

17

CELLULAR AND HUMORAL IMMUNE AGGRESSION AND PANCREATIC FUNCTION IMPAIRMENT IN CHILDREN WITH SPORADIC HYPERGLYCEMIA WITHOUT FAMILIAL HISTORY OF TYPE I DIABETES. Fabiano de Bruno L.; Osinde E.; Doval A.; Basabe J.C.

Diabetes Experimental, Centro de Investigaciones Endocrinológicas (CEDIE), Htal de Niños R. Gutiérrez y Sección Diabetes, Htal. "A. Rosadas", Buenos Aires, Argentina. Forty five children with sporadic hyperglycemias were studied (normal fasting glycaemia, with 2 or more sporadic postprandial hyperglycemias). Controls were healthy children without familial history of diabetes or associated autoimmune diseases. Humoral immunity was detected by the presence of insulin autoantibodies (IAA) according to Palmer; all sera higher than \bar{X} control ± 3 SD were considered positive. Cellular immune aggression (CIA) was evaluated by coculturing lymphocytes with dispersed rat islet cells (control group: $\bar{X} \pm 2$ SD: 29.66 \pm 3.06 insulin U/5000 cells/5 min, n=22) according to the immune markers and taken into consideration the pancreatic function (ins. secr. IS; control group: 137.6 \pm 78.3 insulin U, min ± 3 post i.v. glucose, $\bar{X} \pm 2$ SD, n=15) patients were divided in two groups. Group A: 14/24 with normal IS; 1/4 IAA+ve; 7/14 CIA+ve and 6/14 without any aggression. Group B: 10/24 with impaired IS (than \bar{X} control - 2 SD); 5/10 IAA+ve; 10/10 CIA+ve and 5/10 with both immune markers + ve. The results showed that in children with sporadic hyperglycemia: 1) The presence of CIA is an early marker since it was found in 50% of children without IS impairment or IAA and in all those with impaired IS. 2) IAA were present in 7.14% of children with normal IS and in a 50% of those with impaired IS; 3) 35% of all children with sporadic hyperglycemia showed IS impairment and CIA+ve, suggesting that this could be a group at risk of developing Type I diabetes.

18

SERUM SHBG/IGF-I DURING EARLY AND LATE PREPUBERTY IN CHILDREN WITH IDIOPATHIC (I) AND ORGANIC (O) GH DEFICIENCY. Ciaccio M.; Belgorosky A.; Rivarola M.A.

Laboratorio de Investigación, Hospital de Pediatría Garrahan, Buenos Aires, Argentina. Idiopathic GH deficiency (I) is secondary to multiple ill-defined etiologies. Some children show symptoms in early prepuberty (early onset) while others show a decrease in their growth rate in the late prepubertal years (late onset). We measured two GH-dependent serum parameters (SHBG and IGF-I) in 15 patients with I, either younger (G1, n=10) or older (G2, n=5) than 7 years of age (y) at diagnosis, as well as in 11 patients with organic GH deficiency (O), secondary to intracranial tumors, younger (G3, n=5) or older (G4, n=6) than 7 y, and in 52 control (C) subjects, younger (G5, n=18) or older (G6, n=34) than 7 y. Children younger than 7 y had not started adrenal puberty as evaluated by serum DHA sulfate. Mean \pm SD ages in G1 (2.68 \pm 2.49y), G2 (3 and G5 and in G2 (10.3 \pm 1.95y), G4 and G6 were not statistically different. GH deficiency was diagnosed after 2 pharmacological tests for GH release. Serum T₄ and T₃ were normal in all patients. SHBG was determined by saturation analysis and IGF-I by RIA. Serum SHBG (nmol/L) and serum IGF-I (U/L) were respectively, as follows ($\bar{X} \pm$ SD): G1: 154 \pm 58 and 0.06 \pm 0.06; G2: 79.6 \pm 24.4 and 0.22 \pm 0.16; G3: 132 \pm 47 and 0.47 \pm 0.25; G4: 108 \pm 17.4 and 0.17 \pm 0.11; G5: 113 \pm 72 and 0.32 \pm 0.16; G6: 68.7 \pm 31.7 and 1.04 \pm 0.36. In patients younger than 7 y, both SHBG and IGF-I were statistically different (p < 0.01) when comparing I vs O, while in patients older than 7 y no difference was found. Patients with early onset I seem to differ from late onset I. Lower IGF-I might be related, not only to age, but also to a longer (usually prenatal) and more severe GH deficiency.

