Case Report

Adult Cystic Fibrosis - A Rare Diagnosis from India

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Abstract
Cystic fibrosis (CF) is a multisystem disease characterized by chronic pulmonary infection, bronchiectasis, exocrine pancreatic insufficiency and elevated sweat chloride level. It is commonly considered as a pediatric disease. However increased survival of CF patients due to potent antibiotics, better nutrition and diagnostic facilities results in increased number of adult CF patients. CF is now a problem for adult medicine.

Introduction
Frequency of cystic fibrosis (CF) varies widely in different ethnic groups. It is more prevalent in western countries but rarely reported from India. Exact incidence of CF among Indians is unknown. It is commonly considered as a pediatric disease. However increased survival of CF patients due to potent antibiotics, better nutrition and diagnostic facilities results in increased number of adult CF patients. CF is now a problem for adult medicine.

Case Report
A 29 years Hindu female had persistent cough, sputum production and shortness of breath for last 16 years. She had recurrent wheezing, nasal stuffiness and rhinorrhoea since childhood for which she was treated frequently with bronchodilators, steroids, antihistaminic drugs and antibiotics. At the age of 13 years she was first admitted in hospital with fever, cough and expectoration. She was treated with antitubercular drugs with false impression of pulmonary tuberculosis. She developed Steven-Johnson syndrome with streptomycin with cutaneous eruption, mucosal involvement and subsequent development of thisis bulbri of right eye. After the age of 13 years she had persistent cough and sputum production. She had recurrent exacerbation of symptoms with appearance of fever, increased cough and sputum production and aggravation of breathlessness. She had occasional hemoptysis. She had stunted growth, primary amenorrhea and lack of development of secondary sexual characters. She developed cataract of left eye with progressive dimness of vision. Her bowel habit was normal with passage of well formed stool. She had no abdominal complaints. She had no significant birth history or family history.

Physical examination revealed mild pallor, second degree clubbing, pulse 82/min, regular in rhythm; BP 120/ 78 mm Hg and respiratory rate 22/ min. She had poor nutritional status and glossitis. She did not have any cyanosis, jaundice, edema, lymphadenopathy and neck vein engorgement. Her height was four feet six inches and weight was 35 kg. She had mild hyperinflation of chest, decreased chest movement and diffuse coarse crepitations in both lungs. She had sexual infantilism with Tanner stage II for both pubic hair and breast development. The patient had poor muscle tone and reduced muscle mass.

Complete blood picture during last admission revealed Hb 11.2 gm/ dl, RBC 4.62×10^6/ cu mm, PCV 35.8 %, MCV 77.5 fL, MCH 23.8 pg/ cell, MCHC 30.7 g/ L; TLC 18000 / cu mm with neutrophil 75%, lymphocyte 20%, eosinophil 5% and platelets 3 lacks/ cu mm. Blood sugar, urea, creatinine, Na+, K+ levels and liver function tests (except serum albumin 2.8 gm/ dl) were within normal range. Sputum for AFB was negative, but culture revealed growth of pseudomonas species. Stool examination was normal. ECG and echocardiography were normal. Ultrasoundography of abdomen revealed enlarged liver, but otherwise normal study. Chest x-ray revealed bilateral bronchiectatic changes with honeycombing appearance. Straight x-ray of paranasal sinuses revealed hypoplastic frontal sinus and hazy opacity in both maxillary sinuses suggestive of chronic sinusitis (Figure 1). HRCT scan of thorax revealed cystic bronchiectatic changes in both lungs with dilated thick walled bronchi in right apex and both middle and lower zones (Figures 2, 3). Sweat chloride was 129.5 mEq /L. Repeated sweat chloride tests confirmed high values (124 mEq /L, 132.5 mEq /L). Genetic study was not possible.

The case was diagnosed to have CF with bilateral bronchiectasis, stunted growth and sexual infantilism without pancreatic insufficiency. This is a milder variant of CF, who escaped diagnosis since childhood, but survived till adult age.

