

***Bordetella bronchiseptica* pneumonia in a woman with lymphoma: A case report**

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ABSTRACT

A 62-year-old woman with splenic marginal zone lymphoma presented with fever, cough and bilateral pneumonia 11 days after chemotherapy. A bronchoalveolar lavage showed numerous leukocytes and Gram-negative bacilli that were identified as *Bordetella bronchiseptica* in culture. An antibiotherapy with minocycline and ciprofloxacin helped her to stop coughing. This unusual micro-organism, which has mainly an animal reservoir, is a rarely cause of human infection, almost always in immunocompromised patients. The main problems in *B. bronchiseptica* infection are the difficulties of identification of this micro-organism and the recurrence of infection, which are a challenge for microbiologists and practitioners.

Keywords: *Bordetella bronchiseptica*; Pneumonia; Lymphoma; Case Report

1. INTRODUCTION

Bordetella bronchiseptica is a Gram-negative coccobacillus that commonly causes respiratory tract infections in many mammalian species [1,2]. Human infection with *Bordetella bronchiseptica* is a rare condition that actually occurs almost always in immunocompromised patients, mainly in HIV infected patients [2-4]. The difficulties of identification of this bacterium and the recurrence are the main problems of *B. bronchiseptica* infection [5]. We report herein a case of *B. bronchiseptica* bilateral lung infection in a woman with splenic marginal zone lymphoma.

2. CASE REPORT

A 62-year-old woman was admitted to our hospital for

recurrence of splenic marginal zone lymphoma. Her past medical history included diabetes mellitus, splenectomy and hypothyroidism. HIV serology was negative. She did not have a history of chronic respiratory disease (asthma, emphysema, or chronic bronchitis) or of exposure to tobacco smoke. She lived on a farm in Algeria 20 years ago but returned occasionally from France to Algeria and had significant exposure to cats, dogs and to rabbits. However, at the time of admission she earned no pet. She had severe lymphoma recurrence with liver and bone marrow infiltration and received a single R-CHOP (rituximab, cyclophosphamide, doxorubicine, vincristine, and prednisone) infusion through a central catheter that was taken off after chemotherapy administration. At day 11 after chemotherapy, she presented with cough and fever. Physical examination revealed no hypotension, normal respiratory frequency but diminished oxygen saturation of 86% (arterial haemoglobin) on room air, no abdominal pain, no diarrhoea. Chest examination found bilateral crepitant rales and normal heart auscultation. Laboratory values showed 840/mm³ white blood cells with 15/mm³ neutrophils and 790/mm³ lymphocytes, haemoglobin 8.3 g/dl, platelets 28,000/mm³, normal hepatic tests; C-reactive protein 256 mg/l, serum creatinin 59 µmol/l. Urinary legionella antigen and serum aspergillus antigen were negative. Chest X-ray and Computed Tomography scan showed bilateral pneumonia. Treatment for severe pneumonia was started with cefepim 4 g/day and amikacin 1 g/day. Direct examination of bronchoalveolar lavage showed numerous leukocytes and Gram-negative bacilli. The sample was inoculated onto anaerobic blood agar, chocolate agar in an atmosphere of 5% carbon dioxide, Drigalski agar at ambient atmosphere, and incubated at 37°C. Multiple small, convex, spheroidal colonies approximately 1 mm in diameter were isolated after 24 h (10⁵ bacteria/ml of bronchoalveolar lavage). The isolate was catalase- and oxidase-

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positive, motile and peritrichous, and strictly aerobic. It was also positive in tests for urease, nitrate reduction and citrate utilization, and negative for indole, hydrolysis of esculin and gelatin, and acid production from carbohydrates, including D-glucose, D-mannitol, D-maltose, L-arabinose, D-mannose and D-saccharose. The organism was identified as *Bordetella bronchiseptica* by using the API 20NE systems (bioMérieux, Marcy l'Etoile, France); this identification was confirmed by 16S rRNA sequencing (100% of nucleotide identity with the sequence of *B. bronchiseptica* RB50, GenBank accession No. NC002927) over a 518 bp DNA fragment amplified and sequenced with primers 5'-AGAGTTTGATCC-TGGYTCAG-3' and 5'-CTTTACGCCARTAAWTC-CG-3' and analyzed in the GenBank database: www.ncbi.nlm.nih.gov/genbank. Identification was confirmed by the French National Reference Centre for Bordetellosis. Serologies (IgG anti-pertussis toxin) before infection and one month after the onset of clinical symptoms were negative. Cefepim and amikacin were changed for ticarcillin-clavulanic acid 12,000 mg/day and ciprofloxacin 800 mg/day for 5 days with a good efficacy on fever. Cough was still present. Ticarcillin-clavulanic acid was stopped and replaced by minocycline 200 mg/day. The patient received a treatment with tetracycline and ciprofloxacin for a total of 21 days which helped to stop coughing. She died two weeks after antibiotics discontinuation of lymphoma induced severe lactic acidosis.

