Hospital-Acquired *Bordetella bronchiseptica* Infection following Hematopoietic Stem Cell Transplantation

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Two patients who had undergone nonmyeloablative allogeneic stem cell transplantation 53 and 112 days earlier and were being monitored at the same transplant center developed severe *Bordetella bronchiseptica* infections within 3 days of each other. Pulsed-field gel electrophoresis analysis indicated that the isolates from the two cases were identical. Neither patient had had direct contact with animals since transplantation. These findings strongly support nosocomial transmission of *B. bronchiseptica*.

*Bordetella bronchiseptica* is a small gram-negative coccobacillus that is primarily a veterinary pathogen, causing kennel cough in dogs and atrophic rhinitis in swine. Human disease is rare but has been described to occur in individuals that are immunocompromised and occasionally occurs following contact with sick pets or farm animals (12). To our knowledge, only two previous cases have been described to occur following bone marrow transplantation (2, 5). We describe two cases of *B. bronchiseptica* infection that occurred at a transplant center within 3 days of each other, which strongly suggested the presence of nosocomial transmission.

Patient 1, a 53-year-old man with Hodgkin’s disease, underwent nonmyeloablative allogeneic hematopoietic stem cell transplantation (HSCT) after failing autologous transplantation. On day 53 following allogeneic transplantation, he presented with diarrhea and fatigue. His course had been complicated by graft-versus-host disease (GVHD) of the skin and gastrointestinal tract, requiring high-dose corticosteroid treatment. A week earlier, he had been started on radiation therapy for persistent adenopathy in the left axilla. On the day of admission, he had a temperature of 100.2°F and described profound weakness, mild abdominal discomfort, and shortness of breath. His physical exam was significant for severe anasarca, bilateral wheezing, and an oxygen saturation of 90% on room air. A laboratory exam revealed pancytopenia, with a total white blood cell count of 330/mm³, and renal insufficiency, with a creatinine level of 2.2 mg/dl. He had profound hypoaalbuminemia (1.3 g/dl) and a decreased immunoglobulin G (IgG) level suggestive of a protein-losing gastroenteropathy. A chest radiograph showed pulmonary congestion and bilateral patchy infiltrates. He was begun on renal ultrafiltration and his prophylactic regimen of ciprofloxacin, acyclovir, and itraconazole was altered to include ceftazime and metronidazole. Stool analysis was positive for *Clostridium difficile* toxin A. The next morning, he had an episode of profuse epistaxis followed by a decline in respiratory status necessitating tracheal intubation. His blood pressure began to drop, and he required escalating doses of vasopressors. On the third hospital day, he had an asystolic arrest and was unable to be resuscitated. Autopsy showed diffuse pseudomembranous colitis, as well as diffuse necrotizing bronchopneumonia and extensive alveolar hemorrhage. Cultures of the stool, pre- and postmortem blood, and postmortem lung tissue revealed gram-negative rods that were positive for oxidase and urease and were identified as *B. bronchiseptica* by use of the API 20 NE identification system (1). Culture results were confirmed by the Tennessee Department of Health Laboratory Services by use of the MicroLog identification system (Biolog Inc., Hayward, CA).

Patient 2, a 50-year-old man with IgA(κ) multiple myeloma, had also failed autologous transplantation. He was found to have a cavitory lung nodule in the right middle lobe by chest radiograph 112 days following nonmyeloablative allogeneic HSCT. The patient had no pulmonary symptoms and complained only of fatigue. He had been diagnosed with GVHD of the gastrointestinal tract when he presented with diarrhea on day 68 and was receiving tapering doses of corticosteroids. A computed tomography scan confirmed the presence of an 18-mm cavitory lesion. At bronchoscopy, the patient’s airways appeared normal but he had moderately thick, white secretions in the right middle and upper lobes. Cultures from the bronchoalveolar lavage grew a gram-negative rod that was identified as predominant *B. bronchiseptica* as well as exhibiting light growth of normal respiratory flora. The organism was found to be susceptible to ciprofloxacin, imipenem, and amikacin. Culture results were confirmed by the Tennessee Department of Health Laboratory Services. The patient was treated with ciprofloxacin, with complete resolution of the lung nodule by a subsequent computed tomography scan obtained 2 months later.

