Fatal Pneumonia due to *Bordetella bronchiseptica*

Zvi Shimoni MD[1], Mark Niven MA MB BChir MRCP[1], Margarita Mosenkis MD[1] and Joel Greif MD[2]

[1]Department of Internal Medicine B, Laniado Hospital, Netanya, and [2]Department of Pulmonary Medicine, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

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Infection with unusual organisms in immunocompromised patients is now a familiar and increasing problem. In the absence of an adequate immune response even apparently optimal treatment may fail.

The genus *Bordetella* is well known from its species *pertussis* and *parapertussis*. However, the two other species in the genus, *bronchiseptica* and *avium*, are far less familiar. We present a case of infection with *Bordetella bronchiseptica* in a probably immunocompromised host, in whom therapy was unsuccessful in spite of appropriate treatment according to *in vitro* laboratory sensitivity testing.

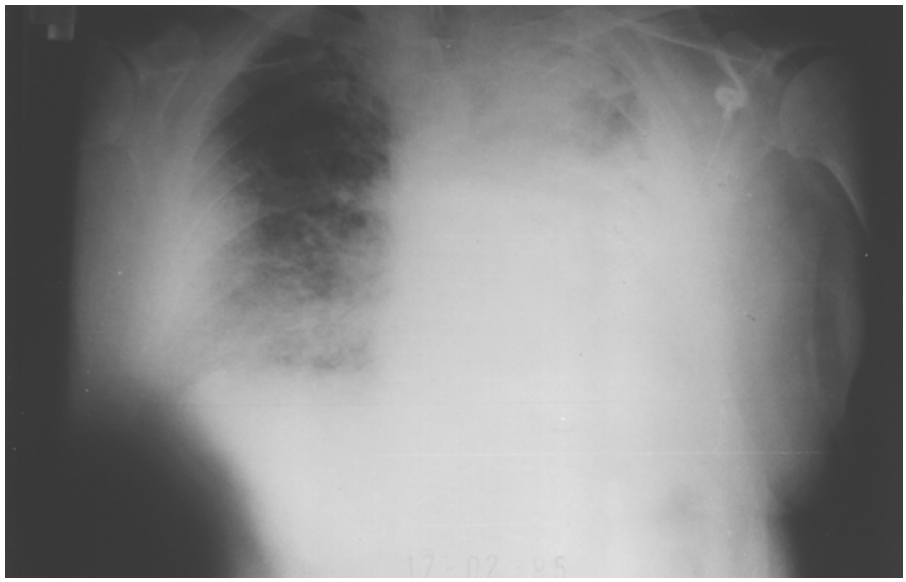

Figure A. Chest X-ray of the patient on admission.

Case Description

A 69-year-old man was admitted with a 7 day history of low grade fever and progressive dyspnea. He received amoxycillin for 5 days prior to admission without improvement. He had smoked for more than 30 years and suffered from pulmonary tuberculosis in his distant past. Seven months prior to admission he underwent a left upper lobectomy because of non-small cell lung carcinoma, and postoperatively received both chemotherapy and radiotherapy from which he apparently recovered well. He received no treatment for at least 4 months prior to the admission. A follow-up chest computed tomography scan a month prior to admission revealed a small infiltrate in the apical segment of the left lower lobe and a small calcified focus at the right apex, but no mediastinal lymphadenopathy.

On admission he was severely breathless but not cyanosed. Temperature was 38.2°C, heart rate 108/min regular, blood pressure 130/80 and respiratory rate 26/min. The heart sounds were normal with no murmurs. There were diminished breath sounds over the left lung and coarse crackles on the right. His abdomen was soft and non-tender with no organomegaly.

Initial laboratory evaluation showed white blood cell count of 10.5×10^9/L with 88% neutrophils, 7% lymphocytes and 5% monocytes. Hemoglobin was 10.8 g/dl and platelet count 209×10^9/L. Electrolytes, renal and liver function tests and coagulation studies were all normal apart from a slightly elevated lactate dehydrogenase. Urine analysis was unremarkable. While the patient breathed room air, arterial blood analysis showed pH 7.40, P_aCO_2 3.9 kPa and P_aO_2 6.3 kPa. The P_aO_2 rose to 7.4 kPa while breathing 100% oxygen via a face mask. The electrocardiogram showed sinus tachycardia. The chest X-ray [Figure A] showed complete opacification of the left lower lobe and infiltrates in the left upper lobe, together with a non-homogeneous infiltrate in the right lower lobe.

