Persistent Pulmonary Infiltrate and Bronchorrhea in a Young Woman*

Kenneth R. Casey, MD, FCCP; and Richard H. Winterbauer, MD, FCCP

42-year-old woman complained of cough of 1-year's duration. Her cough was minimal when upright, severe when supine, and productive of moderate amounts of clear watery fluid. The patient had no fever, hemoptysis, or chest pain. She did not wheeze, and there was no history of asthma. The patient was not dyspneic. Her appetite was good and her weight stable over the year of illness. The patient smoked one-half pack of cigarettes per week for 10 years. Her only medications were estrogen, 0.625 mg daily, and ketoprofen, which was taken on the first day of painful menses. There was no history of tuberculosis exposure and the tuberculin skin test had been negative.

Physical Examination

The BP was 110/70 mm Hg; pulse, 84 beats per minute and regular; respiration, 14 breaths per minute; and temperature, 37°C. Lymph nodes showed no lymphadenopathy. The skin manifested no lesions. Examination of the chest indicated breath sounds suppressed over the lower lobe of the left lung with dullness to percussion but no egophony or whispered pectoriloquy. A cardiac examination yielded normal results. Breast, abdominal, and pelvic examinations all demonstrated normal results. Extremities showed no cyanosis or clubbing.

Laboratory Findings

The WBC count was 4,200/μL with a normal differential cell count, and the hematocrit value was 37%. Screening serum chemistry profiles included values for sodium, 136 mEq/L; potassium, 4.1 mEq/L; creatinine, 0.9 mg/dL; glucose, 120 mg/dL; cholesterol, 186; serum thyroxine (T4), 8.0; calcium, 1442

*From the Section of Pulmonary and Critical Care Medicine, Virginia Mason Medical Center, Seattle. Manuscript received July 2, 1996; accepted August 1.
Reprint requests: Dr. Winterbauer, Head, Section of Pulmonary and Critical Care Medicine, Virginia Mason Medical Center, 1100 Ninth Avenue, PO Box 900 (C7-PUL), Seattle, WA 98111

FIGURE 1. Posteroanterior chest roentgenogram showing persistent airspace disease in the lower areas of the left lung.

FIGURE 2. CT scan images of the lower fields of the left lung demonstrate extensive airspace disease in the lower lobe with patency of associated airways.
9.0; alkaline phosphatase, 39 IU/L; and aspartate aminotransferase, 15 IU/L. The erythrocyte sedimentation rate was 2 mm/h. Urinalysis results were within normal limits. A serum protein electrophoretic pattern revealed an albumin level of 4.1 g/dL with normal globulin values.

The patient had a normal chest roentgenogram 3 years prior to the onset of symptoms. A chest roentgenogram after 3 months of coughing showed a small area of retrocardiac airspace disease on the lateral view only. Eight and 9 months later, films showed an increase in the lower lobe airspace disease of the left lung (Fig 1). A CT scan of the thorax and upper abdomen (Figure 2) showed extensive airspace disease in the lower lobe of the left lung, with normal airways. There was no hilar or mediastinal adenopathy, no pleural effusion, and the upper abdomen manifested no abnormalities.

What is the cause of this patient’s chronic airspace disease?
Diagnosis: Mucin-producing bronchioloalveolar carcinoma (BAC).

Fiberoptic bronchoscopy revealed that the patient had erythema of the mucosa lining the lower lobe of the left lung with dramatic amounts of watery secretions bubbling continuously from all five segments (Fig 3). There was no visual evidence of endobronchial tumor. BAL fluid and brush specimens from the lower lobe of the left lung were cytologically benign; however, transbronchial biopsy revealed a BAC with dramatic mucin production (Fig 4). The malignant cells appeared to be the apocrine type and were discharging mucin through their alveolar margins.

