Clinical Case Reports International

Case Report
Published: 18 Feb, 2020

Cystic Fibrosis with Pancreatic Insufficiency: A Case Report

Luthfun Nahar, Bazlul Karim, Afsana Yasmin, Subarna Rani Das, Kamrun Nahar and Parisa Marjan*

Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Bangladesh

Abstract

Cystic fibrosis is an autosomal recessive disorder; the main responsible gene is Cystic Fibrosis Transmembrane conductance Regulator (CFTR) which is located on long arm of chromosome. Mutation of this gene encoding CFTR protein results cystic fibrosis. This disease involves multiple systems of body as respiratory, gastrointestinal, hepatobiliary, pancreatic, genitourinary and sweat duct. Pancreatic insufficiency presents with symptoms when >95% exocrine function is lost. It is associated about 85% in patient of cystic fibrosis which indicate poor prognosis. This paper presents a case of cystic fibrosis with pancreatic insufficiency and chronic pancreatitis with osteoporosis.

Keywords: Cystic fibrosis; Pancreatitis; Pancreatic insufficiency; Growth failure

Introduction

CFTR protein regulate cyclic Adenosine Mono Phosphate (cAMP) dependent chloride channel of secretory and absorptive epithelium. It is present on apical membrane of epithelial surface. There are more than 2000 mutations occur in CFTR gene and for cystic fibrosis, they can be classified in six types [1]. The most common mutation is ΔF508 and indicates the deletion of phenylalanine in position 508. It is about 66% and under class II which results defective processing or trafficking of CFTR protein on apical membrane [2]. CFTR function is completely absent in class I-III and VI, but partially present in class IV and V. So, class IV and V present with fewer symptoms usually in late childhood or adulthood [3]. Mutations are common in class I-III which are associated with pancreatic insufficiency, whereas less common in class IV, V and VI with sufficient pancreatic secretion. This information have prognostic value in patient of CF. CFTR regulates chloride channel which pumps chloride from intracellular space to the extracellular space. Mutation of CFTR results less chloride secretion, less water transport in the epithelium and sodium hyper absorption. As a result airway surface liquid depletion occur which progress to ciliary collapse and loss of mucociliary clearance. So the secretion become sticky and viscid [4]. Bactericidal activity of airway epithelium required a low NaCl concentration whereas surface fluid in CF has high NaCl concentration which failed to kill bacteria. So after inhalation the bacteria easily deposit on the airway surface and aspirations occur. The continue process of sputum retention, chronic airway infection, and inflammation results viscid secretions which impair mucociliary clearance that lead to progressive lung destruction [5]. It is also known as low volume hypothesis. Patient of cystic fibrosis is 10 times more prone for inflammatory response to bacterial, viral or air droplet pollutants [6]. Pancreatic insufficiency is another important clinical presentation. It usually presents early in life before 1 year of age. The secretory material collect within the acinar duct, it causes obstruction, subsequently fibrosis with variable duct dilatation. So, pancreatic function may deteriorate over time, with or without pancreatitis.

Exocrine pancreatic tissue may damage early but endocrine tissue is relatively preserved. But in patient islets cells also gradually destroyed and 20% to 50% of adolescents and adults may develop Cystic Fibrosis-Related Diabetes (CFRD) [7].

Case Presentation

A 10 year old girl of non consanguineous parents immunized as per EPI schedule got admitted with upper abdominal pain for 4 days. It was severe, dull in nature, aggravated after feeding, relieved by leaning forward position and there was no radiation. She had similar attack for several times in last 2 years. She had also loose stool about 8 to 10 times per day for 1 year which was foul smelling, oily, greasy, float on toilet. She had also history of recurrent respiratory infection since birth and

OPEN ACCESS

Correspondence:
Luthfun Nahar, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, Tel: +880-01716000575; E-mail: dr.mukta27@gmail.com

Received Date: *23 Jan 2019*
Accepted Date: *13 Feb 2020*
Published Date: *18 Feb 2020*

Citation:
Nahar L, Karim B, Yasmin A, Rani Das S, Nahar K, Marjan P. Cystic Fibrosis with Pancreatic Insufficiency: A Case Report. Clin Case Rep Int. 2020; 4: 1139.

Table 1: Laboratory investigations of patient.

