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Multifocal pneumonia caused by *Bordetella bronchiseptica*: Insights from a human case study

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ABSTRACT

This case report describes a 43-year-old man who presented with respiratory distress and was diagnosed with an exacerbation of congestive heart failure and multifocal pneumonia caused by *Bordetella bronchiseptica*. Microbiological work up of a respiratory sample identified the causative organism, prompting antibiotic treatment and recommending vaccination for his dog. This case emphasizes the need to consider diverse origins in respiratory infections for effective clinical management.

Introduction

The genus *Bordetella* consists of small, aerobic, non-spore-forming, non-fermenting gram-negative coccobacilli [1]. These bacteria typically inhabit mammalian upper respiratory tracts, including human upper respiratory tracts, acting as primary pathogens or in commensal relationships and potentially leading to opportunistic diseases [2]. *Bordetella* species cause various respiratory infections. Notably, *B. pertussis* is a key human pathogen causing whooping cough [1]. *B. bronchiseptica*, known for its role in canine infectious respiratory disease complex (CIRDC) or kennel cough (rhinotracheitis), also causes atrophic rhinitis in pigs and respiratory infections in domestic cats, rabbits, and laboratory animals [3–5]. *B. bronchiseptica* infections in humans are mainly reported in immunocompromised pet owners, including those who have undergone hematopoietic stem cell and organ transplants, who are cancer patients, and who have HIV/AIDS [2]. They have also been reported in viral pneumonia contexts [6], with only two cases in immunocompetent individuals [7,8].

Case description

A 43-year-old male presented to the emergency department with a 3-day history of worsening shortness of breath and wheezing, intensified during exertion and when lying flat. He reported a slightly productive cough and left-sided stabbing chest pain, but denied fever, chills, gastrointestinal symptoms, or recent exposure to sick individuals. His medical history included hypertension, stage 2 chronic kidney disease, mild congestive heart failure (grade 1/3), and impaired glucose intolerance. Upon arrival, his vital signs were as follows: blood pressure 162/129 mm Hg, heart rate 96 bpm, respiratory rate 18 breaths per minute, temperature 98.3°F, and pulse oximetry 93 %. Physical examination revealed clear bilateral chest auscultation without murmurs, rubs, or gallops, and minimal bilateral feet edema. Laboratory results showed troponin < 0.03 ng/mL, brain natriuretic peptide 501 pg/mL, creatinine 1.41 mg/dL, white blood cells 7.12 × 10^9/L, platelets 250 × 10^9/L, and hemoglobin 13.8 g/dL. Chest X-ray revealed patchy multilobar airspace disease. The echocardiogram showed an ejection fraction of 30–35 %, moderate to severe left ventricle dilation, and mild global hypokinesis with increased thickness. He was admitted for congestive heart failure exacerbation and multifocal pneumonia, receiving Lasix, ceftriaxone, and azithromycin.

A sputum specimen was collected into a sterile container with a tightly secured screw cap and submitted to the laboratory for culture and sensitivity testing. After performing a direct Gram stain, the sample was inoculated onto primary media plates, including BAP, CHO, MAC, and CNA agar, using a quadrant streak for isolation with a sterile 1 μl disposable loop. The primary media plates were incubated at 35 °C with 5 % CO2 for a minimum of 48 h, according to laboratory policy, and observed at 24-hour intervals. After 24 h post-inoculation a preliminary lab report was submitted, indicating isolates consistent with microorganisms commonly found in the upper respiratory tract. Sputum Gram stain revealed gram-negative rods and gram-positive cocci. At 48 h post incubation cultures on blood and chocolate agars grew oxidase positive, catalase positive, small, grayish-white, shiny, non-hemolytic colonies

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(Fig. 1A-B); on MacConkey agar non-lactose fermenting pale colonies appeared (Fig. 1C). The culture's Gram stain showed gram-negative short rods (Fig. 2). MALDI-TOF identified the *Bordetella* group including *B. pertussis*, *B. bronchiseptica*, and *B. parapertussis*. VITEK 2 ID-GN card was used for gram-negative rods and biochemical test profile (Table 1) confirmed the spp. *B. bronchiseptica* based on oxidase (done as a bench-top test), urease, and citrate positivity. *Bordetella pertussis*, which is urease and citrate negative and does not grow on MacConkey agar, was easily excluded from the group. When comparing *B. bronchiseptica* and *B. parapertussis*, the latter is oxidase negative, while our original CFU was found to be oxidase positive [9].