Although patients 1 and 2 were not hospitalized simultaneously before these events, both had regular follow-up in the transplant clinic and were seen almost daily during the weeks leading up to their illnesses. The initial *Bordetella* isolates from these patients were obtained only 3 days apart. Further questioning revealed that patient 1 had two pet dogs at home, which may have served as a potential source of the organism. Neither patient had had any direct contact with animals since their transplantation. A pulsed-field gel electrophoresis analysis (4) indicated that the isolates recovered from the two patients...
were identical, suggesting infection with the same *B. bronchiseptica* strain (Fig. 1).

Although human disease due to *B. bronchiseptica* was reported as early as 1911 (10), it was not until the 1970s that this organism was clearly distinguished from phenotypically similar microorganisms, such as *Acinetobacter*, *Pseudomonas*, and *Brucella* species (12). *B. bronchiseptica* is a gram-negative, obligate aerobe that grows readily on simple nutritive media and tests positive for catalase, oxidase, citrate utilization, urease, and nitrate reduction. Most isolates are motile due to the presence of peritrichous flagella. It is a respiratory tract pathogen common in wild and domestic animals and is well established as a cause of infectious tracheobronchitis, or “kennel cough,” in dogs. It has been implicated as a cause of otitis media and tracheal bronchitis in rabbits as well as turinate atrophy in swine (12).

*B. bronchiseptica* readily colonizes the upper respiratory tracts of animals and synthesizes virulence factors, including filamentous hemagglutinin and fimbrae, which aid in adherence to respiratory epithelial cells (8, 9). Adherence to cilia results in stasis and difficulty clearing mucous secretions (3). The bacterium also produces the enzyme adenylate cyclase, which suppresses superoxide production by alveolar macrophages and thus contributes to its ability to elude host defense (6, 7).

The organism is also capable of colonizing the human respiratory tract. Despite potentially frequent exposure to sources of this bacterium, human infections are rare. Until 1991, only 25 cases of human infection had been reported, and these are reviewed elsewhere (12). These included reports of pneumonia, sinusitis, whooping cough, meningitis, endocarditis, and nosocomial tracheobronchitis. Underlying immunosuppression was an apparent predisposing factor in many of these cases and included diabetes, leukemia, alcoholism, and Hodgkin’s disease. In many cases, there was also a history of contact with pets or farm animals, suggesting zoonotic transmission. Since that time, over 30 additional cases have been reported. AIDS is increasingly described as the underlying cause of immunodeficiency. To our knowledge, only two cases have occurred following bone marrow transplantation (2, 5). The first was a 20-year-old woman with acute myelogenous leukemia in whom *B. bronchiseptica* was detected by bronchoalveolar lavage 15 days following transplantation (2). She initially improved with ciprofloxacin and doxycycline treatment, but she had persistently positive cultures in the sputum and later the blood and eventually died of multiorgan failure. The second case was a 7-year-old boy with X-linked hyper-IgM syndrome who developed fever and cough 7 days following transplantation (5). Initial chest radiographs were normal, but later radiographs showed bilateral infiltrates. Sputum cultures grew *B. bronchiseptica*. He received erythromycin, ciprofloxacin, and rifampin and cleared the organism, but he eventually died of *Aspergillus fumigatus* pneumonia.

Nosocomial transmission of *B. bronchiseptica* was reported to occur once in a pulmonary ward (11). We describe two cases of *B. bronchiseptica* infection occurring in patients who had contact with each other during frequent visits to the transplant clinic after nonmyeloablative HSCT. Both patients were severely immunocompromised from their transplants and their treatment for GVHD. Pulsed-field gel electrophoresis analysis using restriction enzyme XbaI indicated that the two patients’ isolates were identical. The data strongly suggest that nosocomial transmission occurred, either from one patient to the other or from a third party, presumably a health care worker, to each of these patients. The initial source may have been a pet dog owned by patient 1. Although *B. bronchiseptica* is an unusual pathogen in humans, these cases further document that disease occurs following stem cell and marrow transplantation and that nosocomial transmission is a concern. These cases also show that recent exposure to animals is not necessary for the acquisition of this infection in highly immunocompromised individuals.

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**REFERENCES**


