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Short Communication

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Liver Dysfunction in Children Cause by Metabolic Diseases: Review of 9 Cases

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Abstract

Liver dysfunction can be a form of presentation of some metabolic disease in children. The aim of this study is review all cases of liver dysfunction found in pediatric department and correlate with other clinical and laboratory findings for the diagnosis of metabolic disorder. The results showed 9 cases (8M/1F), with the mean age of 30 months with metabolic diseases: tyrosinemia type 1, alpha1 antitrypsin (A1AT), ornithine transcarbamylase (OTC), citrin deficiency (2 cases), Danon disease, fructose intolerance, lysinuria and glucogenosis type 1. We conclude that clinical presentation and laboratory findings are important for the diagnosis. Molecular studies confirm the final diagnosis and help us for future genetic counseling and prenatal diagnosis.

Keywords: Liver Dysfunction, Children, Metabolic Disease

Introduction

Liver dysfunction is a common presentation of inborn error of metabolism. Renal disease, hepatomegaly, cardiomyopathy are some of clinical findings that can appear at the same time. The suspicious of metabolic disease as responsible for this situation is confirmed by molecular study. The treatment depends on the type of metabolic disease and the time of diagnosis.

Aim

The aim of this study is review all cases of liver dysfunction found in pediatric department and correlate with other clinical and laboratory findings for the diagnosis of metabolic disorder.

Patients and Methods

This is a retrospective study of Pediatric/Neonatology Department of Centro Hospitalar Conde S. Januário of 9 children (8 boys and 1 girl) with the mean age of 30 months, range from 1 month to 13 years, admitted in the Pediatric ward (5 cases) or Neonatal intensive care (2 cases) or follow-up in pediatric outpatient department (2 cases).

Liver dysfunction was defined as the increase of two serum glutamic pyruvic and oxaloacetic transaminase activities (SGPT, SGOT) more than twice the normal value (SGPT: normal = 4-45 IU/I; SGOT: normal = 4-40 IU/1),associated or not with the following symptoms and laboratory findings: hepatomegaly (liver span > or = 5 cm below the right costal margin), hepatic encephalopathy, serum NH3 -> 100 µg/dL , direct serum bilirubin > 30 mmol/1, prothrombin test (PT) < 50% of control value. In case of increased direct serum bilirubin, the serum gamma-glutamyl. Trans peptidase (GGT) activity was determined (normal = 3-30 IU/1). A hepatobiliary ultrasonography study was performed in each patient. Heart ultrasound is performed in case of abnormal heart sounds and alpha fetoprotein (AFP) was also checked in case of suspect of citrin deficiency or tyrosinemia type 1.

Results

All cases showed high levels of SGOT/SGOP. GGT and AFP were elevated in citrin deficiency. CK was very high in Danon disease. Ammonia was increase almost to 500 mg/dl in OTC deficiency. Citruline was increase in citrin deficiency but reduced in OTC defect, a common laboratory presentation of these both diseases. Ornithine was reduced in OTC. Tyrosine was high in tyrosinemia and this result is according to deficiency of fumaryl acetoacetate. Heart ultrasound showed a very severe hypertrophy cardiomyopathy in Danon syndrome (Table 1).

Table 1: Most important laboratory findings

Patients/ Age (months)	SGOT	SGPT	GGT	AFP ng/ml	A1AT mg/dl	* NH3 (µg/dL) ** CK (U/L) *** Glycose (mg/dl)	Lysine in urine micromol/ mmol creatinine in urine	* Citrulline ** Ornithine *** Tyrosine mmol/l	DNA	Diagnosis

A/23	+	+				*** 35 (>45)		*** 145 (25-60)	FAH	Tyrosinemia type 1
B/3	+	+			27 (78-200)				PiZ	A1AT
C/8	+	+				* 467 (45-80)		* 3 (15 -30) ** 14 (49 -151)	OTC	OTC
D/1	+	+	+	125380 (1480-58887)				* 379 (14-32)	SLC25A13	Citrin
E/1	+	+	+	114013 (16-1995)				* 445 (14-32)	SLC25A13	Citrin
F/156	+	+				** 1804 (< 190)			LAMP2	Danon
G/3	+	+				*** 35			ALDOB	Fructose intolerance
H/36	+	+					641 (10-46)		SLC7A7	Lysinuria
I/1	+	+				*** 25			G6PC	Glucogenosis type 1

