Hepatorenal Fibrocystic Diseases: disease spectrum, clinical presentations and complications

Thesis

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Presented by

Rehab El Sayed Mohamed Abd El Salam

Under supervision of

Prof. Dr. Rokaya Mohamed El Sayed Mohsen

Professor of pediatrics

Faculty of Medicine – Cairo University

Prof. Dr. Mona El Said El Raziky

Professor of pediatrics

Faculty of Medicine – Cairo University

Prof. Dr. Rascha Essam El Din Abd El Aziz

Lecturer of Pediatrics

Faculty of Medicine – Cairo University

Cairo University

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Abstract

In this case series descriptive study, we aimed at describing the clinical presentations and complications of congenital hepatic fibrosis. The study was conducted on patients attending the hepatology clinic Cairo University Pediatric Hospital (CUPH) from November 2011 to June 2013. **Methods:** Patient's data were retrieved from patient's files. Twenty nine patients with age range from 0.6 to 13.2 years were included; they were 19 males and 10 females. History of the presenting illness, clinical examination, and laboratory investigations were recorded. Ultrasound and upper endoscopic findings as well as liver biopsy findings were recorded as well. Diagnosis of congenital hepatic fibrosis depends on clinical, ultrasonographic findings as well as liver biopsy. **Results:** The main presenting symptoms were abdominal distension in 15 patients (51.7%), followed by hematemesis in 11 patients (37.9%). Failure to thrive was detected in the form of weight below 3rd percentile in 10 patients (38.5%). Hepatomegaly was the main clinical finding in the studied patients as it was detected in 24 patients (82.8%). Evidence of portal hypertension, manifested by splenomegaly was detected in 21 patients (72.4%) and esophageal varecies in 20 patients (69%) of patients. Recurrent cholangitis presenting with fever, jaundice in an already diagnosed CHF patients was detected in 3 patients (10.3%). Intra-hepatic biliary radical's dilatation was found by ultrasound examination in 5 patients (17.2%). Increased kidney size was detected in 10 cases (34.5%), renal calcification was detected also in 10 cases (34.5%), renal cysts in 9 cases (31%), hyperechogenic kidney in 4 patients (13.8%), loss of cortico-medullary differentiation in 4 cases (13.8%), and renal stone was found in one case (3.4%). Unfortunately one of the studied patients died of hematemesis complicating esophageal varices. **Conclusion:** Portal hypertension was the main clinical presentation of congenital hepatic fibrosis. Renal involvement,

the other spectrum of fibrocystic hepatorenal disease, is somewhat common in our cases.

Key words:

Congenital hepatic fibrosis, children, Hepatorenal fibrocystic diseases, portal hypertension.

First and foremost thanks to

Allah

The beneficent and merciful of all

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Contents

List of abbreviations:

ADPKD	Autosomal dominant polycystic kidney disease
ALP	Alkaline phosphatase
ALT	Alanine transferase
ANA	Anti nuclear antibody
ARPKD	Autosomal recessive polycystic kidney disease
ASMA	Anti smooth muscle antibodies
AST	Aspartate transferase
BBS	Bardet-Biedl syndrome
CD	Caroli disease
CDC	Centers for disease control
CDG-Ib	Congenital disorder of glycosylation type 1b
CED	Cranioectodermal dysplasia
CHF	Congenital hepatic fibrosis
CS	Caroli syndrome
CT	Computed tomography
CUPH	Cairo University Pediatric Hospital
DHPLC	Denaturating high performance liquid chromatograpgy
DPM	Ductal plate malformation
EGD	Esophago-gastro-duodenoscopy
ERCP	Endoscopic retrograde cholangiopancreatograopy
ESR	Erythrocyte sedimentation rate
ESRD	End stage renal disease
EVC	Ellis-Van creveld syndrome
FCDs	Fibrocystic diseases
GGT	Gamma glutamyl transferase
HRFCDs	Hepatorenal fibrocystic diseases
IQ	Intelligence quotient
JATD	June asphyxiating thoracic dystrophy
JSRDs	Joubert syndrome and related disorders
MHz	Mega Hertezs
MKS	Meckel syndrome
MRCP	Magnetic resonant cholangiopancreatography
MRI	Magnetic resonant
MTS	Molar tooth sign
NIH	National Institutes of Health
NPHP	Nephronophthisis
NSAIDs	No steroidal anti-inflammatory drugs
OFD1	Oral-facial-digital syndrome type 1
PANCA	Perinuclear Anti-Neutrophil cytoplasmic antibodies
PBC	Primary biliary cirrhosis

PFIC	Progressive familial intrahepatic cholestasis
PH	Portal hypertension
PKHD1	Polycystic kidney and hepatic disease 1
PSC	Primary sclerosing cholangitis
PT	Prothrombin time
RHPD	Renal-hepatic-pancreatic dysplasia
TIPS	Transjugular intrahepatic portosystemic shunts
VMC	Von meyenburg complex
VOD	Veno-occlussive disease

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Introduction
And aim of the work

Introduction:

Congenital hepatic fibrosis (CHF) is a histopathologic diagnosis that refers to a developmental disorder of the portobiliary system characterized by ductal plate malformation (DPM), abnormal branching of the intrahepatic portal vein, and progressive fibrosis of the portal tracts.

Ductal plate malformation results in a range of abnormalities depending on the level of the biliary tree primarily involved:

- CHF without macroscopically visible cystic dilatation of the intrahepatic biliary ducts.

- CHF associated with macroscopic liver cysts in continuity with the bile ducts, sometimes referred to as Caroli's syndrome (CS) ***(Desmet, 1998).***

Most frequently CHF\CS is associated with ciliopathies (disorders of the primary cilia) that have associated renal disease: polycystic kidney disease, nephronophthisis (NPHP), and chronic tubulointerstitial disease, collectively referred to as the hepatorenal fibrocystic diseases (HRFCDs) ***(Summerfield et al.,1986).***

The characteristic clinical picture of the CHF is portal hypertension (PH) which is strictly defined as an increase in the portal venous pressure ***(Kerr et al., 1978 & Summerfield et al., 1986).***

In general, as hepatic fibrosis increases and PH worsens, the spleen increase in size, platelets and white blood cells decrease in number (hypersplenism) and porto-systemic vascular collaterals develop, including esophageal and gastric varices. As varices enlarge, the risk of bleeding increases ***(Kerr et al., 1978; Summerfield et al., 1986; Fonck et al., 2001).***

Pulmonary hypertention (portopulmonary hypertention) and vascular shunts in the pulmonary parenchyma (Hepatopulmonary syndrome) are complications of PH that can also be rarely seen in CHF ***(Kerr et al., 1978; Summerfield et al., 1986; Fonck et al., 2001).***

Cholangitis should be considered and investigated in individual known to have biliary dilatation that develop unexplained fever or right upper-quadrant pain with or without jaundice ***(Shneider & Magid, 2005).***

Ultrasound examination is the most informative diagnostic modality in CHF which often reveals: increased echogenicity of the liver, cysts in the hepatic parenchyma, enlarged spleen and accompanying fibrocystic changes in the kidneys ***(Premkumer et al., 1988 & Akhan et al., 2007).***

Histopathologic finding on liver biopsy are the gold standard for diagnosis of CHF ***(Fonck et al., 2001)***.

There is no known treatment for the underlying defect in CHF because no therapies can repair the primary ductal plate malformation or reverse the fibrosis or biliary tree abnormalities ***(Shneider & Magid, 2005).***

Aim of the work:

To describe the clinical presentation and complications of CHF patients presenting and following up in the hepatology unit of Cairo University Pediatric Hospital (CUPH).

Review of literature