Discussion
CF is an autosomal recessive disorder due to mutation in CF transmembrane conductance regulator (CFTR) gene. CFTR gene is located on long arm of chromosome 7 at position 7q3. More than 1200 mutations in the gene have been recognized. Mutation in CFTR gene results in failure of cAMP regulated chloride conductance by epithelial cells leading to dehydration of secretions and formation of thick, sticky mucus, along with...
very salty sweat due to elevated sweat chloride. Prevalence of mutations varies in different populations. Commonest mutation is \( \text{delta F}_{508} \) (resulting in absence of phenylalanine at amino acid position 508 of CF gene protein product, CFTR) in Caucasians, which constitutes about 70% of total cases.\(^1\) Panel of common mutations is not yet known for Indian patients. Few small studies indicate that frequency of \( \text{delta F}_{508} \) mutation in India is between 19% and 44%.\(^2\),\(^3\)

Common clinical presentations of CF include meconium ileus in neonatal period, recurrent bronchiolitis, pneumonia and failure to thrive in infancy and early childhood. Chronic lung disease and bronchiectasis develop as child grows older. Persistent cough and wheezing may be early symptoms misleading the diagnosis as bronchial asthma. Digital clubbing is common. Exocrine pancreatic insufficiency leads to fat malabsorption. Mild variants of CF may not have pancreatic insufficiency. Dehydration secondary to gastroenteritis or sweating especially in summer months is common. CF patients have increased risk for diabetes mellitus or osteoporosis. Male infertility occurs due to obstructive azoospermia. Thick tenacious cervical mucus may block sperm migration in female. Cataract may develop due to disease itself or due to steroid use for lung problems.

Significant changes in conjunctival cytology, lens opacity and abnormal tear tests are noticed especially in patients with severe digestive insufficiency.\(^4\) Many patients with CF are now being diagnosed after the age of 18 years. Higher survival rate is seen in males. Greater resting energy expenditure in female with CF may explain their difficulty in maintaining normal growth and contribute to their shorter life expectancy.

Two separate groups are seen in adult CF patients. One group has the diagnosis of CF from their early childhood and presents in adolescent and youth life with severe complications (nutritional deficiency, chronic pulmonary infections, severe hemoptysis, end stage lung disease, CF related diabetes, bone disease etc.). Second group is diagnosed in adulthood with milder CF. These patients have higher mean age, better nutritional status, pancreatic sufficiency and rare chronic bronchial colonization with pseudomonas aeruginosa. Second group may have unique presentation like congenital absence of vasa deference, chronic sinusitis, nasal polyps, and recurrent pancreatitis.

Milder variants of CF may escape diagnosis or diagnosis may be delayed until adulthood. Our case had milder variant of CF diagnosed at the age of 29 years. She had recurrent respiratory infection (including pseudomonas), bronchiectasis, sinusitis and short stature. She had premature cataract but digestive insufficiency or pancreatitis was absent.

Diagnosis of CF is confirmed by typical phenotype, demonstration of high sweat chloride and / or by identifying two CF mutations. Sweat chloride is measured by collecting sweat after pilocarpine iontophoresis into the forearm. Positive sweat chloride (>60 mEq/L) test is nearly pathognomonic of CF. A single positive test should be confirmed by a repeat sweat test or genotyping. Normal sweat chloride values are <40 mEq/L. Values between 40-60 mEq/L are indeterminate. Average sweat chloride values in CF patients are around 100 mEq/L. Nasal potential difference measurement is an adjunct to sweat test but is not readily available.

CF patients may have low or low-normal serum sodium, metabolic alkalosis and hypochloremia. CF patients may be infected with pseudomonas aeruginosa, staphylococcus aureus or non-typable haemophilus influenzae. Isolation of pseudomonas aeruginosa or burkholderia cepacia from sputum is suggestive of CF. X-ray chest may show hyperinflation, peribronchial thickening, cystic changes and lobar or segmental collapse. Findings on HRCT scan of thorax include cystic or varicose bronchiectasis, peribronchial thickening, segmental collapse, mucus impaction and subpleural bullae formation. Imaging of sinuses may show delayed pneumatization or mucosal thickening.

Adult patients with features of chronic asthma, sinusitis and low body weight should be searched for CF. Sweat chloride test should be done in bronchiectatic patients without other etiological factors to prevent under diagnosis of CF. Identification of CF mutations is not cost-effective and is not readily available. Large number of uncommon mutations in CF gene also makes genetic diagnosis impossible in every case. Hence sweat chloride test remains the most important diagnostic test in India. Early diagnosis of CF may retard the decline in lung function and prolong the life with proper antibiotics, rehabilitation therapy and nutritional support. Special adult clinic along with facilities for psychosocial rehabilitation is helpful for adult CF patients. Awareness is needed for early
diagnosis and proper management of CF patients.

References