Parameter	Findings	References
Hemoglobin (gm/dl)	9.2	13.5 ± 1.3
TC of WBC (× 10^9/L)	14 × 10^9	7.0 ± 3
Differentials: Neutrophil Lymphocyte Eosinophil Monocyte Basophil	 69% 21.30% 4% 5.20% 0.50%	 40% to 80% 20% to 40% 1% to 06% 2% to 10% <1%
Platelet count	332 × 10^9/L	150-400 × 10^9/L
ESR (mm in 1st hour)	35	0-10
Serum amylase (U/L)	106	Up to 95
Serum lipase (U/L)	92	13-60
Random blood sugar (mmol/L)	5.12	<7.8
Sweat chloride test (mmol/L)	133	>60: Consistent with cystic fibrosis 40-60: Borderline <40: Normal
Serum lactate dehydrogenase (U/L)	154	230-450
Serum calcium	9.96	7.6-10.8
C reactive protein (mg/dl)	9.33	Up to 5.0
Prothrombin time (second)	15	12-16
INR	1.42	
Vitamin D (ng/ml)	7.59	Deficient: <15 Insufficient: 15 - <20 Sufficient: 20-100
Fecal elastase1 ug/gm stool	113	>200
Chest X-ray	Normal	
Ultrasonography of hepatobiliary system	Pancreatic duct calculi	
MRCP	Pancreas is smaller in size with irregular outline; main pancreatic duct is dilated with multiple signal void structure suggestive of chronic Calculus pancreatitis.	

Figure 1: Patient with growth failure.

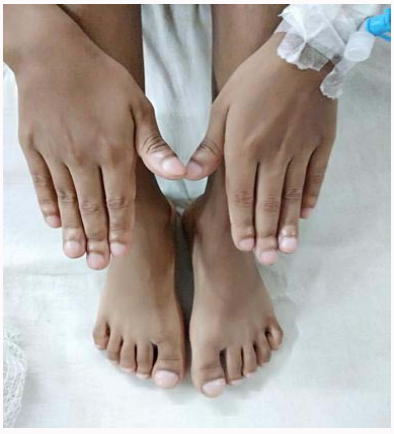

Figure 2: Digital clubbing on both limbs.

was hospitalized for several episodes. She had no history of polyuria, polyphasia, polydypsia, abdominal trauma or surgery. Her brother was died at 14 years of age who had similar type history and he was diagnosed case of cystic fibrosis. On general examination she was a febrile, anicteric, mildly pale, vitally stable, severely wasted and moderately stunted and developmentally age appropriate (Figure 1). Patient had clubbing (Figure 2), skin survey was normal and BCG mark was present. On abdominal examination epigastric tenderness was present but had no organomegaly and ascites. Other system examinations showed normal findings. After admission we did some investigations. Complete blood count was normal other than mild anemia. Liver function test, blood glucose, serum calcium, lactate dehydrogenase was normal. Serum amylase, lipase was slightly high, vitamin D level was significantly low, and chest X-ray was normal. Ultrasonography of whole abdomen and MRCP showed pancreatic duct calculi (Figure 3). Sweat chloride test was high and suggestive for cystic fibrosis and fecal elastase 1 was low (113 ug/gm stool). We also did DEXA (Dual energy X-ray absorptiometry) scan to measure bone mineral density and the report showed low bone mass in lumber vertebra and in both femoral neck (Figure 4). So this patient finally

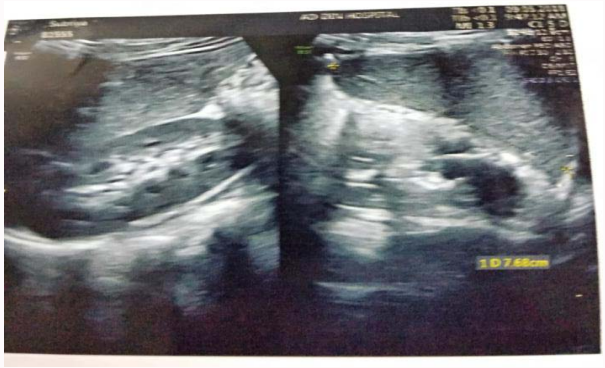

Figure 3: Ultrasonography showing pancreatic duct calculi.

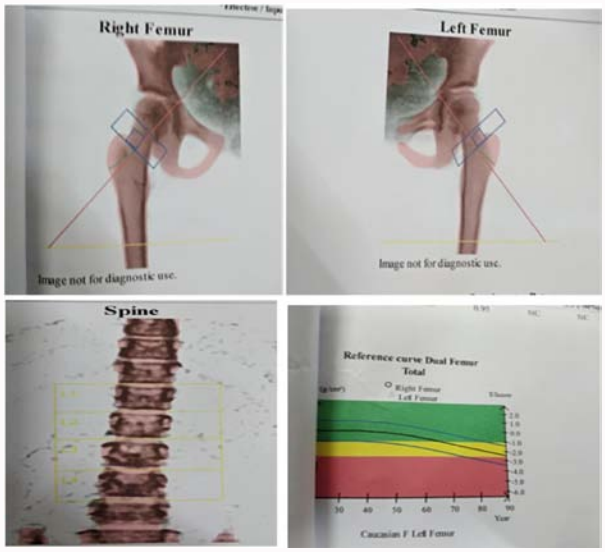

Figure 4: DEXA scan of patient showing osteoporosis.

