Case Report

Cystic Fibrosis- A Deadly, Dear and Agonizing Tale

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Abstract

Cystic fibrosis (CF) is a life constraining autosomal recessive disorder common in Caucasians.Customary presentations are chronic productive cough, recurrent and persistent pneumonia, failure to thrive, chronic diarrhoea.However, pancreatitis is a kenned complication of CF. Now a days, CF is increasingly detected in South and East Asia.Prevalent notion is that, CF does not subsist in our community.Lack of awareness regarding CF among physicians, poor index of suspicion and unavailability of diagnostic facilities cause consequential delay in diagnosis. Living with CF is expensive and also colossal sufferings. It is associated with enormous economic burden for family and has a great impact on life of patient and parents. Here, we report the tragic tale of a girl of 13 years , who was diagnosed as CF with chronic pancreatitis and pancreatic calculi at the age of 10, though her symptoms commenced to manifest as early as 3 months and finally she died at her 13 in our hospital after 54 days of battling for life.

Introduction

Cystic fibrosis (CF) is a complex recessive disorder caused by mutation in cystic fibrosis transmembrane conductance regulator (CFTR) gene resulting in defective epithelial transport of chloride through CFTR Channel.[1] Patients with CF conventionally present in the first two years of life with chronic productive cough, recurrent pneumonia, resistant asthma, failure to thrive, chronic diarrhea (steatorrhea) and dehydration.[2]However, Pancreatitis is a known complication of cystic fibrosis (CF) and may be the first manifestation of the disease in some cases.[3]CF is a life limiting genetic disorder common in Caucasians of North America, Australia and Europe.[4] CF is increasingly detected in South and East Asia, Africa and Latin America in these days.[5]

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Living with CF is extravagant. The disease is associated with considerable economic cost. Our case report highlights the encumbrance of CF in terms of its impact on quality of life for both patient and parents and expenditure. Here, we report a case of a 13 years old girl, who had been suffering since early infancy and was diagnosed as a case of CF with chronic pancreatitis with pancreatic calculi at her 10,but unfortunately she succumbed to her malady at 13 in our hospital after 54 days fighting for life.

Case Summary

SY, a girl of 13, was born at term at home normally with unremarkable perinatal and neonatal period. Until the age of 3 months there was no symptoms, post that she got first episode of “pneumonia” and was hospitalized, received antibiotic and ameliorated.But subsequently she developed recurrent episodes of homogeneous respiratory issues. Most of the time she had to visit in regional government or private hospital, got hospitalizedand was considered as a case of recurrent pneumonia but was never referred to a Paediatric Pulmonologist in the early stage of her life. She additionally failed to gain her expected weight since early infancy. Three years back, at the age of 10 years, she experienced for first time severe agonizing generalized abdominal pain aggravated after taking fatty meals. That time she was suggested by some relative to consult to PaediatricPulmonologist in Ad-din medical college

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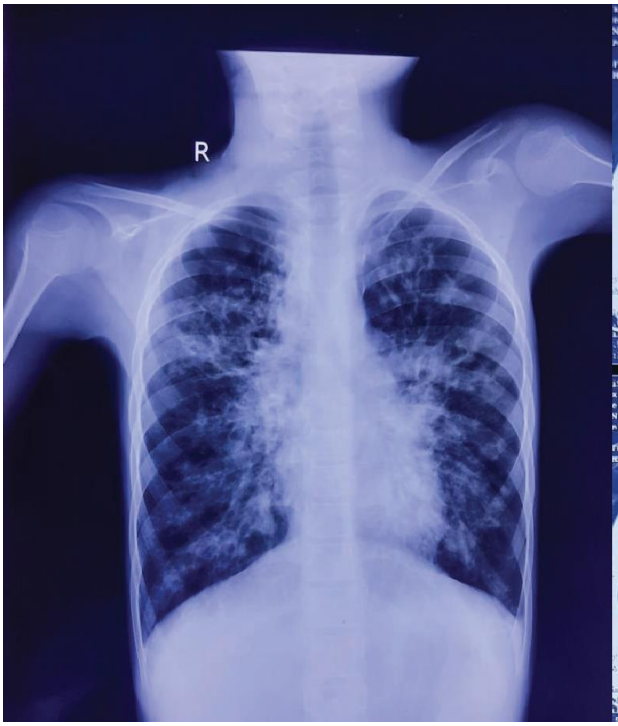