Discussion

All patients had liver dysfunction. When is associated with cardiomyopathy, Danon disease is the most probably diagnosis. The heart contractibility was poor, with risk of sudden dead and early indication for heart transplant [1,2]. Hepatomegaly is a common feature of glycogenosis and tyrosinemia [3,4]. In this last disease, the Fanconi syndrome was responsible for the growth delay and rickets [5]. In other situations, hypoglycemia was a important sign in fructose intolerance and cause coma in the patient, so as in Glycogenosis type 1 and Tyrosinemia type 1 [3,4]. Encephalopathy was the main presentation of OTC secondary to high level of NH3. Although OTC is an x-linked disorder, when appear in girls can be severe. In case of high level of ammonia (>200 mg/dl), we need to consider a great possibility to be a metabolic disease [6]. When we find a patient with persistent increase level of SGOT/ SGOP, we need to exclude A1AT deficiency [7]. The confirmation is important for the future avoidance of smoke that will increase the risk of pulmonary emphysema. Lysinuria can also present with these changes but will have others symptoms particularly protein intolerance and vomiting [8]. In patients with citrin deficiency, cholestasis jaundice is the most common presentation and amino acid screening associated with molecular study will confirm or not the clinical suspicious (Table 2) [9].

Table 2: Clinical presentation

Patients/ Age (months)	Cholestatic jaundice	Hepatomegaly	Ritkets	Coma	Cardiomyopathy	Fanconi syndrome	Diagnosis
A/23	-	+	+	-	-	+	Tyrosinemia 1
B/3	-	-	-	-	-	-	A1AT
C/8	-	+	-	+	-	-	OTC
D/1	+	-	-	-	-	-	Citrin
E/1	+	-	-	-	-	-	Citrin
F/156	-	-	-	-	+	-	Danon
G/3	-	-	-	+	-	-	Fructose intolerance
H/36	-	+	-	+	-	-	Lysinuria
I/1	-	+	-	-	-	-	Glucogenosis

Conclusions

Liver dysfunction in children can be caused by metabolic diseases. The clinical presentation and laboratory findings are important for the diagnosis. Molecular study will confirm the final diagnosis and help us for future genetic counseling and prenatal diagnosis.

References

1. D'souza RS, Levandowski C, Slavov D, Graw SL, Allen LA, et al. (2014) Danon disease: clinical features, evaluation, and management. Circ Heart Fail 7: 843-849.
2. Hedberg Oldfors C, Máthé G, Thomson K, Tulinius M, Karason K, et al. (2015) Early onset cardiomyopathy in females with Danon disease. Neuromuscul Disorder 25: 493-501.
3. Masurl-Paulet A, Poggi-Bach J, Rolland MO, Bernard O, Guffon N, et al. (2008) "NTBC treatment in tyrosinemia type 1: long –term outcome in French patients". Journal of Inherited Metabolic Disease 31: 81-87.
4. Chen M A, Weinstein DA (2016) Glycogen storage diseases: Diagnosis, treatment and outcome. Translational Science of Rare Diseases 1: 45-72.
5. Hsu SY, Tsai IJ, Tsau YK (2005) "Comparison of growth in primary Fanconi syndrome and proximal renal tubular acidosis" Pediatric Nephrology 20: 460-464.
6. Venkateswaran L, Scaglia F, McLin V, Hertel P, Shchelochkov OA, et al. (2009) Ornithine transcarbamylase deficiency: a possible risk factor for thrombosis. Pediatr Blood Cancer 53: 100-102.
7. Primhak RA, MS Tanner (2001) Alpha-1 antitrypsin deficiency. Arch Dis Child 85: 2-5.
8. Riccio E, Pisani A (2014) Fanconi syndrome with lysinuric protein intolerance. Clinical Kidney Journal 7: 599-601.
9. Chen R, Wang XH, Fu HY, Zhang SR, Abudouxikuer K, et al. (2013) "Different regional distribuition of SLC25A13 mutations in Chinese patients with neonatal intrahepatic cholestasis". World Journal of Gastroenterology 19: 4545-4551.