Cystic Fibrosis in an Elderly Woman*

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Cystic fibrosis (CF) is thought of by most physicians as a disease of children. Advances in therapy have extended the life span of patients so that many pulmonary internists have responsibility for the care of young adults with CF. Nevertheless, the initial diagnosis of CF after the age of 30 years is unusual, and a diagnosis after the age of 60 years is rare. Such a case is reported here.

(CHEST 1997; 112:1124-26)

Key words: bronchiectasis; cystic fibrosis

Abbreviations: CF = cystic fibrosis

Cystic fibrosis (CF) is thought of by most physicians as a disease of children. Until the relatively recent past, almost no general internists and very few adult pulmonologists could expect to care for any patients with CF, in part because of early mortality and in part because pediatric specialists maintained control of their care for the generally brief period of postadolescent survival. Advances in therapy have extended the life span of patients so that many pulmonary internists now have responsibility for the care of young adults with CF, and specialized centers routinely offer lung transplantation to this group, thus extending life farther. However, most of this added contact with CF for specialists in thoracic diseases of the adult occurs with patients for whom the diagnosis was established long before; the initial diagnosis of CF after the age of 30 years is unusual, and a diagnosis after the age of 60 years is rare. This is the report of a case with such a late diagnosis, and many reasons why this may occur more frequently in the future are discussed.

CASE REPORT

In February 1991, a 65-year-old woman presented with cough and exertional dyspnea. She dated the onset of her symptoms to pneumonia 2 years prior to presentation. Since that time, she noted increased sputum production, dyspnea on exertion, and occasional hemoptysis. She had a history of one prior episode of pneumonia 15 to 20 years prior to presentation.

The patient had smoked one pack of cigarettes daily for 20 years but quit 30 years prior to evaluation. She produced more than 1 oz of sputum daily. She had a history of sinusitis but no other recurrent infections. She had no GI symptoms; specifically, she had no symptoms suggestive of malabsorption or steatorrhea. Her reproductive history included four normal live births. Her family history disclosed emphysema and muscular dystrophy; there was no family history of stillbirths or children who died in infancy.

A physical examination disclosed that she was a thin but well developed white woman in no apparent distress. Her height was 154.9 cm and her weight was stable at 48.4 kg (96% of the ideal body weight). A chest examination revealed faint basilar crackles bilaterally with a prolonged inspiratory phase but no wheezing. She had no signs of pulmonary hypertension and no digital clubbing.

Spirometry tests revealed an FEV₁ of 1.2 L (56% of predicted), an FVC of 2.1 L (79% of predicted), and an FEV₁/FVC ratio of 57%. Her chest x-ray film is shown in Figure 1. A CT scan revealed bilateral bronchiectasis. The α₁-antitrypsin level, IgE level, and quantitative immunoglobulins were normal. X-ray films of the sinuses were normal. Aspergillus precipitins and hypersensitivity pneumonitis precipitins were negative. A high resolution CT scan (Fig 2) confirmed diffuse panlobar bronchiectasis.

The patient was treated with β-adrenergic and anticholinergic bronchodilators. Prednisone was given based on improvement in pulmonary function tests; intermittent but prolonged courses of daily prednisone were reduced successfully to alternate-day therapy, with a dose ranging from 10 to 25 mg every other day. Supplemental calcium and estrogen, intermittent administration of antibiotics, inhaled steroids, and oral theophylline were also given. Recurrent sinusitis, documented by x-ray films of the sinuses, required endoscopic sinus surgery in November 1992.

In August 1994, she presented with hemoptysis and worsening upper lobe infiltrates (Fig 3). Bronchoscopy revealed mucus plugging. Cultures grew Pseudomonas aeruginosa and, later, Aspergillus fumigatus. Subsequent IgE and Aspergillus precipitins were negative. She was treated with oral ciprofloxacin and showed improvement. From August 1994 to May 1995, she had recurrent exacerbations, accompanied by mucoid impaction evidenced on chest radiographs, which required intravenous administration of antibiotics at home. In June 1995, sputum culture grew a mucoid strain of P aeruginosa. Pilocarpine iontophoresis resulted in a chloride value of 58 mEq/L. Subsequent genetic testing documented two abnormal CF alleles, ΔF508 and R117H.

