridement including polyethylene replacement was performed and antibiotic treatment was continued for 3 months. After a 2-year follow-up period, the patient remained asymptomatic and physical examination showed normal function of the prosthesis.

Conclusion: *B. holmesii* is an uncommon cause of bone and joint infections. This case indicates that this microorganism is a potential pathogen of prosthetic or native arthritis, and it should be considered when cultures are negative and in cases presenting torpid evolution.

Keywords

*Bordetella* holmesii, prosthetic infection, torpid evolution, 16 S gene

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Introduction

*Bordetella holmesii* was described as a new species of the genus of *Bordetella* in 1995.¹ Initially, this microorganism was typically associated with invasive infections in asplenic patients,² but today it is considered a common pathogen in adolescents and adults with pertussis-like respiratory infections.³ This microorganism is associated with a diversity of invasive infections mostly described in case reports including septic arthritis. Prosthetic joint infections are rare. Here, we present the third report of *B. holmesii* in a patient without functional or anatomical splenic dysfunction.

Case report

The patient was a 62-year-old female with a medical history of HLA-B27 positive ankylosing spondylitis receiving treatment with anti-inflammatory drugs, osteoporosis, hypertension and fibromyalgia. The patient had a fracture of the right femur in 2010 fixed with an...
bacilli. In the subculture, colonies of B. holmesii were visible and the Gram stain showed small Gram-negative rods. After 58 hours of incubation the culture was positive for B. holmesii. White blood cell count (WBC) was 80,000 cells/mm³, erythrocyte sedimentation rate (ESR) 62 mm/h and C-reactive protein (CRP) 4.53 mg/dL. An arthrocentesis was performed showing 80,000 red blood cells/mm³, 72 mg/dL of glucose and 53 g/L of proteins. After 58 hours of incubation the culture was positive and the Gram stain showed small Gram-negative bacilli. In the subculture, colonies of B. holmesii were identified. Therefore, a surgical debridement was performed with polyethylene replacement and empirical intravenous treatment with meropenem and vancomycin was started.

The AST of this second strain of B. holmesii showed identical susceptibility profile and after 7 days of intravenous treatment, the patient was started on oral levofloxacin 500 mg/24 hours and the treatment was continued for 3 months. Synovial fluid cultures remained negative a month later. The clinical status of the patient improved with resolution of the infection and physiotherapy was initiated. After 2 years of follow-up, the patient had no signs of infection and physical examination demonstrated an angle of motion of 0° to 120°.

### Discussion

B. holmesii is a slow-growing, fastidious, Gram-negative coccobacillus that causes respiratory diseases including pertussis-like illness in healthy individuals, bacteremia, meningitis, pneumonia, pericarditis, arthritis, diskitis, and cellulitis mainly in asplenic patients with sickle cell disease. In Spain, reports describe the emergence of B. holmesii as a causative agent of whooping cough with a peak incidence reported in 2015. Invasive infections have been reported in immunocompetent patients; however, septic arthritis is rarely reported. To our knowledge, this is the third case associated with a prosthesis. Prior cases of prosthetic joint infection were described in a 20-year-old male with history of osteosarcoma with femoral prosthesis and in 54-year-old female with bilateral knee arthroplasty (Table 2). In concordance with prior cases reported, the route of acquisition of B. holmesii is unknown. It is, however, plausible that both the presence of capsule and the production of lipopolysaccharides play an important role in the pathophysiology of bacterial invasion. This infection is commonly transmitted through respiratory tract; first, a primary respiratory infection develops followed by a dissemination to secondary infection sites. However, our patient did not report any signs of respiratory infection prior to the surgery.

The diagnostic of B. holmesii is complex, and available commercial diagnostics as the Vitek 2 (bioMérieux USA) system usually fail to identify B. holmesii and misidentifies it as Acinetobacter iwoffii. MALDI-TOF MS library include this Bordetella species, and in our case this was the first identification technique. However, since there is a high similarity between B. holmesii and B. pertussis, we used the 16S rRNA gene sequencing as a confirmation method. Other methods that can be used to avoid misidentification is the recA gene amplification using a real-time polymerase chain reaction (PCR) or a loop-mediated isothermal amplification (LAMP).

At the moment, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) do not have

| Antibiotic          | Interpretation result | MIC values (µg/mL) |
|---------------------|-----------------------|--------------------|
| Cefotaxime          | Resistant             | >32                |
| Cefazidime          | Susceptible           | 0.032              |
| Ciprofloxacin       | Susceptible           | 0.023              |
| Cotrimoxazole       | Susceptible           | 0.004              |
| Imipenem            | Susceptible           | 0.5                |
| Meropenem           | Susceptible           | 0.016              |
| Piperacillin/tazobactam | Susceptible     | 0.016              |
| Amikacin            | Susceptible           | 0.25               |
standardized breakpoints for \( B. \, holmesii \). The AST analysis was performed by the disk-diffusion method using the interpretation values of the inhibition halo for \( \text{Enterobacteriaceae} \) and MIC values were calculated using E-test. In previous reports of prosthetic joint infections, third-generation cephalosporins followed by oral fluoroquinolones were the selected options\(^7\) but currently, there is no specific recommendation for bone and joint infections. Resistance to \( \beta \)-lactams and cotrimoxazole have been reported in respiratory infections.\(^8\) In our case, the strain was resistant to cefotaxime, and the patient was initially treated with ciprofloxacin and cotrimoxazole and after the second surgical intervention with meropenem and levofloxacin, the patient responded favorably.

This is a rare infection which can be diagnosed with microbiological techniques such as MALDI-TOF MS, routinely implemented in many microbiology laboratories. However, it is important to consider this fastidious microorganism as a possible aetiological agent in cases of prosthetic or native arthritis with negative cultures and torpid evolution.

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