Bordetella bronchiseptica or Brucella: report of one case misidentification and review of the literature about Bordetella bronchiseptica infection

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Investigation of a clinical case of Brucella infection, in which the cause initially indicated Bordetella bronchiseptica, using automated identification techniques prompted a retrospective analysis of previously published cases of B. bronchiseptica infections in China and elsewhere. B. bronchiseptica infection is rarely found in humans, but more frequently in animals. Automated microbial identification systems may confuse B. bronchiseptica with Brucella sp. Brucella by contrast causes a notifiable communicable zoonotic disease. We summarize here the pathogenesis, epidemiology, clinical symptoms and microbiological identification of B. bronchiseptica infection in humans.

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Introduction

Bordetella bronchiseptica is a small Gram-negative coccobacillus, belonging to genus Bordetella. Up to now, the basic studies on Bordetella pertussis, B. bronchiseptica and Bordetella parapertussis in genus Bordetellae have been relatively clear. The whole-genome sequencing of these three bacteria was completed in the British Sanger Center in 2003. Although it was found that B. bronchiseptica genome was the largest, while the genes present in B. pertussis and B. parapertussis were included in B. bronchiseptica [1], their pathogenicity is significantly different. B. bronchiseptica widely exists in the water and soil. It was first isolated from the respiratory tract of dogs suffering from distemper in 1910s by Ferry [2] who found that B. bronchiseptica can cause diseases in a variety of wild and domestic animals. In 1979, B. bronchiseptica was first isolated from a child with pharyngolaryngitis by Ghosh [3]. After that, literatures about B. bronchiseptica infection gradually increased, especially in immunocompromised patients [4–6]. The insufficient knowledge about B. bronchiseptica epidemiology is related to the inefficiency of laboratory diagnosis technology. In December 2011, our hospital treated a 63-year-old fever patient without apparent cause, whose blood culture yielded a bacterium initially identified as B. bronchiseptica and then verified as Brucella using 16S rRNA sequencing [7]. Combining the experimental analysis of misidentification of Brucella as B. bronchiseptica by using an automatic identification instrument, we performed a review of Chinese and other national literatures on Bordetella in order to provide some insight into the further study of B. bronchiseptica.

Clinical case

In December 2011, a 63-year-old woman with intermittent fever but without apparent cause was admitted to our hospital, with symptoms of splenomegaly. Detailed laboratory investigations mainly showed a WBC count of 2.7–4.5 \times 10^9/l, with significantly higher proportion of lymphocyte (41.1–52.4%) and mildly elevated transaminase levels.
Positive blood culture from the patient yielded a Gram-negative coccobacillus initially identified as *B. bronchiseptica* (maximum identity 99%) through the VITEK 2 Compact microbial identification system and GN identification card. Serological tests for *Brucella melitensis* were negative (titers lower than 1:8), so the Brucella infection was not considered initially. However, *B. bronchiseptica* bacteremia is rare, so 16S rRNA PCR amplification and sequencing were performed for this strain. The results showed that the isolate had identity to *Brucella abortus* ACBJ01000075.1, *B. melitensis* ACEM01000005.1 and *Brucella microti* NC_013118.1 in *Brucella* sp., as well as *Ochrobactrum anthropi* ATCC 49188 NC_009668.1 (query coverage 100%; maximum identity 99%). But the *O. anthropi* could be excluded by the negative result of a motility test. Hence, the initial identification of *B. bronchiseptica* was incorrect.

During the last 30 years, eight clinical cases of *B. bronchiseptica* infection have been reported in China. Among the eight cases, four patients had significant underlying disease including asthma, brain trauma, rheumatic heart disease and iron-deficiency anemia, respectively [8–11]. Exposure to animals was documented in three cases [8–10]. Except for two patients with sepsis and shock as initial symptoms [8,10], the others mainly manifested as respiratory infection, including one with symptoms of bronchitis and five with pneumonia, one of which was associated with kidney abscess. Two patients with sepsis copresented with splenomegaly. In the bacteriology laboratory, the isolates were identified as *B. bronchiseptica* by Vitek-GN card (two cases), API 20NE [9] (one case) and ordinary biochemical reaction identification (one case). No details were given as to the identification of other cases.

*B. bronchiseptica* infection in humans has been reported elsewhere in the world, thereby providing much relevant information. We summarize here two groups of cases, the first including eight cases and the second including 25 cases.