Treatment of intravenous ceftriaxone was begun with an initial dose of 2 g and then 1 g/24 hourly. Over the next 3 days his condition remained fairly static with a persistent fever of up to

38°C and breathlessness. On the fourth hospital day, the lack of improvement raised concern about infection with *Pneumocystis carinii* and *Legionella* and therefore intravenous trimethoprim-sulphamethoxazole and erythromycin were added to the treatment regimen. During the next 12 hours there was an apparent response with a fall in his temperature to 36.6°C.

However his condition deteriorated again the next day with persistent hypoxemia, and he was intubated and mechanical ventilation initiated. He required an inspired oxygen concentration of 70–100% with 14 breaths/min in order to maintain P_aO_2 above 10.5 kPa. Broncheoalveolar lavage was performed on the sixth day. Examination of the lavage showed many polymorphonuclear cells but no evidence of malignancy. His condition continued to deteriorate with the development of septic shock, and he died on the eighth day after admission. No autopsy was performed. Initial blood and urine cultures had shown no bacterial growth. Culture of the broncheoalveolar lavage revealed *B. bronchiseptica*, with results of *in vitro* sensitivity to ceftriaxone,trimethoprim-sulphamethoxazole, amoxycillin-clavulanic acid and piperacillin.

Comment

The genus *Bordetella* consists of four species: *pertussis*, *parapertussis*, *bronchiseptica* and *avium*. *Bordetella pertussis* and *parapertussis* are common human pathogens, and until recently most experimental work on this genus was with *Bordetella pertussis*. *B. bronchiseptica* is a small, pleomorphic, gram-negative coccobacillus. It is a common respiratory tract commensal of mammals, and although relatively rare in humans it has been recognized since 1910 as a human respiratory tract pathogen [1]. When infections occur in humans they are often acquired through animal contact and typically involve immunocompromised patients, with reports of infection in Hodgkin's disease, chronic lymphocytic leukemia, other chronic debilitating conditions, and recently in human immunodeficiency infected patients [2]. The respiratory tract is the most common site of infection, with a range of clinical manifestations including sinusitis, tracheobronchitis, whooping cough and pneumonia [3]. Radiographic appearances of lower respiratory tract infections include diffuse infiltrates, interstitial and lobar pneumonia. There have also been reports of septicemia in humans including endocarditis.

The patient described here had not had any contact with animals. However, he was presumably immunocompromised because of his lung cancer, major surgery and later treatment with chemotherapy and radiotherapy. The results of *in vitro* sensitivity testing showed the cultured organism to be sensitive to the antibiotic therapy that he had taken, both the initial ceftriaxone and the subsequently added trimethoprim-sulphamethoxazole. Nevertheless, there was no significant clinical response to the multiple antibiotic therapy that he received. It is of interest that the specimen from which the organism was cultured was obtained while he was receiving these drugs, suggesting lack of *in vivo* efficacy despite the laboratory results.

The optimal therapy for *Bordetella* has not yet been established. Reports of *in vitro* susceptibility testing suggest that aminoglycosides, anti-pseudomonal penicillins, tetracyclines, ciprofloxacin and chloramphenicol should all be effective [3], and indeed the isolate from our patient was sensitive to all these agents. Some authors believe that when initial antibiotic therapy fails, erythromycin is the preferred antibiotics for the treatment of *B. bronchiseptica* pneumonia. In contrast, Kurzynski et al. [4], in an *in vitro* study of 11 isolates of *B. bronchiseptica*, found none of them to be susceptible to erythromycin.

There are many potential reasons for a lack of correlation between *in vitro* sensitivity and *in vivo* efficacy, including host factors such as inability to mount an immune response, injury caused by non-viable organisms, and failure of delivery of an adequate concentration of the antibiotic to the organism. Mechanisms specific to the organism may also be important. *B. bronchiseptica* has been reported to produce an enzyme, adenylate cyclase, that enters host polymorphonuclear cells and macrophages, and disrupts chemotaxis, superoxide production and bacterial killing [5], thus protecting the bacterium from attack *in vivo*. This mechanism may, at least in part, explain the disparity between the laboratory sensitivities and clinical response in our patient.

We would suggest that *Bordetella bronchiseptica* is a potentially serious, albeit rare cause of pneumonia, particularly in immunocompromised patients. The optimum antibiotic therapy remains uncertain, necessitating intensive empirical therapy.

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Correspondence: Dr Z. Shimoni, Dept. of Internal Medicine B, Laniado Hospital, Netanya 42150, Israel. Tel: (972-9) 860 4610; Fax: (972-9) 860 4781
email: mniven@trendline.co.il