Fig.-1: *CXR showing hyperinflation, increased*

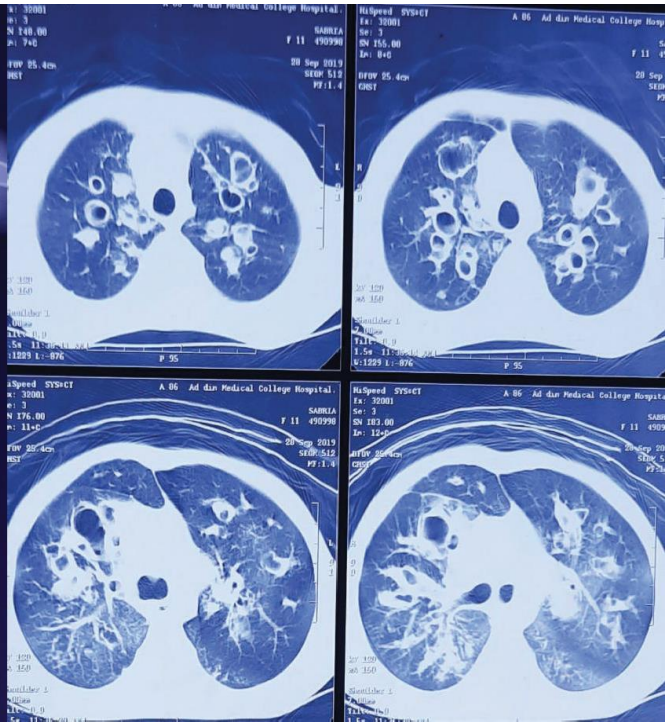

Fig.-2. *CT scan chest. bilateral bronchiectasis*

Bronchovascular markings, patchy opacities.(signet rings, dilated bronchi).

