



Case report

***Bordetella bronchiseptica* in non-cystic fibrosis bronchiectasis**Elham Karamooz^{a,*}, Vanessa L. Yap^{b,1}, Alan F. Barker^a, Mark L. Metersky^b^a Division of Pulmonary and Critical Care Medicine, Oregon Health and Science University, Portland, OR 97239, USA^b Division of Pulmonary, Critical Care and Sleep Medicine, University of Connecticut, Farmington, CT 06030, USA

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ABSTRACT

Bordetella bronchiseptica is a rare pulmonary infection, often associated with zoonotic transmission. It has been described in immunocompromised patients and those with underlying pulmonary disease. However, there are no case series describing the spectrum of disease caused by *Bordetella bronchiseptica* in patients with non-cystic fibrosis bronchiectasis. Here, we report three cases of *Bordetella bronchiseptica* infection in patients with non-cystic fibrosis bronchiectasis and highlight the pathophysiology of the microbe. While the clinical presentation can be quite variable, it is important to note that *Bordetella bronchiseptica* can be a cause of pulmonary exacerbations and can be difficult to eradicate.

1. Introduction

Bordetellae are gram-negative, aerobic bacterial pathogens that can infect the respiratory tract of mammals [1]. Four species can infect humans: *B. pertussis*, *B. parapertussis*, *B. holmesii*, and *B. bronchiseptica* [1]. *B. pertussis* and *B. parapertussis* evolved from *B. bronchiseptica*, and while *B. pertussis* and *B. parapertussis* cause whooping cough in humans, *B. bronchiseptica* does not produce pertussis toxin [1,2]. However, *B. bronchiseptica* is capable of infecting animals and humans and is the cause of “kennel cough”, a form of tracheobronchitis in dogs [3]. Importantly, *B. bronchiseptica* is capable of zoonotic transmission [4].

The spectrum of disease caused by *B. bronchiseptica* is highly variable, ranging from asymptomatic or transient carriage, to persistent infections and even death [4–6]. Thus far, there have been case series describing *B. bronchiseptica* infections in patients with underlying lung disease such as chronic obstructive pulmonary disease (COPD) and cystic fibrosis, and with systemic immunodeficiency or immunosuppression [5–9]. Occasionally, infection can involve healthy hosts who have come in contact with sick pets [5]. There are no case series on *B. bronchiseptica* infection in non-cystic fibrosis (non-CF) bronchiectasis. We present 3 cases. We observe that in patients with non-CF bronchiectasis, *B. bronchiseptica* may be associated with or without the symptoms of a pulmonary exacerbation. We describe the symptoms, the circumstances associated with isolation of the organism, and the treatment each patient received in this case series.

2. Case presentations

2.1. Case 1

The patient is a 53-year-old woman with primary ciliary dyskinesia who had previously grown *Pseudomonas aeruginosa* (*P. aeruginosa*) in 2 sputum cultures. She returned for an exacerbation with increased sputum production, worsening dyspnea, and weight loss. Sputum culture grew *B. bronchiseptica*. She responded well to a 14 day course of tetracycline. She had multiple other exacerbations and had 5 other sputum cultures isolating *B. bronchiseptica* exclusively over the next 2 years despite being on long courses of doxycycline. She reported animal contact with her pet dog but it was well and did not exhibit any symptoms of “kennel cough”.

2.2. Case 2

The patient is a 66-year-old man who was evaluated for persistent, productive cough. His cultures had grown *B. bronchiseptica* as well as *Mycobacterium avium* complex in the past. A follow-up sputum culture again grew *B. bronchiseptica* and methicillin sensitive *Staphylococcus aureus*, for which he was placed on levofloxacin. He demonstrated some improvement, but shortly thereafter had increased sputum production. He was again started on levofloxacin while awaiting another sputum culture, which isolated *Aspergillus* and *Pantoea* sp. Another sputum culture a few weeks later grew *P. aeruginosa* but the patient has since

Abbreviations: CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease

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been lost to follow up. The patient also reported having several pet cats and dogs that were all in good health.

