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Case report

# *Brucella* vertebral osteomyelitis misidentified as an *Ochrobactrum anthropi* infection

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ABSTRACT

*Ochrobactrum anthropi* is a Gram-negative bacillus widely distributed in nature. It is a low virulence and low pathogenic microorganism and human infection by this agent is considered rare. This microorganism can cause bacteremia and in some cases can lead to osteomyelitis and endocarditis. Included in *Brucellaceae* family, this bacterium is phenotypically and genetically closely related to the *Brucella* genus and may be misidentified by rapid identification systems. The authors describe a patient admitted to the Infectious Diseases Department with vertebral osteomyelitis initially identified as *Ochrobactrum anthropi*. Despite appropriate antimicrobial therapy, the blood cultures remained positive and there were no signs of clinical improvement. This raised suspicion of a possible misidentification. It was decided to initiate antimicrobial therapy to include the *Brucella* genus, with slow but progressive clinical improvement. Samples were sent to Instituto Nacional de Saúde Doutor Ricardo Jorge (INSA) for genotyping, confirming the initial suspicion of misidentification and identifying *Brucella melitensis* as the causal agent. Timely diagnosis of brucellosis is essential for the correct management and prevention of its consequences for the patient and for safe handling of the laboratory samples, preventing laboratory-acquired infection

## Introduction

Brucellosis is a major zoonotic disease worldwide caused by *Brucella* species, the infection is transmitted through consumption of unpasteurized milk and raw or undercooked meat from infected animals or by handling material and body fluids of these animals including inhalation of contaminated aerosols [1], which makes it a potential agent for biological warfare purposes [2]. At risk professionals are shepherds and cattle breeders, tannery factories and slaughterhouses workers, veterinarians, butchers and microbiology laboratory technicians. Despite great progress in controlling the disease for most of the world, brucellosis is still considered endemic in certain regions such as South America, the Mediterranean Basin, Middle East and Arabian Peninsula [1], and even in these regions it is often misdiagnosed, unrecognized and clearly underreported [1,3]. The family *Brucellaceae* contains the genera *Brucella*, *Crabtreella*, *Daeguia*, *Mycoplana*, *Ochrobactrum*, *Paenochrobactrum* and *Pseudochrobactrum*. *Brucella* species are Gram-negative bacilli, facultative intracellular pathogens that can survive within phagocytic cells (), with variable degrees of virulence. In Portugal, the species most often implicated in human disease is *Brucella melitensis* [3], capable of causing serious complications in any organ or system.

Contrarily to *Brucella*, *Ochrobactrum* spp rarely causes disease in humans; within the various species, *O. anthropi* seems to be the most clinically relevant. Due to being phenotypically and genetically closely related [4] several cases of misidentification have been reported [5–10]. *Ochrobactrum* is considered an opportunistic and nosocomial pathogen and mostly associated with central venous catheters infections, especially in dialysis patients [11,12] that lead to bacteremia and may cause localized infections such as endocarditis and osteomyelitis mainly in critically ill or immunocompromised patients [13,14]. The misdiagnosis of brucellosis can delay the correct treatment, implying a longer course of the disease, risk of relapse and greater probability of sequelae and other complications. Furthermore, brucellosis poses an occupational hazard for any laboratory personnel working in a clinical microbiology laboratory and staff may be exposed to *Brucella* if an isolate is incorrectly identified and there is no clinical suspicion of brucellosis [9,15].

## Case report

A 46-year-old woman presented to the emergency department with

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night sweats and severe neck pain lasting for three weeks. She denied any other symptoms. The patient brought a magnetic resonance imaging (MRI) result that was previously requested by her family physician that showed evidence of cervical vertebral osteomyelitis (C4-C5). She had no relevant past medical history and took no medications. The patient worked as a shopping mall manager, lived in an apartment in the city and she had no contact with animals. She denied outdoor activities and had no history of recent travel abroad. Sporadically, she consumed fresh cheese. Her physical examination was unremarkable except for pain when mobilizing the cervical region. Laboratory testing showed only a slight elevation of the erythrocyte sedimentation rate (ESR). Two sets of blood cultures were obtained and the patient was admitted for further investigation.

*Ochrobactrum anthropi* was identified using the VITEK® MS system in all of the four blood cultures collected at admission. The Antimicrobial Sensitivity Test (AST) showed susceptibility to imipenem, gentamicin, ciprofloxacin and trimethoprim/sulfamethoxazole, and resistance to amoxicillin and cefotaxime. Guided by the AST, antimicrobial treatment was initiated with ciprofloxacin. Despite antimicrobial therapy, there was no clinical improvement and the patient developed bicytopenia (anemia and leukopenia). An additional two sets of blood cultures were collected and on the 14th day of hospitalization, they were again identified as *O. anthropi*. Considering the poor clinical outcome with persistent positive blood cultures in a patient with no known underlying disease, added to the fact that the initial serological tests (Rose Bengal test and Wright agglutination) came back positive, and later through the detection of specific antibodies by enzyme-linked immunosorbent assay (ELISA) made a strong case for the possibility of misidentification. Samples were sent to Instituto Nacional de Saúde Doutor Ricardo Jorge (INSA) for genetic analysis. We decided to start antibacterial therapy for brucellosis with doxycycline, rifampin plus gentamicin, and the patient improved slowly but progressively. Despite evidence of efficacy in treating brucellosis with regimens containing ciprofloxacin, there is clinical and laboratorial evidence of its inferiority relative to regimens containing doxycycline [16,17] due to its decreased activity in a low pH environment, which is the case with *Brucella*, as an intracellular organism capable of surviving within macrophage phagolysosomes [17].

