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Case Report

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Recurrent anemia in an infant with pneumonia: be vigilant for uncommon presentation of cystic fibrosis

Abstract

Background: Cystic fibrosis (CF) is an autosomal recessive disorder usually presented with meconium ileus in neonatal period. Other symptom of classic presentation of CF is recurrent pulmonary infections, exocrine pancreatic insufficiency, failure to thrive, loss of salt, and infertility may present later in life. Recurrent anemia is not a common feature of CF in infancy.

Case: First born infant presented with recurrent pallor and pneumonia at 3 months of age. He had history of twice packed cell transfusion in last one month. He was admitted with some chest infection at 2 months of age. On examination he had severe pallor with pneumonia and features of malnutrition. Complete blood count showed hemoglobin of 5.2g/dl, WBC21800/ mm^3, platelets 108000/mm^3. Stool for fat globules were present. He had severe sepsis with procalcitonin of 100µg/l. He received invasive ventilation but succumbed to sepsis. Clinical exome sequencing revealed a homozygous nonsense variation in exon 8 of the *CFTR* gene.

Conclusion: Pneumonia with recurrent transfusion dependent anemia should be raise suspicion of CF. In asymptomatic individual, neonatal screening may lead to early detection and allows immediate treatment of CF related consequences.

Keywords: cystic fibrosis, anemia, pneumonia

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Introduction

Cystic fibrosis (CF) is an autosomal recessive multisystem disorder characterized by the formation of thick, sticky mucus that can hamper our various organs.[1] CF is caused by the alteration of a gene located on the long arm of chromosome7 that encodes a protein, the cystic fibrosis trans membrane conductance regulator (CFTR), which functions as a chloride channel on the apical membrane of epithelial cells.[2] The disorder's common symptomatology is due to progressive damage to the respiratory system, digestive system, exocrine pancreatic insufficiency (diarrhea and failure to thrive), though their severity varies among affected individual.[3] Those infant who are not having classical clinical manifestations suggestive of CF or uncommon presentation, neonatal screening or early suspicion is helpful in detection of disease which allows prompt treatment of CF related complications, improving survival and conceptualizing the treatment strategies.[4] Meconium ileus may be the first manifestation of CF in the neonatal period, occurring in approximately 20% of patients with pancreatic insufficiency.[5] Though iron deficiency anemia may be present due to malabsorption in children,[6] transfusion dependent severe anemia in early infancy associated with CF is not mentioned in literature. Our objective of the present publication is to report the case of an infant who had uncommon presentation of CF with recurrent anemia and pneumonia without full blown evolution of the disease despite the clinical suspicion of CF.

Case

This infant was first born to a non-consanguineous marriage Asian descendant couple, full term normal vaginal delivery, APGAR score of 9 and 10 at 1 and 5 minutes of birth respectively, with birth weight of 3.8 kilograms. He was apparently well till 2 months of age then he developed progressive pallor. He had history of packed cell transfusion twice at 2.5 months of age and once hospitalization due to episode of pneumonia. He had no similar illness in other paternal or maternal family members. At the age of three months he admitted with us with recurrent progressive pallor, pedal edema and cough. On examination he had severe pallor, bilateral pitting edema, failure to thrive (weight 2.8 kilograms), and bilateral crepitating in chest, without hepatosplenomegaly. His hematological parameter during hospitalization is mentioned in (Table 1). Complete blood count showed hemoglobin of 5.3g/dl, WBC21800/mm^3 (polymorphs 62% and lymphocytes 38%), platelets 108000/mm^3. Peripheral smear showed macrocytic normochromic anemia with target cells, polychromatophilia and 5-6nRBC/100WBC. Direct coombs test was negative. Correct reticulocyte was 2.8%. RBS was 130mg/dl. High performance liquid chromatography (HPLC) showed HbF 15.5%, HbA 75.9%, HbA2 2.8%. Serum ferritin was 38ng/ml, total iron binding capacity (TIBC) 129. Renal function was normal. Liver function had total serum bilirubin of 2.85mg/dl with direct fraction of 2.84 mg/dl, ALT and AST was 40 U/L and 69 U/L respectively, serum albumin 1.59g/dl. Work up for dengue, scrub typhus and malaria were negative. Lymphocyte subset analysis and immunoglobulin levels were normal. Stool for fat globules were present. He was given 10ml/kg of B positive packed cell transfusion. Chest x-ray showed bilateral infiltrates in all lungs fields. He got severe sepsis with procalcitonin of 100ng/dl though blood culture and other secretions were sterile. On suspicion of cystic fibrosis due to pneumonia, failure to thrive, genetic study was sent. Further, he received invasive ventilation with in tropes but unfortunately succumbed to sepsis. Clinical exome sequencing revealed a homozygous nonsense variation in exon 8 of the *CFTR* gene (chr7:117180352G>A; Depth: 129x) that results in a stop codon and premature truncation of the protein at codon 356 (p.Trp356Ter; ENST00000003084).

