Respiratory Medicine Case Reports 30 (2020) 101110

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: http://www.elsevier.com/locate/rmcr

Unusual presentation of CF in an infant

José Dario Portillo Miño, MD [a,*], Efrén Esteban Cerón Muñoz, MD; MSc [b]

[a] School of Medicine, San Martin University Foundation, Hospital Universitario Departamental de Nariño, From Department of Pediatrics, Hospital Infantil Los Angeles, Pasto (Nariño), Colombia
[b] Valle of University, From Department of Pediatrics, Hospital Infantil Los Angeles, Pasto (Nariño), Colombia

ARTICLE INFO

Keywords:
Cystic fibrosis
Hepatobiliary
Infant

ABSTRACT

This case report attempts an approach to the clinical findings of hepatobiliary manifestations in Cystic Fibrosis. Infant less than 1-month-old with an insidious clinical picture that debut with hepatobiliary manifestations and jaundice, upper respiratory infection and gastrointestinal sepsis non-specific. Cystic Fibrosis is the most frequent autosomal recessive clinical condition in Caucasians. It is associated with liver involvement around 30%. In children, hepatobiliary symptoms occur at puberty when damage to the liver system is in advanced stages. The atypical presentation of Cystic Fibrosis with liver involvement is very rare and lethal. Understanding the different form of Cystic Fibrosis, it is essential for early diagnosis and to achieve integral management.

1. Introduction

Cystic Fibrosis (CF) is the most common autosomal, recessive, genetic clinical condition in Caucasians, occurring in approximately 1 of every 2,000 to 3,000 live births [1]. Hepatic abnormalities in patients with CF have usually been reported in about 30–40% of pediatric patients. It is a multisystemic, progressive and lethal disease that is distinguished by the relationship of several organic components, mainly; pulmonary, pancreatic, gastrointestinal and hepatic [2]. The disorder is characterized by an abnormality in the Cl and Na transporter through the defective transmembrane conductance regulation protein Cystic Fibrosis transmembrane regulator (CFTR), which causes an increase in the density of the exocrine secretions of the bronchial, intestinal, pancreatic duct, reproductive and biliary systems [3]. Currently, the hepatobiliary involved is considered the third cause of death after lung disease and complications of transplantation. The diagnosis is subscribed to the clinical evaluation, laboratory tests, ultrasound, and liver biopsy. The hepatic transplantation is the definitive treatment in advanced stages of the disease.

1.1. Case report

Infant less than 1-month-old with an insidious clinical picture of 5 days of evolution consist of fever, coughing, polypnea, tachycardia, and nasal flaring accompanied by episodes of diarrheic stools of high expenditure in current jelly and dysentery, bleeding profuse in venipuncture sites, distended abdomen, mild jaundice in the mucosa. No outstanding prenatal and pathological history. On admissions, with vital signs of HBP 82/50 mmHg, average blood pressure 68 mmHg, HR 182 beats per minute, BR 30 breaths per minute, saturation 92%, weight 3.5 kg, height 52 cm. At a physical examination in ill general conditions, widespread skin pallor and ecchymosis chest stigmas, signs of low expenditure, capillary refill greater than 3 seconds, hypoactive, a cardiopulmonary system without alterations and the testicular genitourinary system with edema and perianal erythema. He patient arrive the Pediatric Intensive Care Unit (PICU) where orotracheal intubation is performed due to respiratory failure and infusion of inotropic due to hemodynamic compromise. In laboratory control tests, severe anemia is evidenced that requires transfusion of blood products. Further; white blood cells 18,060, neutrophils 78.5%, lymphocytes 16.3%, monocytes 4.6% and platelets 397.000. Arterial blood gases with metabolic alkalosis and electrolytes alterations. Liver function; with transaminases and bilirubin levels elevated. The Procalcitonin 4.51 ng/dl with a high risk of sepsis and C-reactive protein 42 mg/l. The molecular study of the respiratory system by nested PCR (Film Array*) does not detect pathogens. The exam for viral load reveals infection by Cytomegalovirus treated with Ganciclovir. In the diagnostic images, in the chest X-ray shows scattered alveolar infiltrates in both pulmonary fields and perihilar and bibasal bronchial dilatations (Fig. 1). On abdominal X-ray, moderate gas distension is observed in the colon, without the presence of air-fluid levels or pneumoperitoneum (Fig. 2). The diagnostic suspicion of CF is approached due to clinical evaluation and by liver biopsy, which reports