After microbiology consultation, the provider inquired about the patient's potential exposure to sick animals. The patient disclosed having a pet dog, however, the patient denied observing any symptoms indicative of kennel cough in the dog. Antimicrobial susceptibility testing was performed using the Vitek 2 system (Automated broth microdilution, bioMérieux, France) using AST-GN69 and AST-XN06 cards according to the manufacturer's instructions (Table 2) with the latest CLSI standards interpretation. This led to a change in treatment to ciprofloxacin 500 mg twice daily for 5 days. Upon improvement, the patient was discharged with a recommendation to administer vaccination against kennel cough for his dog.

Discussion

Originally, *B. bronchiseptica* was characterized as a pathogen causing respiratory diseases in various animals, particularly dogs. However, its association with human infections has gained increasing recognition [10]. Similar to other *Bordetella* species, *B. bronchiseptica* shows a tendency for respiratory colonization, leading to respiratory tract infections in humans, though less frequently than those in animals. Since 1911, nearly a hundred cases of human infection have been reported in the USA, with 62 cases documented worldwide [2,4,6,10,11]. The majority of these cases involve immunocompromised patients, often with a history of exposure to dogs or cats [12]. Some cases were reported following exposure to recently vaccinated dogs [13].

B. bronchiseptica organisms are small, gram-negative, aerobic, non-endospore forming bacilli. They are motile and oxidase and urease positive [1]. The genome of *B. bronchiseptica* is approximately 4400 kilobase pairs (kbp), akin to *B. parapertussis* but larger than *B. pertussis*, which is about 4000 kbp. This difference in genome size is believed to be due to genes needed for survival in the environment by both *B. bronchiseptica* and *B. parapertussis*. This is supported by the specific growth requirements of *B. pertussis*, which is fastidious and cannot survive at temperatures below 37 °C [14]. The virulence factors of *B. bronchiseptica* are categorized into three groups: a) adhesins aiding in respiratory tract colonization, like filamentous hemagglutinin (FHA), fimbriae, and pertactin; b) immunosuppressive factors such as BrkA; and c) toxins, including adenylate cyclase toxin and dermonecrotic toxin [15].

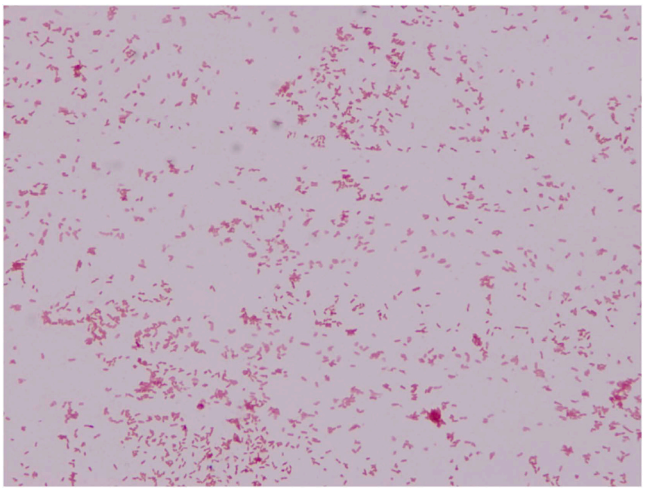

Fig. 2. Gram stain of *B. brochiseptica* pure culture showing gram-negative short rods.

The main clinical sign of *B. bronchiseptica* infections is respiratory tract symptoms, seen in over three-quarters of cases. Pneumonia is the most common, with other respiratory issues like sinusitis, bronchitis, and empyema also reported [4,16]. Extra-pulmonary manifestations like bacteremia, peritonitis, and pancreatic abscess have been observed in some cases [17,18].

Diagnosing a *B. bronchiseptica* infection involves a thorough patient history. Clinical suspicion should arise with prolonged respiratory symptoms like shortness of breath and cough, especially in those with pet exposure [4,16,19]. In immunocompromised or chronically ill patients, sputum sampling is recommended for culture and sensitivity [20]. Gram stains show gram-negative coccobacilli, and on blood agar, small, grayish-white, shiny, non-hemolytic colonies (Fig. 1A). On MacConkey agar (Fig. 1C), *B. bronchiseptica* forms small, clear-white, non-fermenting colonies [1]. Our lab uses FDA-approved MALDI-TOF MS (VITEK MS, bioMérieux, France) with Myla software for identifying routine isolates based on a published protocol[21] adapted to our