diagnosed as cystic fibrosis with chronic calcified pancreatitis with osteoporosis. We managed the patient by analgesic, pancreatic enzyme supplement therapy, vitamin D supplementation and pancreatic stone was removed by ERCP procedure (Figure 5). For osteoporosis we consulted with Pediatric Rheumatology department and advised to treat by inject able bisphosphonates, but parents refused it.

Though it is a genetic disease, so specific treatment couldn't be given and we discharged the patient with counseling the parents about nature of disease, treatment options, available treatment, complication, genetic counseling, prognosis and follow up plan (Table 1).

Discussion

Children with Cystic Fibrosis (CF) presented with a variety of manifestations including pancreatic insufficiency, chronic obstructive pulmonary disease and malnutrition [8]. The most common clinical and laboratory manifestations at first admission were gastrointestinal problems. Gastrointestinal manifestations are failure to thrive, neonatal cholestasis, pancreatitis with pancreatic insufficiency, hyper transaminesemia or hepatitis and neonatal cholestasis [9]. In general, pancreatic insufficiency is present in about 85% of the CF population in early in life (before the age of 1 year). The progress of pulmonary diseases, affecting the quality of life and survival of the

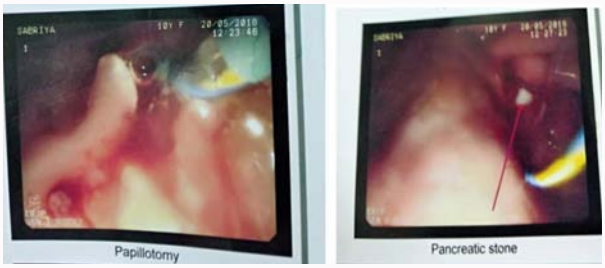

Figure 5: Pancreatic stone is removed by ERCP.

patients depends on the nutritional state of the patient and the early introduction of preventive therapy [10,11]. The presenting case also had history of not growing well, recurrent abdominal pain, greasy loose stool for long duration. She had history of recurrent respiratory tract infection since birth. On physical examination of children with cystic fibrosis usually we can found growth failure, clubbing, according to system involvement respiratory findings like nasal polyp, fast breathings, features of consolidation; GIT findings like organomegaly, epigastric tenderness. Clubbing was present in 9% of cystic fibrosis patients [9,10]. The presenting case also had wasting, growth failure, clubbing and abdominal tenderness for pancreatitis. The diagnostic criteria of cystic fibrosis are newborn screening positive or presence of symptoms and or signs of cystic fibrosis or family history of cystic fibrosis with evidence of CFTR gene mutation by either sweat chlorite test positive or 2 CF causing mutation found or positive nasal potential difference [12]. In the presenting case had sign and symptoms of cystic fibrosis along with history of sib death due to cystic fibrosis. Cystic fibrosis was confirmed by sweat chloride test. There are so many direct and indirect tests for diagnosis of pancreatic insufficiency. But there is no gold standard for the diagnosis or degree of severity of pancreatic exocrine insufficiency. Moreover, available tests are positive only when the exocrine pancreatic function is severely impaired [13]. Quantitative fecal fat estimation was considered as gold standard for steatorrhoea. But it has limitation for inconvenience nature [14]. Nowadays fecal elastase 1 is used for diagnosis of pancreatic insufficiency [15]. In this 1949 patient fecal elastase 1 was 113 ug/gm stool which indicate mild pancreatic insufficiency. Fat soluble vitamin deficiency is common in people with cystic fibrosis having pancreatic insufficiency and adverse clinical consequences have occurred [16]. There was low level of vitamin D level in this patient. DEXA scan also showed markedly reduced bone mineral density. Radiologic and endoscopic imaging is highly accurate for diagnosing the morphologic changes of chronic Pancreatitis. In this patient USG of HBS showed pancreatic calculi. MRI of HBS showed small irregular pancreas with pancreatic calculi suggestive of chronic pancreatitis. Shwachman et al. [17] reported 10 patients with cystic fibrosis presented with acute or recurrent pancreatitis. But none of them had pancreatic calcification [17]. There was no curative treatment of cystic fibrosis. Early diagnosis and interventional therapy improve life expectancy. For respiratory symptoms antibiotic and hypertonic saline inhalation is needed for airway clearing [18]. The management of pancreatic insufficiency in individuals with CF is a lifelong therapy. It is crucial that treatment include age-appropriate education through the lifespan, emphasizing the importance of good nutrition in prolonging survival in CF and the effective use of PERT (pancreatic enzyme replacement therapy). Fat soluble vitamin supplementation needed along with PERT [17]. We manage the patient with PERT, vitamin and mineral supplementation.

