Section: Neonatology

Case Report

CASE REPORT: PANCREATIC INSUFFICIENCY AS AN EARLY MANIFESTATION OF CYSTIC FIBROSIS IN AN INFANT

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ABSTRACT

We had an infant who presented with unusual symptoms of pancreatic insufficiency and diarrhea along with failure to thrive. He was diagnosed to have cystic fibrosis with genetic testing showing CFTR gene mutation. Cystic fibrosis (CF) is an autosomal recessive disorder with variable presentation in infancy. Clinical manifestations include pancreatic insufficiency in majority of cases followed by respiratory manifestations and failure to thrive. Pancreatic insufficiency can lead to gastrointestinal symptoms such as malabsorption, steatorrhea and Failure to Thrive. Early recognition is critical for timely interventions and improved long-term outcomes.

Keywords: Cystic fibrosis (CF), CFTR gene, Pancreatic insufficiency (PI)

INTRODUCTION

Cystic fibrosis (CF) is a serious and life-shortening genetic disorder affecting approximately 70,000 persons worldwide.[1] Respiratory failure is the foremost cause of death in CF patients, and lung transplantation is often considered in end-stage CF disease. For those born with CF in the last five years, median predicted survival age is now 44, which is decades longer than survival rates in the recent past.[2] Indeed, new advances in CF modulator therapy and CF gene therapy may eventually provide a normal life expectancy for these individuals. Cystic fibrosis (CF) is an autosomal recessive disorder caused by pathogenic variants in cystic fibrosis transmembrane conductance regulator (CFTR) gene, leading to defective chloride transport across epithelial surfaces. This results in thickened secretions affecting multiple organs, particularly respiratory and gastrointestinal systems. While respiratory symptoms are often considered as the hall mark of CF, gastrointestinal complications such as pancreatic insufficiency can be initial presentation, especially in infants.[3] Clinical manifestations of CF include pancreatic insufficiency (90-95%), pulmonary involvement (80- 90%), failure to thrive (70-80%), meconium ileus (20-25%) and liver dysfunction (5-7%).[4] Gastro intestinal manifestations include pancreatic insufficiency, meconium ileus, hepatobiliary manifestations, distal intestinal obstruction syndrome and GERD. Early recognition is essential for initiating pancreatic enzyme replacement therapy and nutritional support to improve growth and long-term outcomes.

Case Report

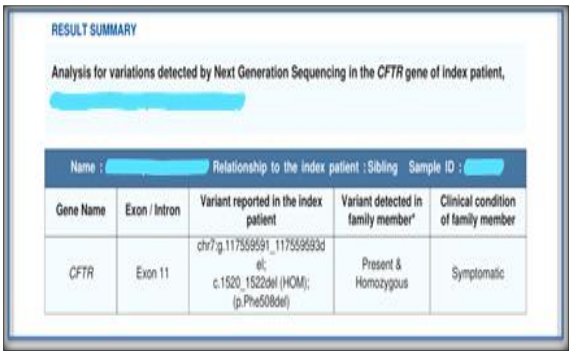
A 2 months 16 days old male infant second born to a third degree consanguineous marriage, presented with complaints of inadequate weight gain, 1 month history of pale colored and sticky stools, 1 week history of non-bilious vomiting and 3 days history of abdominal distension. He had multiple OP visits for diarrhoea.

Birth history - He was born through Lower segment Caesarean section (LSCS) in view of previous LSCS with birth weight of 2.6kgs. He was admitted in NICU for abdominal distension and operated on day

4 of the life for ileal atresia. He had smooth post operative course and discharged after 10 days from NICU.

On arrival to the emergency room examination revealed pallor, dehydration and parameters suggestive of failure to thrive on anthropometry. He was admitted in hospital, dehydration was corrected and further evaluation was resumed. Initial work up showed severe anemia, thrombocytopenia and hypoalbuminemia. Leukocyte-reduced red blood cells (LRBC) transfusion was given in view of severe anemia. Stool routine examination was normal and Ultrasound of the abdomen and kidneys, ureter, bladder (KUB) was unremarkable. Pediatric gastroenterologist was consulted. In view of lactose intolerance low lactose feeds were initiated which he tolerated well. Gradually feeds were increased and weight gain was noticed.