* Corresponding author. Tel.: +57 322 5136609.
E-mail addresses: josedariopm83@gmail.com, josedariopm@hotmail.com (J.D. Portillo Miño).

https://doi.org/10.1016/j.rmcr.2020.101110
Received 20 January 2020; Received in revised form 24 May 2020; Accepted 26 May 2020
Available online 30 May 2020
2213-0071/© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

cholestasis, hepatitis with marked fibrosis and hepatobiliary involvement through liver function tests and bilirubin in the blood. The diagnosis of CF is confirmed with molecular studies of complete sequencing of the CFTR gene. The CFTR gen analysis results with mutation c.2353C > T (transition of cytosine by thiamin at position 2353 of cDNA), p. Arg785* (in the protein produces a change of arginine by stop codon), in a homozygous state, this change has been reported in the literature as a pathogenic change related to CF. For the second image test with the MLPA technique, no deletions or duplications were found (see Table 1). The patient is discharge with good prognosis to your home and control for Pediatrics, Gastroenterology, Neumology and Genetics specialist in this hospital.

2. Discussion and conclusions

The CF displays numerous types of portrayal because it covers a multisystemic spectrum. The typical clinical manifestations are localized in the respiratory and gastrointestinal tracts. It is common for the hepatobiliary disease to be expressed at the end of the first decade of life; that is, in the children's puberty. It has a prevalence in a range of 5.7%–39% [4]. Pathology is the third cause of fatality in patients with CF only preceded by lung damage and the complications inherent to transplantation. Besides, some researches have shown that patients with significant hepatic injury have a higher risk of worsening additional extrahepatic manifestations such as malnutrition, diabetes mellitus, hepatic osteodystrophy, and pulmonary disease which leads to an accentuation of morbidity into the underlying illness. For that reason, the hepatobiliary disease has been recognized as a jeopardy factor to unfavorable development, and disadvantageous prognosis. The most typical histological abnormality in the pediatric population is hepatic steatosis with a recorded predominance of 70% and *Nascimento FS* et al. [5] revealed that 16.4% of patients with CF had the hepatobiliary disease. This repetition is similar to that detailed by *Wegener* et al. with 16.3% in Canada and the United States. In Colombia, there are no known data that report the predominance of CF linked to hepatobiliary pathology. Therefore, this description is of valuable academic interest, regarding hepatobiliary condition associated with CF is insufficient as a predominant manifestation in pediatric patients in the biological behavior of the pathology, prognosis and therapeutic management.

It is of vital importance to the recognition of this phenotype as a clinical manifestation that exhibits CF to avoid severely complications such as portal hypertension and liver cirrhosis. It is a rare pathological entity, but with energetic disabling potential. In the case presented, we found that hepatic involvement is feasible and lethal. Although

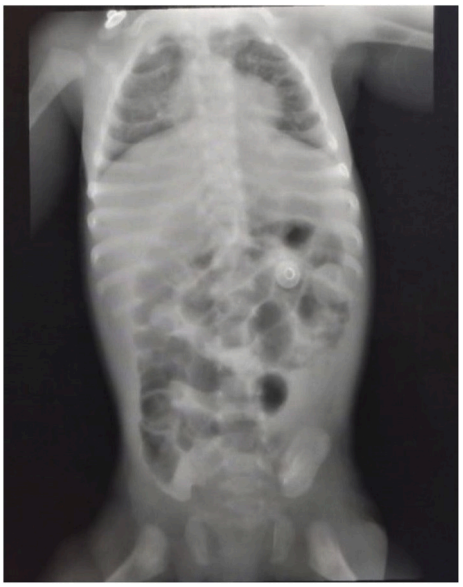

Fig. 2. Image X-ray abdominal of moderate gas distension is observed in the colon, without the presence of air-fluid levels or pneumoperitoneum.
Source**:** Archive of Hospital Infantil Los Angeles, Pasto. Colombia.

Table 1
Results CFTR gen analysis.

GEN	CHANGE DETECTED			REFERENCE
MIM*602421	Condition	Refseq NM_000492.3	Protein NP_000483.3	None
CFTR	Homocigosis	c.2353C > T	p.Arg785*	rs374946172 *Frentescu I* et al. J Cyst Fibros. 2008; 7 (5):423-8.