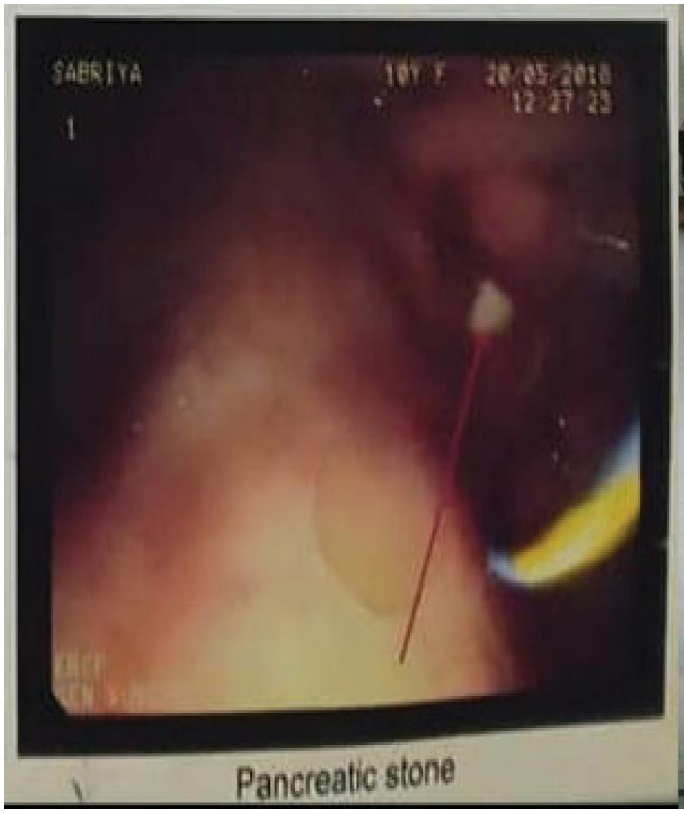

Fig.-3: *Pancreatic stone in ERCP.*

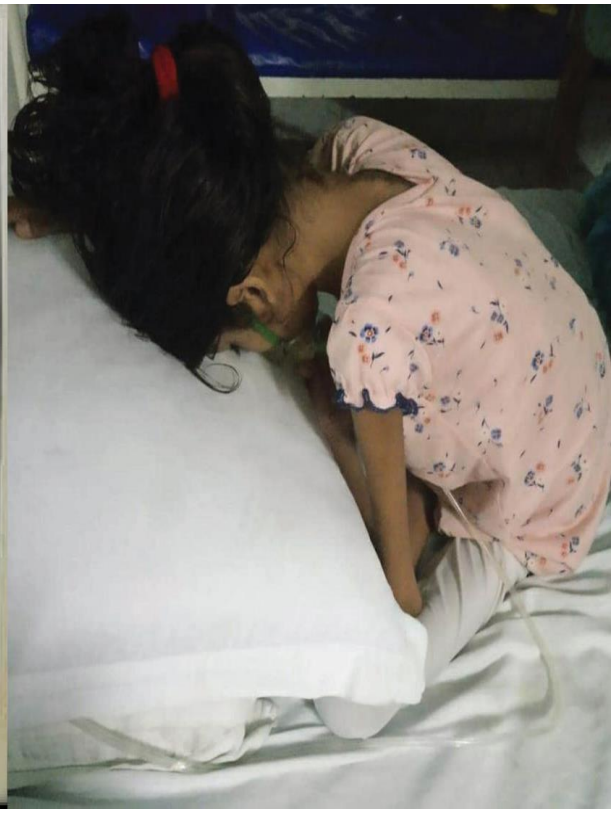

Fig.-4: *Girl sitting bending forward.*

hospital. Her severity of cough further incremented for last two years, became productive, almost persistent and worsening at morning. So, at the age of 10, her diagnosis was substantiated by us with sweat chloride test as cystic fibrosis with persistent pneumonia with bronchiectasis with chronic pancreatitis with pancreatic calculi with growth failure. Pancreatic calculi were partially extracted by ERCP, and she was on all ancillary measures, maintained regular follow up and also required subsequent hospitalization.

Family history: SY was the third issue of a non-consanguineous marriage. One of her elder sisters died at the age of 14 years who also had unresolved persistent pneumonia. SY's younger brother additionallydied at the age of two months with some undiagnosed respiratory issues.Two of her siblings are in good health.

Socioeconomic background of her family: Her father studied upto class 8 and is an electrician. Mother completed class 5 and is a housewife. Father is the only earning member and his monthly income is on average 10-12 ThousandTaka. They live in a tin-shed house and own a modicum of land.

Encumbrance of disease cost for family: SY used to fall ill so often that she needed frequent hospitalization since her early infancy. On average, she required hospitalization for 3/4 times per year. So, she was admitted to hospital around 50 times in her lifetime. Average duration of hospital stay was around 2-3 weeks or more. To bear her treatment cost (investigations, medicines,transport, hospital charge etc.) and to run the family, her father was compelled to sell his 2 autorickshawsfor 8 Lakhs Taka. He has also,sold the land owned by him for 12 Lakhs Taka. Moreover, he has taken a loan of 25 Lakhs Takato accommodate the cost. Total expenditure for her treatment was around 30-40 lakhs Taka.

The tragic end of a cystic fibrosis patient: SY was admitted to paediatric ward on 16th May 2020 for the last time with worsening of respiratory distress and cough. She was dyspneic having clubbing of nails and toes. Respiratory rate was 64/min, SPO2-87%, chest movement and expansibility of chest were restricted on both sides, air entry was poor and bilateral extensive crepitations were present on both lung fields. Her BMI-10.55, below 3rd centile (underweight), HAZ -4.46(severe stunting).

In-spite of several episodes of antibiotic therapy, oxygen inhalation and other ancillary measures her pneumonia unfortunately failed to amend rather deteriorated gradually and complicated with type 2 respiratory failure, compensated hypochloremic metabolic alkalosis and hypokalemia. At that critical stage of patient,parents were asked about the need to shift her to pediatric intensive care unit(PICU) for metabolic derangement but to bear the cost was beyond their capabilities. So, parents were ready to accept the grievous consequences. We endeavored our best with all ancillary measures within our capabilities but could not able to alleviate her sufferings. Most of the time she used to spend bending forward in a pillow to surmount hypoxia. But, whenever she felt better, never forgot to live, to smile, even she relished optically canvassing cartoon etc. on mobile in her last days. But alas! After 54 days of hospital stay, she took her last breath.