The patient was discharged, back to her home, continuing antibacterial therapy and follow up at our outpatient clinic. The genetic analysis confirmed the presence of DNA from *Brucella melitensis* and the absence of DNA from *O. anthropi*. The patient maintained antibacterial therapy for four months. There was a re-evaluation with MRI after 6 months that showed slight attenuation of the previous enhancement of epidural and paravertebral soft tissues, suggesting a favorable response.

## Discussion

Belonging to the same family, genus *Brucella* and *Ochrobactrum* share a large phylogenetic similarity but have important and significant differences in their ability to cause disease, mainly because of their interaction with the host cell [18]. *Ochrobactrum* is a saprophytic soil bacteria with a low virulence that does not replicate inside human cells or animals and only occasionally causes human disease [18,19]. *Brucella* is an extremely effective pathogen with replication inside the cells and that can cause disease in a large number of animal species, including humans [20]. Another important difference lies in the structure of the cell membrane of these two bacteria, which confers intrinsic resistance of the genus *Brucella* to the polymyxins, something that does not happen with *Ochrobactrum* [4] and may help to differentiate between the two bacteria.

Regarding the initial antimicrobial therapy, ciprofloxacin is active against *Brucella* and can be used as an alternative in combination with other agents, mainly in non-localizing infections, but it shouldn't be used as a single agent due to its low efficacy and unacceptable high relapse rates [17,21,22]. Several cases of misidentification with *Brucella* and *Ochrobactrum* have been reported [5–10]. These cases have led some laboratories to implement a safety measure with an automatic alert message whenever similar species to *Brucella* are identified, so that the laboratory staff may take the necessary safety precautions. In this case report, all blood cultures were initially identified as *Ochrobactrum anthropi*. However, because of the positive serology for *Brucella*, and the fact that an immunocompetent patient maintained persistent positive blood cultures for *O. anthropi* despite antimicrobial therapy, the possibility of misidentification was raised. Although mortality from brucellosis is low, a late diagnosis and treatment can be responsible for significant morbidity, with debilitating consequences. The risk of a wrong diagnosis is, therefore, of great clinical relevance.

## Conclusions

Previous cases of misidentification have been described using several methods for rapid identification of microorganisms, namely by API® 20NE system, misidentifying *Brucella* species as *Moraxella phenylpyruvica* [9,10] and *O. anthropi* [7]; by RapID® NF plus as *O. anthropi* [5]; by Baxter MicroScan® panels as *Haemophilus influenza* biotype IV [10] and *Moraxella* species [10] and by MicroScan WalkAway® system as *Bergeyella zoohelcum* [8]. In some of this cases, the samples were later evaluated and correctly identified using Vitek®2 system [5,8]. More recently there was a case report with Vitek®2 system misidentifying *Brucella suis* as an *O. anthropi* [6]. To our knowledge, this is the first reported case of a misidentification of a *Brucella* species with *O. anthropi,* using a system based on MALDI-TOF technology (Vitek® MS). Despite the great breakthroughs in microbial identification and the wide use of fast and reliable commercial systems in some cases, correct identification remains challenging, furthermore this case demonstrates the difficulties of identifying *Brucella* species and the importance of clinical context for differential diagnosis. It also highlights the importance of not relying on a single identification method especially when the diagnosis is not firmly established. In the present case, there was also the risk of exposure for the laboratory personnel and timely identification may prevent laboratory-acquired infection.

## Consent

Written informed consent was obtained from the patient for publication of this case report. This case report doesn't include images or videos. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## References