Source: Archive of Hospital Infantil Los Angeles, Pasto. Colombia.

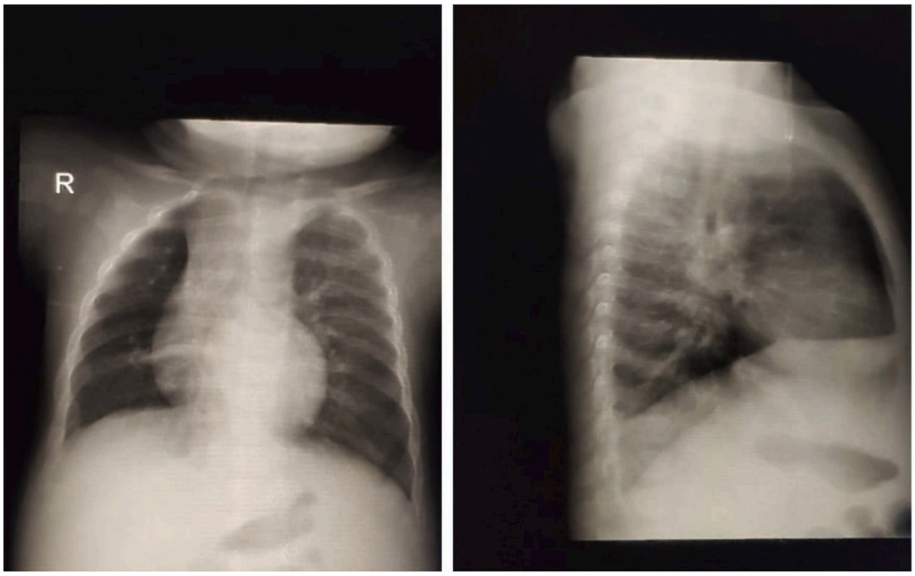

Fig. 1. Image chest X-ray shows diffuse alveolar infiltrates in both pulmonary fields and parahilar and bibasal bronchial dilatations
Source: Archive of Hospital Infantil Los Angeles, Pasto. Colombia.

hepatobiliary symptoms are unusual at the beginning in the natural history of the disease. The conventional approach of CF is highlighted by respiratory and gastrointestinal compromise, which is aimed at diagnosis with clinical suspicion of these findings and complement with aids is necessary as; laboratory tests, ultrasound and liver biopsy for an accurate diagnosis due to the complexity of the disease. Regarding treatment, it must be identified early; since, it deserves an adequate, comprehensive and individualized the approach implemented by a multidisciplinary organization formed of a gastroenterologist, pediatrician, nutritionist, pulmonologist, etc., in charge of providing all the therapeutic support early to the patient to improve their prognosis.

Funding

This manuscript is funding for Hospital Infantil Los Angeles, ID: Cra. 32 No. 21A-30 – AV. Los Estudiantes, Pasto, Nariño, Colombia.

Declaration of competing interest

The authors declare no conflict of interest for this article.

Acknowledgment

To the noblest hospital, humanist and committed to health care in childhood, The Hospital Infantil Los Angeles, in Pasto, Colombia.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2020.101110.

References

[1] C. Colombo, P.M. Battezzati, A. Crosignani, A. Morabito, D. Costantini, R. Padoan, et al., Liver disease in cystic fibrosis: a prospective study on incidence, risk factors, and outcome, Hepatology 36 (6) (2002 Dec) 1374–1382.
[2] Ana Luiza Melo dos Santos, et al., Cystic fibrosis: clinical phenotypes in children and adolescents, Pediatr Gastroenterol Hepatol Nutr 21 (4) (2018).
[3] G.F. Parisi, G. Di Dio, A. Gennaro, N. Rotolo, E. Salvatori, E. Lionetti, et al., Liver disease in cystic fibrosis: an update, Hepat. Mon. 35 (2013) 783–790.
[4] R. Somerville, A. Lackson, S. Zhou, C. Fletcher, P. Fitzpatrick, Non pulmonary chronic diseases in adults with cystic fibrosis: analysis of data from the Cystic Fibrosis Registry, Ir. Med. J. 106 (2013) 166–168.
[5] F.S. Nascimento, N.A. Sena, T.A. Ferreira, C.D. Marques, L.R. Silva, E.L. Souza, Hepatobiliary disease in children and adolescents with cystic fibrosis, J. Pediatr. 94 (2018) 504–510.