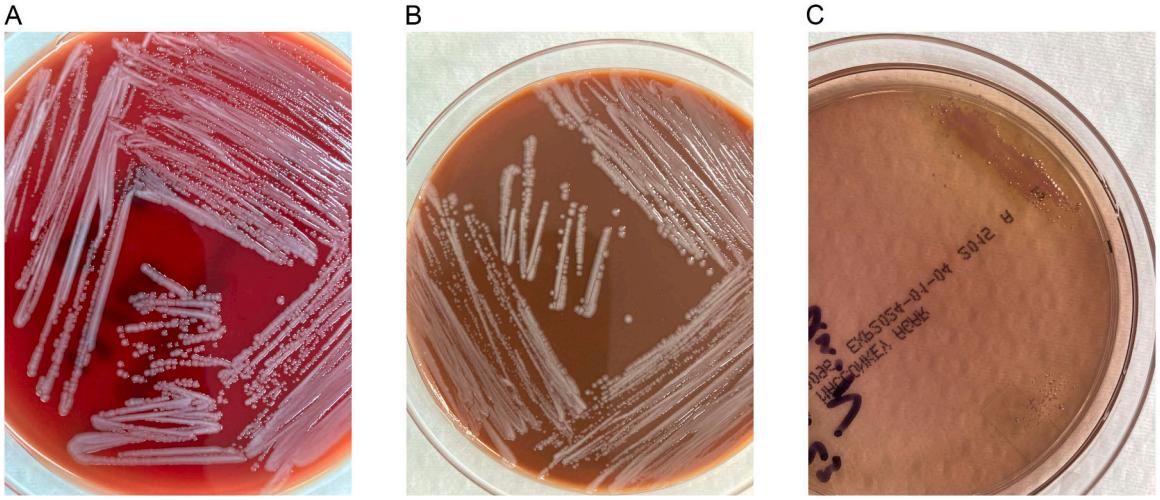

Fig. 1. *Bordetella brochiseptica* morphology. A. blood agar: small, grayish-white, shiny, non-hemolytic colonies. B. chocolate agar: small, grayish-white colonies C. MacConkey agar: small, clear-white, non-lactose fermenting colonies.

Table 1
Biochemical tests for *Bordetella bronchiseptica*: Results of 47 tests using Vitek 2 ID-GNB Panel.

Biochemical Test Details											
APPA	-	ADO	-	PyrA	+	lARL	-	dCEL	-	BGAL	-
H2S	-	BNAG	-	AGLTp	+	dGLU	-	GGT	-	OFF	-
BGLU	-	dMAL	-	dMAN	-	dMNE	-	BXYL	-	BAlap	-
BGLU	-	dMAL	-	dMAN	-	dMNE	-	BXYL	-	BAlap	-
ProA	+	LIP	-	PLE	-	TyrA	-	URE	+	dSOR	-
SAC	-	dTAG	-	dTRE	-	CIT	+	MNT	-	5KG	-
lLATk	-	AGLU	-	SUCT	-	NAGA	-	AGAL	-	PHOS	-
GlyA	-	ODC	-	LDC	-	lHISa	-	CMT	-	BGUR	-
O129R	-	GGAA	-	IMLTa	-	ELLM	-	ILATa	-		

List of table abbreviations.

APPA	Ala-Phe-Pro-Arylamidase	*BAlap*	Beta-Alanine Arylamidase pNa	*AGAL*	Alpha-Galactosidase
ADO	Adonitol	*ProA*	L-Proline Arylamidase	*PHOS*	Phosphatase
PyrA	L-Pyrrolydonyl-Arylamidase	*LIP*	Lipase	*GlyA*	Glyicine Arylamidase
lARL	L-Arabitol	*PLE*	Palatinose	*ODC*	Ornithine decarboxylase
dCEL	D-Cellobiose	*TyrA*	Tyrosine Arylamidase	*LDC*	Lysine Decarboxylase
BGAL	Beta-Galactosidase	*URE*	Urease	*lHISa*	L-Histidine Assimilation
H2S	H2S Production	*dSOR*	D-sorbitol	*CMT*	Coumarate
BNAG	Beta-N-acetyl-glucosaminidase	*SAC*	Saccharose/Sucrose	*BGUR*	Beta-glucuronidase
AGLTp	Glutamyl Arylamidase pNa	*dTAG*	D-Tagatose	*O129R*	2,4-Diamino-6,7-DiisopropylpteridineResistance
dGLU	D-Glucose	*dTRE*	D-Trehalose	*GGAA*	Glu-Gly-Arg-Arylamidase
GGT	Gamma-Glutamyl-Tranferase	*CIT*	Citrate	*IMLTa*	L-Malate Assimilation
OFF	Fermentation/Glucose	*MNT*	Malonate	*ELLM*	ELLMAN
BGLU	Beta-Glucosidase	*5KG*	5-Keto-D-Gluconate		
dMAL	D-maltose	*lLATk*	L-Lactate Alkalinisation		
dMAN	D-Manitol	*AGLU*	Alpha-Glucosidase		
dMNE	D-Mannose	*SUCT*	Succinate Alkalisation		
BXYL	Beta-xylosidase	*NAGA*	Beta-N-Acetyl-Galactosaminidase		

Table 2
Antimicrobial susceptibility profile of *Bordetella bronchiseptica*.