Family history was significant. The infant's elder sibling had died at 9 months of age following repeated respiratory tract infections and was found to have CFTR gene mutation on whole exome sequencing. Given the suggestive family history, genetic testing via Sanger sequencing was performed for the current patient, confirming the presence of the same CFTR gene mutation, consistent with cystic fibrosis. (Report was mentioned below)


RESULT SUMMARY

Analysis for variations detected by Next Generation Sequencing in the *CFTR* gene of index patient,

[redacted] Name : [redacted] Relationship to the index patient : Sibling Sample ID : [redacted]

Gene Name	Exon / Intron	Variant reported in the index patient	Variant detected in family member*	Clinical condition of family member
CFTR	Exon 11	chr7:g.117559591_117559593del; c.1520_1522del (HOM); (p.Phe508del)	Present & Homozygous	Symptomatic

Figure 1: Sanger sequencing report

DISCUSSION

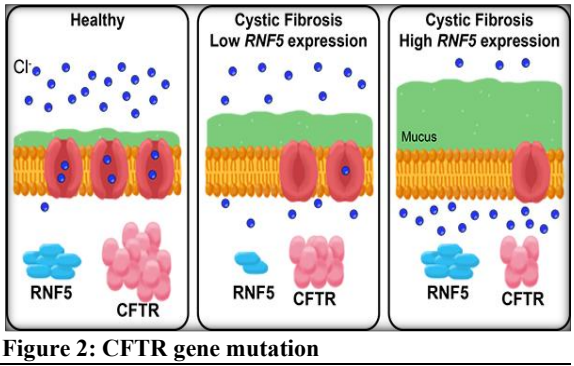


Figure 2: CFTR gene mutation

The cystic fibrosis transmembrane conductance regulator (CFTR) gene, located on chromosome 7q31.2, encodes a chloride channel essential for fluid transport across epithelial cells in multiple organs, including the lungs, pancreas, intestine, and hepatobiliary system. Over 2,000 mutations have been identified in the CFTR gene, varying in prevalence and severity. The most common pathogenic variant worldwide is the F508del mutation, accounting for approximately two-thirds of CF alleles in Caucasian populations.[5] However, mutation frequencies vary geographically and ethnically, with rare or private mutations often encountered in certain regions, particularly among consanguineous families.

Mutations in the CFTR gene disrupt chloride and bicarbonate transport, leading to thickened secretions, obstruction of ducts, and subsequent organ dysfunction. In the pancreas, inspissated secretions obstruct pancreatic ducts, resulting in exocrine pancreatic insufficiency, malabsorption, and failure to thrive, as observed in this case.[6]

Cystic fibrosis is the most common cause of exocrine pancreatic insufficiency. Pancreatic insufficiency (PI) is the most common gastrointestinal complication of CF affecting 90% of patients. Thickened secretions from the pancreas block the exocrine movement of digestive enzymes into the duodenum and cause irreversible damage to the pancreas.[7]

Clinical manifestations include steatorrhea, flatulence and abdominal distension, fat soluble vitamin deficiencies, coagulation abnormalities. Approximately 60% of CF infants have PI at birth, while 90% will develop PI by 1 year of age.[8]

CF-related meconium ileus is a recognized neonatal complication; however, this child presented with ileal atresia requiring early surgical intervention. While meconium ileus and bowel obstruction are commonly linked to CF, congenital intestinal atresia itself is less frequently associated but has been reported.[9-11]

Diagnosis includes 72 hour fecal fat collection as gold standard but practically not feasible. Fecal elastase has high sensitivity and specificity. Other tests include stool trypsin/chymotrypsin, serum immunoreactive trypsinogen and secretin/cholecystokinin infusion test.[12-13]

This case emphasizes the diagnostic challenge of CF in infants presenting with predominant gastrointestinal symptoms, especially in regions where respiratory symptoms are often considered more typical.

Management includes pancreatic enzyme replacement therapy and symptomatic support. Diet should include high calorie, high quality protein and fat soluble vitamins and trace elements. Medical management has Aspergillus oryzae pancreatic enzyme tablets. Lumacaftor-Ivacaftor (Orkambi) is indicated for the treatment of CF in children older than 6 years.[14]

CONCLUSION

This case highlights that cystic fibrosis should be considered in infants presenting with persistent gastrointestinal symptoms, failure to thrive. Genetic

analysis should be employed for an early diagnosis of CF.[15-16]

Pancreatic enzyme replacement therapy is beneficial for improving digestive function and preventing respiratory complications with adequate treatment and frequent follow up will improve survival rate

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