Branhamella (Neisseria) catarrhalis—a Lower Respiratory Tract Pathogen?

MARY ANNE JOHNSON,† W. LAWRENCE DREW,* AND MARILYN ROBERTS

Departments of Pathology and Laboratory Medicine and Medicine, Mount Zion Hospital and Medical Center, San Francisco, California 94120,† and Department of Microbiology and Immunology, University of Washington School of Medicine, Seattle, Washington 98105

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Branhamella (Neisseria) catarrhalis was identified as a probable respiratory tract pathogen in seven patients, four with pneumonia and three with bronchitis. Five of the B. catarrhalis isolates produced β-lactamase. Production of β-lactamase correlated with penicillin resistance by the standardized disk diffusion method and also with high minimal inhibitory concentrations of penicillin for the two strains which were tested.

In the past year, we have observed two characteristics of Branhamella (Neisseria) catarrhalis which have not been widely recognized. The first is the apparent capacity to produce acute respiratory infections in patients with chronic lung disease, and the second is the ability to produce β-lactamase. In seven patients—all of whom had underlying pulmonary pathology—bronchiectasis or pneumonia was documented by clinical presentation, roentgenographic findings, and sputum examination. We used one method for plasmid extraction and found no plasmid deoxyribonucleic acid in the β-lactamase-positive or -negative strains of B. catarrhalis.

CASE REPORTS

Patient 1. Patient 1 was a 53-year-old man admitted 19 April 1978 with fever and an acute episode of wheezing following aspiration. In the past, the patient had undergone surgery for a giant hiatal hernia and now had an intrathoracic stomach. Recurrent episodes of aspiration pneumonia had prompted numerous hospitalizations. Examination upon this admission showed an acutely ill man in respiratory distress. Wheezing was heard throughout the chest. A chest X-ray showed a large infiltrate in the right lower lobe and a smaller infiltrate in the left lower lobe. The patient was treated with bronchodilators, steroids, and penicillin. The sputum Gram stain showed 3+ polymorphonuclear leukocytes, 3+ gram-positive cocci in pairs and short chains, and 3+ gram-negative cocci (see below). The culture subsequently grew 3+ Streptococcus pneumoniae and 2+ oral flora. The patient improved only slightly after treatment with penicillin and then ampicillin, and he continued to aspirate. Repeated sputum Gram stains showed persistence of leukocytes and gram-negative cocci. Repeated cultures grew only 3+ B. catarrhalis and were β-lactamase positive. Because of persistent fever, leukocytosis, and pulmonary infiltrates, therapy was changed to oral tetracycline to treat the B. catarrhalis infection. The subsequent course of the patient was one of gradual clinical and roentgenographic improvement, and he was discharged afebrile with a clear chest X-ray after 7 days of oral tetracycline.

Patient 3. Patient 3 was a 75-year-old woman admitted 19 November 1978 with acute pulmonary edema. She had a history of diabetes mellitus, refractory congestive heart failure, cranial arteritis treated with steroids, and chronic bronchitis with emphysema. The patient responded to therapy for her congestive failure but was noted to have a productive cough 1 day after admission. She had no fever and no roentgenographic evidence of pneumonia. A sputum Gram stain revealed 4+ polymorphonuclear leukocytes and 4+ gram-negative diplococci. The patient was started on oral tetracycline, and there was an improvement of her cough and a decrease in sputum production. The sputum culture subsequently grew 3+ B. catarrhalis and was β-lactamase positive but susceptible to tetracycline.

MATERIALS AND METHODS

Patients with suspected B. catarrhalis infection were identified by reviewing sputum Gram stains and culture results. Charts of patients with apparent infection were then reviewed to obtain information on clinical course, roentgenographic findings, treatment, and outcome.

All sputum specimens received in the laboratory were initially processed in the same way. A purulent portion of sputum was selected for Gram staining and culturing. Blood and chocolate agars were inoculated and incubated in 5% CO2. Another blood agar plate was incubated anaerobically, and a MacConkey agar plate was incubated aerobically. Quantitation of organisms, leukocytes, and epithelial cells by the Gram stain was assessed on a 1+ to 4+ scale: 1+ indicates 1 per oil immersion field; 2+ indicates 1 to 5 per oil

† Present address: Department of Family Practice, San Francisco General Hospital, San Francisco, CA 94110.
immersion field; 3+ indicates 5 to 30 per oil immersion field; 4+ indicates 30 or more per oil immersion field. Quantitation of bacterial growth was assessed on a 1+ to 4+ scale: 1+ indicates light growth in the primary streaking zone of the original plate; 2+ indicates heavy growth in the primary streaking zone; 3+ indicates growth in the primary and secondary streaking zones only; and 4+ indicates growth in the primary, secondary, and tertiary streaking zones.

_B. catarrhalis_ was identified by the following characteristics: gram-negative diplococci; oxidase positive; growth on chocolate and blood agars, at 36°C in air or 5% CO₂, o-nitrophenyl-β-D-galactopyranoside negative; citrate negative; and nitrate reduced. Carbohydrate fermentation was tested with the Minitek system (BBL Microbiology Systems, Cockeysville, Md.) and was negative for glucose, maltose, and lactose. Identification of the isolates as_B. catarrhalis_ was confirmed by the San Francisco Department of Public Health.