Wernl *et al.* [4] reported an evaluation of eight cases confirmed as *B. bronchiseptica* infection. All patients except one had significant underlying disease, including four patients with severe lung disease, two patients with AIDS and one patient with autoimmune neutropenia. Cat exposure was documented in three cases, and in one case, the cat itself had respiratory symptoms. In this group, specimens of seven cases were retrieved from the airways and one isolated from the placenta of a pregnant woman undergoing cesarean section. She was an asymptomatic carrier and laboratory contamination could be reasonably excluded. Five patients had symptoms of pneumonia or bronchitis, two were asymptomatic carriers of the organism, and the remaining patients presented with colitis and septic shock unrelated to *B. bronchiseptica* airway colonization.

All organisms isolated from these cases were identified as *B. bronchiseptica* by API 20NE gallery or VITEK 2 (bioMerieuxSA, Marcy-l’Etoile, France) phenotypic identification systems, four of which were then verified by 16S rDNA sequencing. Unfortunately, the strain from the placenta was not confirmed by 16S rDNA sequence. Blood leukocyte counts from these cases were not provided. Their analysis confirms the tropism of *B. bronchiseptica* for the respiratory tract, leading to occasional upper airway colonization.

Woolfrey and Moody [12] reported 25 cases. Of these, 12 patients had significant underlying disease, including two trauma patients with vertebral fractures and orbital fractures, respectively, two patients with chronic lymphocytic leukemia, two patients with alcoholism, three patients with diabetes, Hodgkins disease and peritoneal dialysis, respectively, and three endocarditis patients, two of whom had aortic valve replacement. Most patients showed symptoms of respiratory tract infection (11 cases), which included eight with pneumonia, tracheobronchitis and three with sinusitis, epiglottitis and catarrh, respectively. Six patients presented with whooping cough, three patients presented with septicemia and three patients presented with meningitis, pleurisy and endocarditis, respectively. Of the 25 cases, only two had detailed information on laboratory tests; both had neutrophil leukocytosis. Of the 25 cases, 13 had some contact with animals. Specimens were obtained in nine cases from the respiratory tract, six from blood, two from cerebrospinal fluid and peritoneal dialysis fluid, respectively; the rest were unknown.

In only 10 cases was *B. bronchiseptica* identified using reliable microbiological ID systems, including eight by the API and VITEK systems and two by current stringent microbiological criteria. The remaining cases were identified as *B. bronchiseptica* mainly on the basis of biochemical reactions only.

For the three patients with symptoms of septicemia, two were confirmed as *B. bronchiseptica* infection by blood culture. The first isolate was identified by API 20E and the second by API 20E, VITEK and standard microbiological methods. But no identification details were provided for the patient with aortic valve replacement for endocarditis. In addition, the identification information of the strains isolated from other two endocarditis patients was also not presented, and one of them had bacteremia with blood culture yielding a Gram-negative coccobacillus only initially suspected to be *B. bronchiseptica* without further reliable identification. Obviously, although the endocarditis patients presented with bacteremia or sepsis, there was no reliable evidence to confirm they were infected by *B. bronchiseptica*.

For immunocompromised patients, especially those in some contact with animals, approximately 70 cases of...
infection with *B. bronchiseptica* have been described in the literature. The majority of cases have occurred among immunocompromised patients, such as AIDS patients, blood cancer patients and those with organ transplants. These patients were directly exposed to infected or colonized animals [6,13–16]. Unfortunately, many of these isolates were identified only by API 20NE or VITEK identification instruments. However, in one case of alcoholic liver disease, idiopathic pneumonia caused by *B. bronchiseptica* was described with the isolate, further bacteria being identified by 16S rRNA gene sequencing [17].

**Conclusion**

In summary, *B. bronchiseptica* rarely causes infection in humans. It is usually encountered as a pathogen in immunocompromised patients, especially those in contact with animals. The description of the manifestations and symptoms of *B. bronchiseptica* infection in the literature were somewhat similar to that of Brucella infection. Not all of these isolates were identified by the molecular biology methods. In our study, we found that Brucella might be misidentified as *B. bronchiseptica* by the VITEK 2 Compact microbial identification system. For this reason, it is recommended that all isolates initially identified as *B. bronchiseptica* by the VITEK 2 Compact microbial identification system be confirmed by molecular biology methods. In the absence of such instrumentation, special attention should be paid by the clinicians to exposure history of patients, especially the strains isolated from blood and other sterile sites, which should be highly suspected as Brucella rather than *B. bronchiseptica*.

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**Conflicts of interest**

R.X.Q. is a postgraduate of the Institute of Graduate Studies, Liaoning Medical University. She is engaged in the research in Clinical Laboratory, General Hospital of Shenyang Military Area Command, guided by X.W.C. and M.D.Y. There are no conflicts of interest and ethical adherence.

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