Antimicrobial	MIC	Interpretation
Piperacillin/Tazobactam	≤ 4	Sensitive
Cefazolin	≥ 64	Resistant
Ceftazidime	4	Sensitive
Ceftriaxone	≥ 64	Resistant
Cefepime	8	Sensitive
Imipenem	0.5	Sensitive
Amikacin	16	Sensitive
Gentamicin	2	Sensitive
Tobramycin	2	Sensitive
Ciprofloxacin	1	Sensitive
Levofloxacin	1	Sensitive
Trimethoprim/ Sulfamethoxazole	≤ 20	Sensitive

MIC = Minimum Inhibitory Concentration.

laboratory Standard operation Protocol. Briefly, using a sterile 1-μl loop, a portion of a single bacterial colony is removed from the Blood agar plate and applied as a thin layer to a target slide spot. Then, 1 μl of a saturated solution of CHCA matrix in 50 % acetonitrile and 2.5 % trifluoroacetic acid is added to each control and sample spot. The spots are allowed to air dry at room temperature. The slide and sample barcodes are read on the VITEK MS prep station to identify inoculated spots, and the data are then sent to Myla. After the colony is chosen and inoculated onto the target slide with matrix and slide information entered, the slide is fed into the VITEK-MS, where all further analysis steps are performed automatically by the instrument.

MALDI-TOF-MS based *Bordetella* spp identification has not been widely reported. A few recent studies have used it to distinguish the three main clinically relevant species in *B. bronchiseptica B. parapertussis* and *B. pertussis*. One study reported the possibility of distinguishing them without additional testing, although they also noted difficulty in differentiating them from *B. parapertussis* [22]. Another report confirmed the correct differential identification of *Bordetella* species but developed customized libraries for this purpose [23]. This practice is challenging for CLIA laboratories which used FDA approved/cleared MALDI-TOF-MS platforms. As a CLIA laboratory, we are unable to use customized libraries on our FDA-approved platform. However, this paper confirms that combining MALDI with the VIEK2 ID card yields successful results.

While MALDI-TOF identifies *Bordetella* group (*B. pertussis*, *B. bronchiseptica*, *B. parapertussis*), biochemical tests help differentiate between them [4]. *B. bronchiseptica* distinguishes itself from *B. pertussis* by its capacity to grow on MacConkey agar, along with positive reactions for nitrate reduction, urease, and citrate utilization. In contrast, *B. bronchiseptica* can be differentiated from *B. parapertussis* through its oxidase positivity and nitrate reduction capability [1].

Like other *Bordetella* species, *B. bronchiseptica* is resistant to beta-lactams, including penicillins and some cephalosporins, but has low minimum inhibitory concentrations (MICs) to antipseudomonal penicillins, carbapenems, tetracyclines, and quinolones. Treatment, based on case reports and in vitro data, often involves monotherapy or, less frequently, combinations of these drugs for one to two weeks [4,6,19].

In conclusion, this case underscores the evolving clinical picture of *B. bronchiseptica* infections in humans, highlighting its potential role in pneumonia cases, particularly in those with close contact with dogs. While most cases occur in immunocompromised individuals, our case shows that infections can also happen in immunocompetent patients with underlying cardiac disease. The identified antibiotic susceptibility profile informs targeted treatment, emphasizing the need for clinician awareness for timely diagnosis and effective management of *B. bronchiseptica*.

Author's contributions

All authors contributed to the study conception and design. Patient data and clinical description were collected by DN and MD. Microbiological diagnosis, taxonomy and antibiotics susceptibility tests were performed by SJR. The first draft of the case report was written by MD and edited by DN. All authors read and approved the final manuscript.

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CRediT authorship contribution statement

Dhammika H Navarathna: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Nada Mohamed:** Writing – review & editing, Writing – original draft, Validation, Resources, Investigation, Data curation. **Ma Rowena San Juan:** Methodology, Investigation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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