β-Lactamase was detected by a modification of the chromogenic cephalosporin procedure (11). Penicillin susceptibility was tested by the standardized disk diffusion method. For two of the β-lactamase-producing strains, susceptibility to penicillin was also tested by a broth dilution procedure utilizing inocula of 10⁵ and 10⁶ colony-forming units per ml.

To screen for the presence of extrachromosomal deoxyribonucleic acid, _B. catarrhalis_ was grown over-night in the presence of penicillin (1 μg/ml). Ethanol-precipitated deoxyribonucleic acid was prepared in duplicate from cleared lysates and was electrophoresed in a 0.7% agarose gel as described by Meyers et al. (10).

**RESULTS**

_B. catarrhalis_ was identified as a probable respiratory tract pathogen in seven patients. In all seven patients identified as infected, sputum plus Gram stains showed 3+ to 4+ polymorphonuclear leukocytes, few epithelial cells, and 3+ to 4+ gram-negative diplococci located intracellularly and extracellularly. Other bacteria were seen only in small numbers (rarely to 1+), and _B. catarrhalis_ was the predominant organism recovered in culture (3+ to 4+ growth).

Of the seven isolates of _B. catarrhalis_, five were found to produce β-lactamase. Penicillin resistance, as determined by the standardized disk diffusion method, correlated in all instances with the production of β-lactamase. For the two β-lactamase-producing strains which were tested by the broth dilution procedure, the minimal inhibitory concentrations for penicillin were 25 and 12 μg/ml, respectively, with an inoculum of 10⁵ colony-forming units per ml, and 100 and 25 μg/ml, respectively, with an inoculum of 10⁶ colony-forming units per ml.

No plasmid deoxyribonucleic acid could be detected in either β-lactamase-positive or -negative strains grown in broth or on agar containing penicillin.

**DISCUSSION**

The recognition of _B. catarrhalis_ as a possible pathogen in our patients prompted a review of the literature. _B. catarrhalis_ has been isolated from middle ear aspirates in a small percentage of children with otitis media (7). Sporadic cases of meningitis (3, 4), endocarditis (14), urethritis (8), and bacteremia with and without purpura fulminans (1, 5) have also been reported. To our knowledge, only one patient with _B. catarrhalis_ pulmonary infection has been previously reported from the United States (9). This patient was immunosuppressed, and he died from overwhelming _B. catarrhalis_ pneumonia.

The role of _B. catarrhalis_ in pulmonary infections has been demonstrated best by Ninane and colleagues in Belgium (12). These investigators performed transtracheal aspiration on retired coal miners with acute bronchitis and chronic lung disease. _B. catarrhalis_, in pure culture, was the third most common isolate from these patients. (_Haemophilus influenzae_ and _S. pneumoniae_ were isolated more frequently.) _B. catarrhalis_ was also isolated in combination with _H. influenzae_ in one patient. Of particular interest is the fact that one patient had β-lactamase-producing _B. catarrhalis_ with a minimal inhibitory concentration of ampicillin of 16 μg/ml. This patient failed to respond to ampicillin, but he improved rapidly when treated with cefuroxime (minimal inhibitory concentration, 2 μg/ml). Ninane et al. reported another anthracosilicotic coal miner with acute bronchitis who had β-lactamase-producing _B. catarrhalis_ grown in pure culture from a transtracheal aspirate (13). This patient responded to therapy with amoxicillin combined with clavulanic acid, a β-lactamase inhibitor.

All seven of our patients whose sputum yielded _B. catarrhalis_ as the predominant organism had some underlying lung pathology. Most of these patients had received ampicillin or penicillin intermittently for past pulmonary infections. The finding of several β-lactamase-producing _B. catarrhalis_ strains in this patient population may be related to this prior antibiotic usage; we postulate that prior penicillin use may have allowed selection of a resistant population.
of organisms. Since the patients were compromised in terms of pulmonary function, these organisms were then able to express their pathogenic potential.

In Gram stains of respiratory secretions from several of our patients, *B. catarrhalis* was mistaken for *Neisseria meningitidis*, a well-known respiratory tract pathogen (6, 15), and therapy with penicillin was initiated. Of two patients with pneumonia presumably caused by β-lactamase-producing strains, one did respond to high-dose intravenous penicillin therapy; thus, the question is raised of etiology or the susceptibility of β-lactamase-producing strains to high-dose penicillin. The other patient with pneumonia required a change in therapy from ampicillin to tetracycline before clinical improvement occurred.

β-Lactamase production by our strains was apparently not plasmid mediated. Similar findings have been reported for β-lactamase-producing *B. catarrhalis* strains isolated in France and England (2, 16). However, we did not try variations of the extraction procedures that may be necessary for demonstrating plasmids in this particular organism.

Further studies of the etiological role of *B. catarrhalis* and the clinical importance of its β-lactamase production will require a prospective evaluation of a large group of patients with acute respiratory infections. Isolation of the organism from normally sterile areas, such as pleural fluid and blood, will resolve the question of pathogenicity. However, our preliminary observations suggest that *B. catarrhalis* may be another organism that is capable of causing acute bronchitis or pneumonia in patients with underlying lung disease.

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**LITERATURE CITED**