Investigations:

Complete blood count (CBC) Hb%- 8.3 gm/dl,white blood cell(WBC) 9580/cmm, neutrophil-60.8%, lymphocytes -32.5%

ESR-90 mm in first hour, **CRP-** 188.24 mg/L

Sputum for C/S-growth of klebsiella species, **gram stain**- gram negative bacili

Chest X ray-hyperinflated lungs, thickened bronchial wall and prominent bronchovascular markings, bilateral patchy opacities

CT scan of chest- Bilateral bronchiestasis(signet ring apperrance, septal thickening, ground glass appearance, dilated bronchi)

Arterial blood gas analysis: PH- 7.4, pCO2- 68.4 mmHg (H),pO2-89.3 mmHg(L),HCO3-43.3 mmol/L(H), Na-136.3, K -2.78(L),Cl-84.7(L)

Sweat chloride test- 133mmol/L (H)

In favor of pancreatitis

Amylase-106U/L (N-95U/L) , **Lipase**- 92 U/L(N-13-60 U/L)

USG of whole abdomen- chronic calculus pancreatitis

MRCP- chronic calcific pancreatitis with mild to moderate dilatation of pancreatic duct with intraluminal calculi

ERCP-chronic calcific pancreatitis, papillectomy followed by stone extraction(incomplete) done.

Discussion

A large scale study in Bangladesh with 95 CF patients on clinical and sociodemographic characteristics over a period of 17 years has been conducted for first time by Kabir et al. .Clinical features were categorized as 1) major triad symptoms (persistent cough 100%, respiratory distress 90%, purulent sputum 73.7%), 2)minor triad of signs(crepitation83%, clubbing 71%, chest in drawing 58%) and 3)minor duet from history (recurrent/ persistent pneumonia 83%, bronchiolitis 57%).[6]Our patient presented with almost all above mentioned recurrent respiratory symptoms since early life and she developed pancreatitis in older age. Several other studies also revealed predominant pulmonary manifestations. Shah et al[7]reported 80.6% pulmonary symptoms in Pakistan, and 48.8% reported by North American CF Registry in CF patients.[8] She had several episodes of recurrent/persistent pneumonia, that ultimately complicated into irreversible bronchiectasis. Aziz et al[9]and Kabra et al[10] reported persistent pneumonia in 98% patients in their studies. There was evidence of bronchiectasis in 60% and 80.7% patients in HRCT of chest in studies done by Kabir et al[6] and Aziz et al respectively.[8]

Pancreatitis is a rare manifestation of CF, affecting < 2% of patient with CF.[11] The girl experienced 3 episodes of exacerbation of chronic pancreatitis commenced at the age of 10, with pancreatic calculi which was partially extracted by ERCP. Shwachman et al. reported 10 patients of cystic fibrosis with acute or recurrent pancreatitis but without calcification.[12]Nahar et al also reported a case of CF with chronic pancreatitis with pancreatic calculi.[13]In our previous observation malabsorption was present in 37% and fecal fat in stool in 53%cases that clearly reflected exocrine pancreatic insuflciency.[6]However, none of them suffered from frank pancreatitis.

Most of the morbidity and more than 90% of the mortality of CF are related to chronic pulmonary infection and its complications.[14]The girl also died from recurrent lower respiratory tract infections that leaded to bronchiectasis, compromising lung function and consequently type 2 respiratory failures.

Kabir et al showed 87% children were underweight (81% severe, 6% moderate). Overall stunting in under 5 children was 87% and short stature in 68% in elder children > 5 years.[6] These results are consistent with Kabra et al [10]and Aziz et al[9]. The girl was also severely underweight and stunted as well. The growth failure in Cf is the consequences of chronic illness, malabsorption, anorexia, inadequate nutritional supply due to poverty and increased metabolic demand.

