Short communication

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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, 16S 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

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Table 1. Results of AST of both strain of *B. holmesii* identified in synovial fluid inoculated in blood cultures bottles; MIC minimum inhibitory concentration.

Antibiotic	Interpretation result	MIC values (μg/mL)
Cefotaxime	Resistant	>32
Ceftazidime	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

intramedullary nail. A total knee prosthesis in the left knee was implanted in 1997 requiring multiple replacements of the femoral component due to aseptic loosening in 2004, 2008 and 2015, with negative synovial cultures in all cases. In May 2016, the patient complained of knee pain, radiological signs of aseptic loosening were observed and the patient was admitted to our hospital for an elective replacement surgery. Samples were taken for histopathological study and microbiological cultures. Cytochemical analysis of the synovial fluid was not performed. The histopathological study reported presence of fibrous tissue with chronic reactive changes and no evidence of infiltrates or malignancy. Synovial fluid was inoculated in blood culture bottles and *B. holmesii* was isolated after 75 hours of incubation. Bacterial colony identification was performed by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) and was confirmed with the amplification and sequencing of the 16S gene of the bacterial rRNA using the following primers: 5′-AGA GTT TGA TCC TGG CTC AG-3′and 5′-GGA CTA CCA GGG TAT CTA AT-3′ followed by Sanger sequencing. Sequences were identified using the Blast algorithm in the National Center for Biotechnology Information (NCBI) database.

Antibiotic susceptibility test (AST) was performed using the disk-diffusion method which showed resistance to cefotaxime. Minimum inhibitory concentration (MIC) were calculated using espsilometer test (E-test) Table 1 showed the MIC values. Despite the absence of other parameters suggesting infection, it was decided to start antibiotic treatment with ciprofloxacin and cotrimoxazole for 1 week. Fourteen days after, the patient presented pain and joint effusion. White blood cell count (WBC) was 8000 cells/mm^3 (62.1% neutrophils, 27% lymphocytes), 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/mm^3, 3290 white blood cells/mm^3, 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 0º to 120º.

Discussion

B. holmesii is a slow-growing, fastidious, Gram-negative coccobacillus,[4,5] 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.[2,5] In Spain, reports describe the emergence of *B. holmesii* as a causative agent of whooping cough with a peak incidence reported in 2015.[6] Invasive infections have been reported in immunocompetent patients;[5] however, septic arthritis is rarely reported. To our knowledge, this is the third case associated with a prosthesis.[7] Prior cases of prosthetic joint infection were described in a 20-year-old male with history of osteosarcoma with femoral prosthesis and in a 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.[8] This infection is commonly transmitted through respiratory tract; first, a primary respiratory infection develops followed by a dissemination to secondary infection sites.[3] 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*.[2] 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*,[3] 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).[9]

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

Table 2. Cases of prosthetic joint infection by *B. holmesii*.[7]

Case Reference	Age	Medical history	Infection site	Medical treatment	Evolution
1[7]	20	Osteosarcoma	Right femoral prosthesis	Ceftriaxone + doxycycline for 1 week and levofloxacine for 4 weeks	Cure
2[7]	54	Bilateral knee arthroplasty	Right knee prosthesis	Ceftriaxone + ciprofloxacin for 1 month	Cure
3	62	Ankylosing spondylitis, osteoporosis and fibromyalgia	Left knee prosthesis	Ciprofloxacin + cotrimoxazole 1 week, meropenem 1 week and levofloxacin for 2 months	Cure

standardized breakpoints for *B. holmesii*. The AST analysis was performed by the disk-diffusion method using the interpretation values of the inhibition halo for *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 β-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.

Declaration of conflicting interests

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References

1. Pittet LF and Posfay-barbe KM. *Bordetella holmesii*: still emerging and elusive 20 years on. *Emerg Infect* 1995; 10: 239–254.
2. Moissenet D, Leverger G, Merens A, et al. Septic arthritis caused by *Bordetella holmesii* in an adolescent with chronic haemolytic anaemia. *J Med Microbiol* 2011; 60(Pt 11): 1705–1707.
3. Pittet LF, Emonet S, Francois P, et al. Diagnosis of whooping cough in Switzerland: differentiating *Bordetella pertussis* from *Bordetella holmesii* by polymerase chain reaction. *PLoS ONE* 2014; 9(2): e88936.
4. Planet PJ, Narechania A, Hymes SR, et al. *Bordetella holmesii*: initial genomic analysis of an emerging opportunist. *Pathog Dis* 2013; 67(2): 132–135.
5. Abouanaser SF, Srigley JA, Nguyen T, et al. *Bordetella holmesii*, an emerging cause of septic arthritis. *J Clin Microbiol* 2013; 51(4): 1313–1315.
6. Mir-Cros A, Codina G, Martin-Gomez MT, et al. Emergence of *Bordetella holmesii* as a Causative Agent of Whooping Cough, Barcelona, Spain. *Emerg Infect Dis* 2017; 23(11): 1856–1859.
7. Humphrey JM, Lacaille SN, Patel K, et al. Prosthetic-Joint-Associated *Bordetella holmesii* Infection. *Open Forum Infect Dis* 2015; 2: ofv169.
8. Pittet LF, Emonet S, Schrenzel J, et al. *Bordetella holmesii*: an under-recognised Bordetella species. *Lancet Infect Dis* 2014; 14(6): 510–519.
9. Otsuka N, Yoshino S, Kawano K, et al. Simple and specific detection of *Bordetella holmesii* by using a loop-mediated isothermal amplification assay. *Microbiol Immunol* 2012; 56(7): 486–489.