2.3. Case 3

The patient is a 70-year-old woman with a history of sarcoidosis and bronchiectasis who reported a productive cough. Routine sputum culture on her initial visit isolated *B. bronchiseptica*. The patient did not own a dog but she interacted with many dogs passing by her yard and her daughter also had two cats. As she was feeling relatively well during the time of the isolate, she was not started on antibiotics. However, she had an exacerbation 10 months later requiring hospitalization. Her sputum culture grew *Haemophilus influenzae* and was treated adequately with levofloxacin. She improved and was discharged to home.

3. Discussion

Although *B. bronchiseptica* is an uncommon cause of respiratory infections in humans, the clinical manifestations can be quite variable. Our descriptions of *B. bronchiseptica* infection in patients with non-CF bronchiectasis highlight this variability. The patient in case 1 had multiple cultures exclusively growing *B. bronchiseptica*, making this organism the likely culprit of the pulmonary exacerbations. The second case, however, grew *B. bronchiseptica* in association with other more usual respiratory pathogens making it difficult to ascertain a link to the pulmonary exacerbation. The third case points to asymptomatic carriage among patients with chronic lung disease.

Whether these distinct presentations reflect differences in the host immune response to the microbe versus the expression of different virulence factors by the microbe is unknown. There are several virulence factors that likely contribute to persistent infection. First, the microbe has adhesion proteins such as filamentous hemagglutinin (FHA) and fimbriae, allowing for attachment to mammalian airways [1]. These virulence factors are regulated by the *Bordetella* virulence gene, BvgAS [10]. Depending on the environment, BvgAS can adopt one of three phases: Bvg+ (virulent), Bvg- (nonvirulent) and Bvgi (intermediate). It has been shown that *B. bronchiseptica* can form biofilms in the Bvgi phase [10,11]. This could contribute to the persistence of infection, given the difficulty of antibiotics and innate immune cells in penetrating biofilms. Another mechanism by which *B. bronchiseptica* circumvents the immune response is via adaptations allowing for survival in acidified phagosomes in alveolar macrophages [12]. Finally, although there are no data on the exact mechanisms allowing for interspecies transmissibility, a screen of *B. bronchiseptica* mutants revealed that deletion of an extracellular polysaccharide (EPS) locus led to a substantial decrease in transmissibility between mice [13]. Furthermore, it was shown that the EPS mutant was less efficient at colonizing the respiratory tract of mice and demonstrated impaired bacterial shedding. These findings suggest that EPS is integral to the virulence of *B. bronchiseptica*.

Unfortunately, there are no specific guidelines for the treatment of *B. bronchiseptica*. The most effective antimicrobial agents appear to be the aminoglycosides, anti-pseudomonal penicillins, and tetracyclines [5,7]. Variable susceptibility is seen to trimethoprim/sulfamethoxazole and fluoroquinolones, though they can also be effective [3,5,7]. Antibiotic courses of 2–6 weeks may be needed and longer courses, up to 6 months, have been required for treatment of some

immunocompromised patients [3,5,6]. Unlike *B. pertussis*, *B. bronchiseptica* infection does not respond to macrolides and resistance to beta-lactam antibiotics is common [1,5,7]. Chronic or recurrent infection may occur, even after the patient is not in contact with infected animals because of persistence of the bacterium, potentially in macrophages or epithelial cells [14,15]. In addition to antibiotic therapy, source control by identifying potentially infected pets and vaccination of pets to *B. bronchiseptica* is recommended to prevent zoonotic transmission [7].