Mean age of onset of symptoms was 15 months in the studies conducted by Kabra et al[10] and Aziz et al[9]and 16.9 months by Kabir et al[6].But SY presented as early as 3 months. The average age of diagnosis was 54 months and 36 months in 2 studies conducted by Kabra et al[10] in India and Aziz et al[9] in Pakistan, respectively. Kabir et al.[6] showed mean age of diagnosis was 90 months in Bangladesh. Even in America, median age of diagnosis among Indian American was 12 months compared with 6 months among Caucasian American children.[15] Unfortunately SY was diagnosed at the age of 10 years. This wide gap reflects a low index of suspicion, unavailability of diagnostic facilities and lack of awareness about the occurrence of CF in Bangladeshi children. So, it is clearly shown that lack of cognizance regarding CF is a consequential factor for this delayed diagnosis. The girl had been suffering from recurrent episodes of pneumonia with faltering demanding hospitalization for several of times. Recurrent pneumonia with growth failure always reflects underlying chronic lung pathology. But the child was never referred to a Pediatric Pulmonologist for confirmation of diagnosis in her early life. So, at the time of diagnosis most CF patients already develop advanced bronchiectasis.

There is no curative treatment for CF. Patient's lifespans are greatly shortened with alive expectancy of roughly 40 years in western country.[16]In our previous study, 11 out of 95 CF children died at their early teen in Bangladesh.[6]The girl died at the age of 13 years only. So, among several factors, delayed diagnosis is one of the major contributor causing increased morbidity and early mortality of our CF children comparing with western countries.

In Bangladesh, 59% CF children belonged to low, 28% mid income group families with their average monthly budget < 26,675 Bangladeshi taka.[6]SY's family belonged to low income group with monthly income only 12,000 taka.

Consanguinity is associated with increased risk of CF.50% consanguineous marriage of parents of CF patients was reported by Aziz et al [8] in Pakistan and 80% in a Middle Eastern population reported by Al-Mahroos et al[17] and 22% in Bangladesh by Kabir et al[6]. Incase of our patient, though her parents are not involved in consanguineous

marriage, but as their other two children also died from similar respiratory issues, so it clearly reveals autosomal recessive mode of inheritance. Therefore, early and confirmatory diagnosis is very crucial for the patient as well as for parents for proper understanding of genetic background and mode of inheritance of the disease and risk of recurrence in future pregnancy.

Parents faced psychological and economic challenges for the long-term suffering of their child. Diagnostic dilemma further raised their anxiety. Parents were well known about the ultimate fate of CF after confirmation of diagnosis. We can easily assume how much psychological and mental trauma they were going through. Being a poor family, cost of living with CF is truly extravagant. The parents spent around 30-40 lakhs Taka for her treatments. To bear the cost of disease for a poor family is really enormous burden. Chevreul et al showed the total average annual cost of CF was 29,746 Euro per patient in France that is around 28,70,191 Bangladeshi Taka. Total cost was higher in adults than in children and increased with disease duration.[17]

Although nearly all people with CF in USA have health insurance, the treatment and care regimen for CF is expensive even for individuals with comprehensive insurance and health care costs can quickly exceed what a family can afford. Forty five percent people with cystic fibrosis spend 5000 US dollar or more annually in USA. The CF Foundation of USA is working on multiple fronts to support access and to keep CF care affordable by advocating for the CF community with policymakers, payers, and drug manufacturers.[18] In contrast, there is no such health insurance or health care facilities for CF patients in our country, so total cost of a CF patient need to afford by the family.

Conclusion: Cystic fibrosis is a lifelong disease and there is no remedy. Early diagnosis and extensive auxiliary treatment only can reduce child's morbidity; can ameliorate quality of life and increment life expectancy. Common Belief among physician is that CF does not subsist in our community. So, knowledge of physician regarding CF, high index of suspicion, prompt referral of a child with recurrent respiratory issue and early diagnosis and treatment can alleviate child's suffering and financial cost to some extent. Proper counseling of parents regarding disease course, genetic consequences and prognosis should be made empathetically for better understanding.

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