[1] Corbel MJ. Brucellosis: an overview. Emerg Infect Dis 1997;3(2):213–21. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2627605/.
[2] Doganay GD, Doganay M. *Brucella* as a potential agent of bioterrorism. Recent Patents AntiInfect Drug Disc 2013;8(1):27–33.
[3] Pelerito A, Cordeiro R, Matos R, Santos M, Soeiro S, Núncio S. Brucelose humana: análise retrospetiva de casos clínicos suspeitos de infeção entre 2002 e 2013 Instituto Nacional de Saúde Doutor Ricardo Jorge. Observações: Boletim Epidemiol 2013;09:2.
[4] Velasco J, Romero C, Lopez-Goni I, Leiva J, Diaz R, Moriyon I. Evaluation of the relatedness of *Brucella* spp. and *Ochrobactrum anthropi* and description of *Ochrobactrum intermedium* sp. nov., a new species with a closer relationship to *Brucella* spp. Int J Syst Bacteriol 1998;48(Pt 3):759–68. http://dx.doi.org/10.1099/00207713-48-3-759.
[5] Horvat RT, El Atrouni W, Hammoud K, Hawkinson D, Cowden S. Ribosomal RNA sequence analysis of *Brucella* infection misidentified as *Ochrobactrum anthropi* infection. J Clin Microbiol 2011;49(3):1165–8. http://dx.doi.org/10.1128/JCM.01131-10.
[6] Vila A, Pagella H, Vera Bello G, Vicente A. *Brucella suis* bacteremia misidentified as *Ochrobactrum anthropi* by the VITEK 2 system. J Infect Dev Ctries 2016;10(4):432–6.
[7] Elsaghir AAF, James EA. Misidentification of *Brucella melitensis* as *Ochrobactrum anthropi* by API 20NE. J Med Microbiol Engl 2003. http://dx.doi.org/10.1099/jmm.0.05153-0.
[8] Dash N, Al-Zarouni M, Rattan A, Panigrahi D. Misidentification of *Brucella melitensis* as *Bergeyella zoohelcum* by MicroScan WalkAway(R): a case report. Med Princ Pract: Int J Kuwait Univ Health Sci Centre 2012;21(5):495–7. http://dx.doi.org/10.1159/000338391.
[9] Batchelor BI, Brindle RJ, Gilks GF, Selkon JB. Biochemical mis-identification of

*Brucella melitensis* and subsequent laboratory-acquired infections. J Hosp Infect 1992;22(2):159–62.
[10] Barham WB, Church P, Brown JE, Paparello S. Misidentification of *Brucella* species with use of rapid bacterial identification systems. United States: Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America; 1993.
[11] Zakariya-Yousef I, Aller-Garcia AI, Corzo-Delgado JE, Saez-Nieto JA. Catheter-associated bacteremia caused by *Ochrobactrum anthropi* in a patient on parenteral nutrition. Spain: Enfermedades Infecciosas Y Microbiologia Clinica; 2014. http://dx.doi.org/10.1016/j.eimc.2014.01.004.
[12] Alparslan C, Yavascan O, Kose E, Sanlioglu P, Aksu N. An opportunistic pathogen in a peritoneal dialysis patient: *Ochrobactrum anthropi.* Indian J Pediatr 2013;80(1):72–4.
[13] Stiakaki E, Galanakis E, Samonis G, Christidou A, Maraka S, Tselentis Y, et al. *Ochrobactrum anthropi* bacteremia in pediatric oncology patients. Pediatr Infect Dis J 2002;21(1):72–4.
[14] Ashraf F. A case of *Ochrobactrum anthropi*-induced septic shock and infective endocarditis. Rhode Island Med J (2013) 2016;99(7):27–8.
[15] Fiori PL, Mastrandrea S, Rappelli P, Cappuccinelli P. *Brucella abortus* infection acquired in microbiology laboratories. J Clin Microbiol 2000;38(5):2005–6.
[16] Atkins HS, Spencer S, Brew SD, Jenner DC, Russell P, MacMillan AP, et al. Efficacy of ciprofloxacin versus doxycycline as prophylaxis against experimental murine *Brucella melitensis* infection. Int J Antimicrob Agents 2009;34(5):474–6. http://dx.doi.org/10.1016/j.ijantimicag.2009.04.006.
[17] Garcia-Rodriguez JA, Garcia Sanchez JE, Trujillano I. Lack of effective bactericidal activity of new quinolones against *Brucella* spp. Antimicrob Agents Chemother 1991;35(4):756–9.
[18] Barquero-Calvo E, Conde-Alvarez R, Chacon-Diaz C, Quesada-Lobo L, Martirosyan A, Guzman-Verri C, et al. The differential interaction of *Brucella* and *Ochrobactrum* with innate immunity reveals traits related to the evolution of stealthy pathogens. PLoS One 2009;4(6):e5893. http://dx.doi.org/10.1371/journal.pone.0005893.
[19] Hagiya H, Ohnishi K, Maki M, Watanabe N, Murase T. Clinical characteristics of *Ochrobactrum anthropi* bacteremia. J Clin Microbiol 2013;51(4):1330–3. http://dx.doi.org/10.1128/JCM.03238-12.
[20] Christopher S, Umapathy BL, Ravikumar KL. Brucellosis: review on the recent trends in pathogenicity and laboratory diagnosis. J Lab Phys 2010;2(2):55–60. http://dx.doi.org/10.4103/0974-2727.72149.
[21] Falagas ME, Bliziotis IA. Quinolones for treatment of human brucellosis: critical review of the evidence from microbiological and clinical studies. Antimicrob Agents Chemother 2006;50(1):22–33. http://dx.doi.org/10.1128/AAC.50.1.22-33.2006.
[22] Akova M, Gur D, Livermore DM, Kocagoz T, Akalin HE. In vitro activities of antibiotics alone and in combination against *Brucella melitensis* at neutral and acidic pHs. Antimicrob Agents Chemother 1999;43(5):1298–300.