3. DISCUSSION

The genus *Bordetella* comprises three species of Gram-negative respiratory pathogens, *B. pertussis*, *B. parapertussis* (cause whooping cough or pertussis in humans), and *B. bronchiseptica*. The entire genome sequences of *B. pertussis*, *B. parapertussis*, and *B. bronchiseptica* have been published [6]. *B. pertussis* and *B. parapertussis* each are reported to derive from a *B. bronchiseptica*-like ancestor. *B. pertussis* and *B. parapertussis* are extremely fastidious, contrary to *B. bronchiseptica*.

Although human disease due to *B. bronchiseptica* was reported as early 1911, the microorganism was not clearly distinguished until the studies of Johnson and Sneath in 1973 and Bemis *et al.* in 1977 from certain phenotypically nonfermentative similar isolates, particularly some members of the genera *Acinetobacter*, *Alcaligenes*, *Pseudomonas*, and *Brucella* [1,7]. It was known by a variety of names such as *Haemophilus bronchiseptica*, *Brucella bronchiseptica*, *Bacillus suisepiticus*, *Alcaligenes bronchicanis*, and *Alcaligenes bronchiseptica*.

Bordetella bronchiseptica commonly causes respiratory tract infections in many mammalian species, including cats, dogs and laboratory animals [1,2]. *Bordetella bronchiseptica* is a rarely reported cause of human

infection, mainly respiratory infections, although atypical clinical presentations have been reported (like meningitis, endocarditis, peritonitis) [3,8,9]. The respiratory illnesses ranged in severity from mild upper respiratory tract infection to cavitary pneumonia and bacteraemia or shock and could lead to death. *B. bronchiseptica* is considered as an opportunistic infection associated with immunocompromised patients, mainly in HIV infected patients but also malignant haematological underlying disease (leukaemia, Hodgkin's disease, and multiple myeloma), transplant patients or various immunodeficiencies (alcohol addiction, cystic fibrosis...) [3,10,11]. Infections have also been described in immunocompetent persons but always in a specific context such as post-surgery, trauma, hemodialysis, or respiratory infections [9,10]. Often, however not necessary, a contact with an appropriate animal reservoir is reported [3-5,11].

The occurrence of *Bordetella bronchiseptica* infection results on the patient's underlying immunosuppression and the ability of *Bordetella bronchiseptica* to inhibit leukocyte function and to adhere to respiratory epithelial cells [12]. The abilities of *B. bronchiseptica* to colonize and to establish upper respiratory tract infection depend on the production of virulence factors. *Bordetella bronchiseptica* synthesizes all of the factors implicated in *B. pertussis* virulence (adhesins, such as filamentous hemagglutinin, fimbriae, and pertactin and toxins such as dermonecrotic toxin, tracheal cytotoxin, type III secretion system, endotoxin and adenylate cyclase-hemolysin) except for pertussis toxin [5,10,13,14].

The optimal therapy for *B. bronchiseptica* infections has not been clearly established, but the response to a number of antimicrobial agents appears to be similar to that expected for nonfermentative Gram-negative bacilli. However, despite the good *in vitro* activities of these antibiotics, the clinical responses to them have often been disappointing. The *in vitro* susceptibility tests using a disk diffusion technique on Mueller-Hinton agar according to the Antibiogram Committee of the French Microbiology Society showed that this bacterium was susceptible to aminoglycosides (amikacin, tobramycin and gentamicin, but not streptomycin), ticarcillin, piperacillin, ceftazidime and imipenem, fluoroquinolones (although MIC of ciprofloxacin appear near the susceptibility breakpoint), tetracyclins, trimethoprim-sulfamethoxazole and chloramphenicol. It was resistant to ceftioxin, cefamandole, cefotaxime, aztreonam. The amino- and carboxy-penicillins alone appear to be less effective than their association with beta-lactamase inhibitor, it might be explained of the beta-lactamase BOR-1 in *B. bronchiseptica*, a naturally occurring penicillinase [15]. The principal problem in *B. bronchiseptica* infection is the recurrence, needing a long duration of treatment.