Pancreatic duct stone were removed by ERCP.

Conclusion

Our case report highlights cystic fibrosis patient with pancreatic insufficiency may present with pancreatic calcification and osteoporosis secondary to malabsorption. ERCP can use for diagnosis as well as therapeutic purpose for pancreatic calcification. To see severity of fat soluble vitamin malabsorption, along with fat soluble vitamin level assessment DEXA can done to assess bone mineral density.

References

1. Wilschanski M, Uc A. Cystic Fibrosis. In: Guandalini S, Dhawan A, Branski D, editors. Textbook of pediatric gastroenterology, hepatology and nutrition. 1st ed. Springer; 2015. p.471-86.
2. Sathe MP, Feranchak A. Cystic fibrosis liver disease. In: Suchy FJ, Sokol RJ, Balistreri WF, editors. Liver disease in children. 4th ed. Cambridge; 204. p.419-34.
3. Uc A. Pancreatic Insufficiency and Cystic Fibrosis. In: Bishop WP, editor. Pediatric Practice Gastroenterology. 1st ed. McGraw-Hill; 2010. p.441-51.
4. Ratjen FA. Cystic fibrosis: Pathogenesis and future treatment strategies. Respir Care. 2009;54(5):595-605.
5. Smith JJ, Travis SM, Greenberg EP, Welsh MJ. Cystic fibrosis airway epithelia fail to kill bacteria because of abnormal airway surface fluid. Cell. 1996;85(2):229-36.
6. Davies JC, Alton EW, Bush A. Cystic fibrosis. BMJ. 2007;335(7632):1255-9.
7. Singh VK, Schwarzenberg SJ. Pancreatic insufficiency in cystic fibrosis. J Cyst Fibros. 2017;16(Suppl 2):S70-8.
8. Rosenstein BJ, Cutting GR. The diagnosis of cystic fibrosis: a consensus statement. Cystic Fibrosis Foundation Consensus Panel. J Pediatr. 1998;132(4):589-95.
9. Farahmand F, Khalili M, Shahbaznejad L, Hirbod-Mobarakeh A, Najafi Sani M, Khodadad A, et al. Clinical presentation of cystic fibrosis at the time of diagnosis: a multicenter study in a region without newborn screening. Turk J Gastroenterol. 2013;24(6):541-5.
10. Wilschanski M, Durie PR. Pathology of pancreatic and intestinal disorders in cystic fibrosis. J R Soc Med. 1998;91(Suppl 34):40-9.
11. Ranganathan SC, Parsons F, Gangell C, Brennan S, Stick SM, Sly PD, et al. Evolution of pulmonary inflammation and nutritional status in infants and young children with cystic fibrosis. Thorax. 2011;66(5):408-13.
12. Farrell PM, White TB, Ren CL, Hempstead SE, Accurso F, Derichs N, et al. Diagnosis of cystic fibrosis: consensus guidelines from the Cystic Fibrosis Foundation. J Pediatr. 2017;181S:S4-S15.
13. Keller J, Aghdassi AA, LerchMM, Mayerle JV, Layer P. Tests of pancreatic exocrine function clinical significance in pancreatic and non-pancreatic disorders. Best Pract Res Clin Gastroenterol. 2009;23(3):425-39.
14. Van JH, Kamer H, Huinink BO, Weyers HA. Rapid method for the determination of fat in feces. J Biol Chem. 1949;177(1):347-55.
15. Borowitz D, Lin R, Baker SS. Comparison of monoclonal and polyclonal ELISAs for fecal elastase in patients with cystic fibrosis and pancreatic insufficiency. J Pediatr Gastroenterol Nutr. 2007;44(2):219-23.
16. Feranchak AP, Sontag MK, Wagener JS, Hammond KB, Accurso FJ, Sokol RJ. Prospective, long-term study of fat-soluble vitamin status in children with cystic fibrosis identified by newborn screen. J Pediatr. 1999;135(5):601-10.
17. Shwachman H, Lebenthal E, Khaw KT. Recurrent acute pancreatitis in patients with cystic fibrosis with normal pancreatic enzymes. Pediatrics. 1975;55(1):86-95.
18. Goss CH, Ratjen F. Update in cystic fibrosis 2012. Am J Respir Crit Care Med. 2013;187(9):915-9.