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References

- [1] S. Mattoo, J.D. Cherry, Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to *Bordetella pertussis* and other *Bordetella* subspecies, *Clin. Microbiol. Rev.* 18 (2) (2005 Apr) 326–382.
- [2] J. Parkhill, M. Sebahia, A. Preston, L.D. Murphy, N. Thomson, D.E. Harris, M.T. Holden, C.M. Churcher, S.D. Bentley, K.L. Mungall, A.M. Cerdeño-Tárraga, L. Temple, K. James, B. Harris, M.A. Quail, M. Achtman, R. Atkin, S. Baker, D. Basham, N. Bason, I. Cherevach, T. Chillingworth, M. Collins, A. Cronin, P. Davis, J. Doggett, T. Feltwell, A. Goble, N. Hamlin, H. Hauser, R. Deoraj, K. Jagels, S. Leather, S. Moule, H. Norberczak, S. O’Neil, D. Ormond, C. Price, E. Rabinowitsch, S. Rutter, M. Sanders, D. Saunders, K. Seeger, S. Sharp, M. Simmonds, J. Skelton, R. Squares, S. Squares, K. Stevens, L. Unwin, S. Whitehead, B.G. Barrell, D.J. Maskell, Comparative analysis of the genome sequences of *Bordetella pertussis*, *Bordetella parapertussis* and *Bordetella bronchiseptica*, *Nat. Genet.* 35 (1) (2003 Sep) 32–40.
- [3] D.M. Berkowitz, R.I. Bechara, L.L. Wolfenden, An unusual cause of cough and dyspnea in an immunocompromised patient, *Chest* 131 (5) (2007 May) 1599–1602.
- [4] K.B. Register, N. Sukumar, E.L. Palavecino, B.K. Rubin, R. Deora, *Bordetella bronchiseptica* in a paediatric cystic fibrosis patient: possible transmission from a household cat, *Zoonoses Publ. Health* 59 (4) (2012 Jun) 246–250.
- [5] C. García-de-la-Fuente, L. Guzmán, M.E. Cano, J. Agüero, C. Sanjuán, C. Rodríguez, A. Aguirre, L. Martínez-Martínez, Microbiological and clinical aspects of respiratory infections associated with *Bordetella bronchiseptica*, *Diagn. Microbiol. Infect. Dis.* 82 (1) (2015 May) 20–25.
- [6] A.T. Yacoub, M. Katayama, J. Tran, R. Zadikany, M. Kandula, J. Greene, *Bordetella bronchiseptica* in the immunosuppressed population - a case series and review, *Mediterr. J. Hematol. Infect. Dis.* 6 (1) (2014 Apr 7) e2014031.
- [7] C. Brady, P. Ackerman, M. Johnson, J. McNamara, *Bordetella bronchiseptica* in a pediatric Cystic Fibrosis center, *J. Cyst. Fibros.* 13 (1) (2014 Jan) 43–48.
- [8] M.S. Dworkin, P.S. Sullivan, S.E. Buskin, R.D. Harrington, J. Olliffe, R.D. MacArthur, C.E. Lopez, *Bordetella bronchiseptica* infection in human immunodeficiency virus-infected patients, *Clin. Infect. Dis.* 28 (5) (1999 May) 1095–1099.
- [9] Z. Ner, L.A. Ross, M.V. Horn, T.G. Keens, E.F. MacLaughlin, V.A. Starnes, M.S. Woo, *Bordetella bronchiseptica* infection in pediatric lung transplant recipients, *Pediatr. Transplant.* 7 (5) (2003 Oct) 413–417.
- [10] Y. Irie, S. Mattoo, M.H. Yuk, The Bvg virulence control system regulates biofilm formation in *Bordetella bronchiseptica*, *J. Bacteriol.* 186 (17) (2004 Sep) 5692–5698.
- [11] N. Cattelan, P. Dubey, L. Arnal, O.M. Yantorno, R. Deora, *Bordetella* biofilms: a lifestyle leading to persistent infections, *Pathog Dis* 74 (1) (2016 Feb) ftv108.
- [12] B. Schneider, R. Gross, A. Haas, Phagosome acidification has opposite effects on intracellular survival of *Bordetella pertussis* and *B. bronchiseptica*, *Infect. Immun.* 68 (12) (2000 Dec) 7039–7048.
- [13] K.K. Dewan, D.L. Taylor-Mulneix, L.J. Hilburger, I. Rivera, A. Preston, E.T. Harvill, An extracellular polysaccharide locus required for transmission of *Bordetella bronchiseptica*, *J. Infect. Dis.* 216 (7) (2017 Oct 17) 899–906.
- [14] P. Gueirard, C. Weber, A. Le Coustumier, N. Guiso, Human *Bordetella bronchiseptica* infection related to contact with infected animals: persistence of bacteria in host, *J. Clin. Microbiol.* 33 (8) (1995 Aug) 2002–2006.
- [15] H. Schipper, G.F. Krohne, R. Gross, Epithelial cell invasion and survival of *Bordetella bronchiseptica*, *Infect. Immun.* 62 (7) (1994 Jul) 3008–3011.