4. CONCLUSION

Our report underscores that unusual micro-organisms from nonhuman sources are potential serious pathogens in patients who are immunocompromised. The difficulties of identification of these micro-organisms, which can induce a therapeutic delay, are a challenge for practitioners.

REFERENCES

- [1] Bemis, D.A., Greisen, H.A. and Appel, M.J. (1977) Bacteriological variation among *Bordetella bronchiseptica* isolates from dogs and other species. *Journal of Clinical Microbiology*, **5**, 471-480.
- [2] Dworkin, M.S., Sullivan, P.S., Buskin, S.E., *et al.* (1999) *Bordetella bronchiseptica* infection in human immunodeficiency virus-infected patients. *Clinical Infectious Diseases*, **28**, 1095-1099. doi:10.1086/514761
- [3] Woolfrey, B.F. and Moody, J.A. (1991) Human infections associated with *Bordetella bronchiseptica*. *Clinical Microbiology Reviews*, **4**, 243-255.
- [4] Wernli, D., Emonet, S., Schrenzel, J. and Harbarth, S. (2011) Evaluation of eight cases of confirmed *Bordetella bronchiseptica* infection and colonization over a 15-year period. *Clinical Microbiology and Infection*, **17**, 201-203. doi:10.1111/j.1469-0691.2010.03258.x
- [5] Gueirard, P., Weber, C., Le Coustumier, A. and Guiso, N. (1995) Human *Bordetella bronchiseptica* infection related to contact with infected animals: Persistence of bacteria in host. *Journal of Clinical Microbiology*, **33**, 2002-2006.
- [6] Parkhill, J., Sebaihia, M., Preston, A., *et al.* (2003) Comparative analysis of the genome sequences of *Bordetella pertussis*, *Bordetella parapertussis* and *Bordetella bronchiseptica*. *Nature Genetics*, **35**, 32-40. doi:10.1038/ng1227
- [7] Johnson, R. and Sneath, P.H.A. (1973) Taxonomy of *Bordetella* and related organisms of the families *Achromobacteraceae*, *Brucellaceae*, and *Neisseriaceae*. *International Journal of Systematic and Evolutionary Bacteriology*, **23**, 381-404. doi:10.1099/00207713-23-4-381
- [8] Hadley, K., Torres, A.M., Moran, J. and Schiller, B. (2009) *Bordetella bronchiseptica*—Beware of the dog! *Peritoneal Dialysis International*, **29**, 670-671.
- [9] Belen, O., Campos, J.M., Cogen, P.H. and Jantusch, B.A. (2003) Postsurgical meningitis caused by *Bordetella bronchiseptica*. *The Pediatric Infectious Disease Journal*, **22**, 380-381. doi:10.1097/01.inf.0000059766.51912.e8
- [10] Mattoo, S., Miller, J.F. and Cotter, P.A. (2000) Role of *Bordetella bronchiseptica* fimbriae in tracheal colonization and development of a humoral immune response. *Infection and Immunity*, **68**, 2024-2033.
- [11] Huebner, E.S., Christman, B., Dummer, S., *et al.* (2006) Hospital-acquired *Bordetella bronchiseptica* infection following hematopoietic stem cell transplantation. *Journal of Clinical Microbiology*, **44**, 2581-2583. doi:10.1128/JCM.00510-06
- [12] Bauwens, J.E., Spach, D.H., Schacker, T.W., *et al.* (1992) *Bordetella bronchiseptica* pneumonia and bacteremia following bone marrow transplantation. *Journal of Clinical Microbiology*, **30**, 2474-2475.
- [13] López-Boado, Y.S., Cobb, L.M. and Deora, R. (2005) *Bordetella bronchiseptica* flagellin is a proinflammatory determinant for airway epithelial cells. *Infection and Immunity*, **73**, 7525-7534. doi:10.1128/IAI.73.11.7525-7534.2005
- [14] Pilione, M.R. and Harvill, E.T. (2006) The *Bordetella bronchiseptica* type III secretion system inhibits gamma interferon production that is required for efficient antibody-mediated bacterial clearance. *Infection and Immunity*, **74**, 1043-1049. doi:10.1128/IAI.74.2.1043-1049.2006
- [15] Lartigue, M.F., Poirel, L., Fortineau, N. and Nordmann, P. (2005) Chromosome-borne class A BOR-1 beta-Lactamase of *Bordetella bronchiseptica* and *Bordetella parapertussis*. *Antimicrobial Agents and Chemotherapy*, **49**, 2565-2567. doi:10.1128/AAC.49.6.2565-2567.2005