From that time to the present, the patient has been treated with intermittent intravenous administration of antibiotics, inhaled tobramycin, inhaled deoxyribonuclease, low-dose prednisone, bronchodilators, as well as chest percussion and postural drainage. Her children and grandchildren have been referred for genetic analysis and consultation.

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Manuscript received December 17, 1996; revision accepted May 12, 1997.
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Figure 1. Posteroanterior (left) and lateral (right) chest x-ray film after presentation, revealing hyperinflation and increased interstitial lung markings.

Figure 2. High resolution CT scan of the chest, showing bronchiectasis in the upper lobe of left lung.

DISCUSSION

CF is the most common lethal autosomal recessive disorder in the white population. It results in the development of COPD secondary to chronic airway infection and bronchiectasis; pancreatic exocrine insufficiency; and abnormalities of the liver, the GI system, and the reproductive tract. In the United States, median survival for patients with CF is 30.1 years, and median age at diagnosis is 6 months. Greater than 90% of patients are diagnosed by age 8 years. Diagnostic criteria include a combination of clinical characteristics plus an elevated sweat chloride concentration (>60 mEq/L), or identification of two CF mutations, or in vitro demonstration of characteristic abnormalities in ion transport across the nasal epithelium.

In this patient, a diagnosis of CF was made at age 70 years after she was followed up for nearly 5 years for bronchiectasis; this makes her case one of the oldest new diagnoses of CF ever reported. The growth of a mucoid strain of P aeruginosa from the patient’s sputum was the important feature of this case which led to the consideration of CF. While others have reported new diagnoses of CF in persons in their 60s, most of these patients had long-standing medical histories of respiratory illness. Some of these reports of new diagnoses of CF in adults have been criticized, as in the case of a 69-year-old man in whom a diagnosis of CF was made; the diagnosis of CF was questioned because the patient had sweat chloride values in the range of 55 to 61 mEq/L and did not have any evidence of digital clubbing on examination. Sweat chloride values increase with age and are more variable in adults, rendering values <60 mEq/L indeterminate in the diagnosis of CF. The patient reported here had a sweat chloride level of 58 mEq/L and no digital clubbing, but the diagnosis was confirmed by genetic mutation analysis. This
illustrates the utility of genetic testing in confirming a diagnosis of CF in atypical cases.

This patient was found to be a compound heterozygote for the ΔF508 and R117H mutations. This genotype is associated with pancreatic sufficiency in patients with CF, and the reported patient’s apparent pancreatic sufficiency resulted in her normal development and ability to elude diagnosis given her mild pulmonary disease. The R117H mutation has been found to occur on two distinct chromosomal backgrounds, one of which (the 7T variant) has been shown to be associated with milder phenotypes. There are persons with the ΔF508/R117H (7T variant) genotype who are asymptomatic or have congenital bilateral absence of the vas deferens without evidence of CF-related lung disease. While it was not ascertained whether this patient possesses the R117H mutation on a 5T or 7T genetic background, it would be interesting to learn if this patient possesses the 7T intron 8 variant as this conceivably could contribute to the delayed manifestations of CF lung disease in this patient.

This case illustrates that while CF most commonly presents in infancy or early childhood, its diagnosis should be considered even in older adults who present with recurrent respiratory infections, bronchiectasis, and obstructive lung disease. CF gene mutation analysis may be a useful adjunct to sweat testing in atypical cases but only confirms a diagnosis of CF when combined with appropriate clinical manifestations of CF. Genetic testing also may provide valuable information for the patient’s family and allow identification of related CF carriers. As newer therapies for CF become available, earlier case recognition should improve prognosis for patients with CF.

REFERENCES