BAC is the least common variety of bronchogenic carcinoma. The prevalence varies between 1 and 9%. The incidence of BAC appears to be increasing. A recent review of the medical literature determined that the incidence of BAC relative to the total number of occurrences of lung cancer increased from 5 to 24% between 1955 and 1990. Much of this increase appears to have occurred in women. BAC has a lower male-to-female ratio than other lung cancer cell types. Also, the causal link to cigarette smoking is less strong for BAC than it is for other lung cancer cell types. BAC has a tendency to be associated with underlying scarring of the lung parenchyma and has increased prevalence in patients with interstitial pulmonary fibrosis and scleroderma.

There are two subtypes of BAC. One type is associated with marked mucin production and tends to be multicentric while the other produces little mucus and more frequently presents as a solitary nodule. The 5-year survival rates for patients with these two types of BAC have been reported as 26 and 72%, respectively. Electron microscopic studies have found that BACs are composed of cells which resemble either Clara cells or type II pneumocytes or both. As many as 90% of nonmucinous BACs show Clara cell differentiation.

Approximately half of patients with BAC are asymptomatic at the time of diagnosis. As the extent of involvement increases, cough, sputum production, dyspnea, chest pain, hemoptysis, fever, and weight loss become more prominent. Bronchorrhea is a reflection of abundant tumor mucin production, a unique feature of BAC.

The chest radiograph of patients with BAC demonstrates a peripheral lung mass or nodule in about 40% of cases. Thirty percent demonstrate a pattern of extensive airspace disease, sometimes involving an entire lobe, as exemplified by our patient. A clinical impression of "unresolving pneumonia" is common in these patients. Multicentric or diffuse infiltration, which may be bilateral, also may be seen. Air bronchograms usually are prominent. Pleural effusion is seen in 30% of cases, and hilar or mediastinal adenopathy may be present. CT, particularly high-resolution CT, demonstrates characteristic spiculated margins of BAC peripheral nodules; this is sometimes referred to as a "star" pattern. Another common finding is bubble-like lucencies or pseudocavitation, which correlates with patent small bronchi or cystic spaces surrounded and outlined by tumor. True cavitation is uncommon. The so-called CT angiogram sign (caused by low attenuation of mucin-highlighting vessels) is suggestive of BAC but may be seen in other conditions as well.
Confirmation of the diagnosis of BAC may be accomplished by transbronchial biopsy, needle aspiration biopsy, or BAL; however, the tumor cells often are very well differentiated and the diagnostic sensitivity of fiberoptic bronchoscopy has been reported to be as low as 14% and that for needle aspiration has been reported to be as low as 60%. Up to 60% of diffuse lesions and 77% of localized lesions have required thoracotomy to establish a diagnosis.

BAC is managed in a manner similar to other forms of lung cancer. This malignant neoplasm is unusual in that prognosis appears to be more strongly related to local tumor factors, such as extent of involvement, multifocality, and presence or absence of mucin production, than to the stage of lymph node involvement. Demonstration of multicentric or bilateral disease is facilitated by the use of CT scans. Surgical removal of localized diseased tissue offers the potential for cure and is the treatment of choice. If the disease is multicentric but unilateral, resection is again appropriate. The presence of bilateral disease portends a grim prognosis. Nonsurgical treatment of BAC is notoriously ineffective.

Our patient underwent thoracotomy of the left lung with apparent complete resection of the tumor, which extensively involved the lower lobe of the left lung, forming confluent zones as well as multiple small separate foci throughout the lobe. Multiple lymph nodes were sampled and were all free of tumor.

**Clinical Pearls**

1. **BAC should be a strong diagnostic consideration in patients with persistent pulmonary infiltrates.**

2. **Mucin-producing BAC may produce marked bronchorrhea, including dramatic signs of focal production of clear watery secretions at FOB.**

3. The tumor cells of BAC are frequently so well differentiated that specimens removed during fiberoptic bronchoscopy, such as pooled wash cytologic brush cytologic, and transbronchial biopsy specimens, may fail to demonstrate malignant tumors.

4. **Mucin-producing BAC commonly produces diffuse airspace infiltration mimicking infection, is frequently multifocal, and has a lower 5-year survival rate than its nonmucin-producing counterpart.**

**Suggested Readings**