Table 1 Hematological parameters during Hospitalization

Parameters	Day 1	Day 3	Day 4	Day 5
Hemoglobin(g/dl)	5.3	9.7	12.4	15.2
WBC (per mm^3)	21800	14990	18400	25370
Platelets (per mm^3)	108000	18000	22000	19000
Neutrophils (%)	61	65	64	75
Lymphocytes (%)	37	27	27	25
RBC count (per mm^3)	2.35	3.25	4.25	3.55
MCV (fl)	81.7	88.9	89.2	90.7
MCH (pg)	26.8	29.8	29.2	32.8
MCHC (fl)	32.8	33.6	32.7	37.2
MPV (fl)	10.2	10.3	10.5	10.3
Serum Ferritin (ng/ml)	38			
Serum iron (µg/dl)	70			
Total Iron Binding Capacity	129			
Reticulocyte count	1%			
Vitamin B12 (pg/ml)	400			
Serum Folate (ng/ml)	15			
Direct Coombs Test	Negative			
Blood group	B Positive			
Packed cell transfusion given	yes	yes		
Blood gas	Ph-7.443, Pco2-52 mmHg, pO2-65.7mmHg, Cl—89mmol/L, cHCO3—34.2 mmol/L			

Discussion

It is known that diagnosis of CF may be difficult during infancy, but in the presence of recurrent anemia and pneumonia, this differential diagnosis should be compulsorily considered. Meconium ileus may be the first manifestation of CF in the neonatal period specially in premature babies, occurring in approximately 20% of patients with pancreatic insufficiency.[5] Our patient had no meconium ileus in neonatal period which could raise the suspicion for diagnosis of CF. Despite the importance of an early sweat chloride test, we could not perform this test due to non-availability and the bad clinical condition of the patient. Mott et al.,[7] reported that at the time of neonatal screening lungs may be affected in 81% of cases showing structural abnormalities,45% bronchial wall thickening, and 21% lung infection. Our patient also had current episode of pneumonia and one episode at 2 months of age which raised the suspicion of CF and genetic study was sent. So in any infant who present with pneumonia and failure to thrive CF should be included in the list of differential diagnoses. Similar to our case, Armstrong et al.,[8] also reported that lung inflammation may occur early, and may even precede the onset of infection in infants with newly diagnosed cystic fibrosis. Other authors[9,10] also reported that those infants diagnosed with CF as a result of neonatal screening may have lung disease with bacterial infection from few first days of birth and that is linked to early onset of bronchiectasis in later life. Our patient has severe sepsis with pneumonia with procalcitonin of more than 100µg/l. We could not isolate any organism in blood culture or other secretions though. Our child had recurrent anemia that required 3 times packed cell transfusion almost every 15 days. Except sepsis, workup for recurrent transfusion did not show any evident explanation for the anemia. Iron deficiency has reported as more common cause for anemia in almost 60% children with CF due to malabsorption by Uijterschout et al.,[6]; Sismanlar et al.,[11] reported severe anemia as first sign of CF at an early age in 17/231(7.3%) children without respiratory involvement but none of them had recurrent and transfusion dependent anemia. Our patient had normal serum ferritin and serum iron possibly due to recent red cell transfusion and chronic inflammatory state of CF. But why transfusion dependent recurrent anemia at so early age happened is unexplainable with CF. Though iron deficiency anemia due to loss of iron in sputum has been described in adult patients with cystic fibrosis apart from pancreatic insufficiency,[12] but in children no such mechanism is explainable as no sputum production at an early age. Our case highlighted that those infant presented with severe recurrent anemia with pneumonia one should be vigilant for CF. It also emphasizes to include CF in each country neonatal screening programme so that it is diagnosed early to prevent devastating complications. These infants should be followed up and manage as per important published guidelines of Delphi methodology.[13]

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None.

Conflict of interest

None.

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