Nonalcoholic fatty liver disease and fatigue in long-term survivors of childhood-onset craniopharyngioma

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Introduction

Hypothalamic obesity in childhood craniopharyngioma (CP) carries a high risk for development of metabolic syndrome. In metabolic syndrome, the development of non alcoholic fatty liver disease (NAFLD) is known. The aim of this study is to detect the risk for NAFLD in childhood-onset CP.

Patients and Methods

A total of 384 patients recruited in trials HIT Endo and KRANIOPHARYNGEOM 2000 were analyzed. Ninety-four survivors were included by fulfilling the criteria of proven hypothalamic involvement (HI), a minimum interval of 5 years between diagnosis and study, and a minimum age of 18 years at time of evaluation. 19 patients participated.

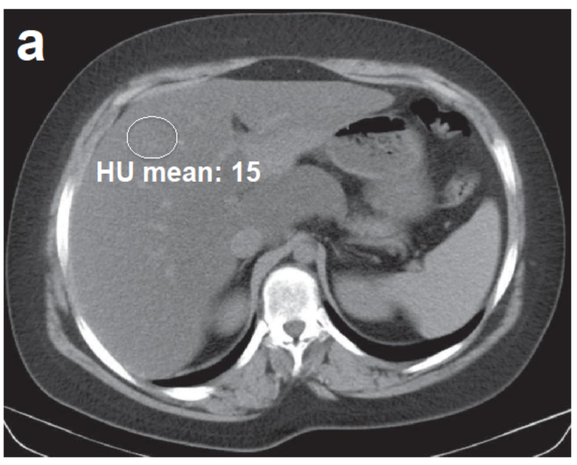

Figure 1: Computed tomography imaging of (a) a patient with severe steatosis hepatis and (b) with a normal liver. Circles depict the regions of interest in which Houns-field units (HU) are measured.

Table 1: Characteristics of 19 patients with CP at time of diagnosis and current study. BMI SDS was calculated according to Rolland-Cachera et al. Bold-formatting indicates significant differences.

Characteristics	Patients without steatosis hepatis	Patients with steatosis hepatis	P
Number of patients (n)	9	10	
Age at diagnosis (years), median (range)	11.9 (2.8–20.5)	9.39 (5.06–19.6)	0.859
Age at study (years), median (range)	23.7 (18.9–29.2)	25.16 (16.9–30.3)	0.591
Follow-up (years), median (range)	12.8 (6.0–24.1)	14.7 (6.1–19.1)	0.765
Gender, n (male/female)	4/5	5/5	
Degree of resection, n (%) Complete resection Incomplete resection	 3 (33.4) 6 (66.7)	 5 (50) 5 (50)	
Hypothalamic involvement, n (%)	9 (100)	10 (100)	
BMI–SDS at diagnose, median (range)	0.66 (K0.6–4.67)	0,70 (K1.6–3.65)	0.530
BMI–SDS at study, median (range)	5.48 (1.51–10.29)	7.30 (3.71–12.62)	0.331
Body composition, %, median (range) **Body fluid** **Body fat**	 **49.9 (41.0–56.7)** **35.4 (23.9–49.3)**	 **45.3 (36.7–51.6)** **42.6 (32.9–55.8)**	 **0.036** **0.033**
Hounsfield units (HU), median (range)	57 (46–63)	32 (15–41)	

Serum parameters	Patients without steatosis hepatis n, median (range)	Patients with steatosis hepatis n, median (range)	P
Cholesterin (mg/dl)	8; 177 (144 – 263)	10; 199 (150 – 271)	0.479
HDL (mg/dl)	8; 40 (26 – 58)	10; 34 (16 – 52)	0.169
LDL (mg/dl)	8; 119 (86 – 213)	10; 147 (59 – 218)	0.818
AST (U/l)	**9; 29 (21 – 39)**	**10; 55 (18 – 126)**	**0.041**
ALT (U/l)	9; 28 (13 – 62)	10; 47 (18 – 232)	0.141
GLDH (U/l)	**9; 2.95 (0.3 – 7)**	**10; 13.4 (3.2 – 26.7)**	**0.006**
ChE (U/l)	9; 9.95 (7 – 11.9)	10; 9.8 (6.6 – 10.9)	0.701
Gamma-GT (U/l)	**8; 23 (7.8 – 99)**	**10; 94 (18 – 216)**	**0.016**
Billirubin (mg/dl)	9; 0.55 (0.2 – 1.7)	10; 0.4 (0.09 – 1.5)	0.428
Insulin (mU/l)	**9; 17.15 (2.3 – 36.2)**	**9; 47.2 (13 .0 – 58.8)**	**0.03**
HbA1c (% of Hb)	9; 5.2 (4.5 – 7.0)	10; 5.8 (5.1 – 6.3)	0.408
Blood glucose (mg/dl)	9; 75 (58 – 101)	10; 79 (58 – 115)	0.429
HOMA	**8; 2.45 (0.3 – 5.5)**	**5; 9.2 (2.2 – 14.8)**	**0.036**

Table 2: Serum parameters of 19 patients CP at time of study. Bold-formatting indicates significant differences. HOMA: homeostasis model assessment index

Medication	Patients without steatosis hepatis		Patients with steatosis hepatis	
	n	%	n	%
Cortisone	8	89	10	100
DDAVP	9	100	10	100
L thyroxine	8	89	10	100
*Rec. GH	6	67	6	60
Sex steroids	8	89	10	100
Methylphenidate	0	0	5	50
Melatonin	4	44	0	0
Anti-diabetics	0	0	1	10
Cardiac medicine	0	0	2	20

Table 3: Medication of the 19 patients with childhood-onset craniopharyngioma (CP) at the time of current study.

Medication	Patients without steatosis hepatis		Patients with steatosis hepatis	
	n	%	n	%
Cortisone	8	89	10	100
DDAVP	9	100	10	100
L thyroxine	8	89	10	100
*Rec. GH	4	44	6	60
Sex steroids	8	89	10	100
Methylphenidate	0	0	6	60
Melatonin	2	22	1	10
Anti-diabetics	1	11	4	40
Cardiac medicine	3	33	2	20

Table 4: Medication of 19 pts with childhood-onset craniopharyngioma during follow-up 2–7 yrs after original study.

Results

NAFLD occurs in about 50% of CP patients with HI and is associated with elevated liver enzymes and homeostasis model assessment index. BMI is not an effective predictive factor but body fat mass measured by near-infrared spectroscopy (NIRS) is. Over half of CP patients (60%) with NAFLD are treated with stimulating agents.

Conclusions

NAFLD is a major adverse late effect in childhood-onset CP. NIRS rather than BMI should be used to measure body composition and predict NAFLD. Stimulating agents for treatment of fatigue and daytime sleepiness in CP should be prescribed judiciously.

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