19

GROWTH AND FINAL HEIGHT IN PATIENTS WITH TURNER SYNDROME. García Rudaz C.; Azanda E.; Martínez A.; Heinrich J.J.; Bergadá C.

División de Endocrinología, Hospital de Niños R. Gutiérrez, Buenos Aires, Argentina. Short stature is a central feature in Turner's Syndrome. In the last years several treatment schedules have been proposed in order to improve final height. So complete knowledge of the variants of this Syndrome and the expected final height for a specific country is needed. We analyzed the final heights of 86 patients with Turner Syndrome, 32 with a 45X chromosome constitution (X45D 138.1 \pm 4.92 cm) and 52 with a mosaicism or a structurally abnormal X (136.8 \pm 4.73 cm). Forty five patients were longitudinally follow trough their pubertal growth period. Nine girls received treatment with low doses of ethinyl estradiol, 100 ng/kg/day (group A), 11 started spontaneous pubertal development and received no treatment (group B) and 26 patients, treated with standard replacement doses of estrogen (17 patients non XO group C and 8 XO group D). In all patients height prediction was calculated by Bayley-Pinnau method at the onset of spontaneous puberty or at the beginning of the replacement therapy and the total height gain between this onset and final height was calculated.

GROUP	CA	BA	PREDICIED HEIGHT	TOTAL GAIN	FINAL HEIGHT
A	10.96 \pm 1.58	9.13 \pm 1.57	142.4 \pm 6.56	17.14 \pm 6.32	137.7 \pm 7.08
B	11.84 \pm 1.40	10.1 \pm 1.53	143.7 \pm 7.76	16.55 \pm 3.02	140.1 \pm 6.36
C	12.91 \pm 2.28	11.21 \pm 1.50	139.41 \pm 6.03	10.61 \pm 6.64	137.02 \pm 4.7
D	14.55 \pm 1.56	12.71 \pm 2.15	136.4 \pm 2.15	7.91 \pm 5.04	137.3 \pm 4.83

In prepubertal girls with Turner Syndrome a slight acceleration of growth velocity under treatment with low doses or a conventional estrogen therapy was seen, but final height was the same in all group. We also noticed that Argentine girls with Turner Syndrome have an ultimate height below the average height reported for European (X 143 cm) or American girls (X 142.6 cm).

20

DIAGNOSIS AND TREATMENT OF 5-ALPHA-REDUCTASE DEFICIENCY. Mendoza B.; Arnold I.J.P.; Vaccinatos C.; Rigan A.C.; Lando V.S.; Goto S.Y.; Bloise W.

Unidade de Genadas e Intersexo-HC-FMSP-Sao Paulo, Brazil. We studied 4 patients with ambiguous genitalia characterized by microphallus, bifid scrotum, blind vagina and bilateral chriptorchidism. The patients were submitted to stimulation test with hCG (50-100) U/Kg x 4 doses in prepubertals and 6,000 U, i.m. in pubertals with dosage of T and DHT by RIA after extraction with organic solvent, celite column chromatography to isolate DHT. The results as compared to the prepubertal and pubertal control groups showed normal response of the test and subnormal of DHT with an increased relation T/DHT, characterizing 5-alpha reductase deficiency. Patients were treated with i.m. exogenous testosterone for 2 months (125 mg IM every 30 days) in prepubertals, and 6 months (250 mg/week), and with 2.5% topic dihydrotestosterone (2.5 gr DHT in 100 gr cold cream) for 1 month in prepubers and for 6 months in intrapubers for the development of the penis.

CASE	AGE (years)	FOBT 'I' (ng/dl)	hCG DHT (ng/dl)	T/DHT	FALO		FOBT DHT
					BEFORE	POST-TEST	
1	6	292	6.6	44	1.7	4.0	4.7
2	9	255	7.0	36.4	2.3	2.5	4.2
3	13	1288	21	53	4	6.2	6.5
4	14	1453	16	76	4	5.8	6.8

Prepub-controls 384 \pm 59 29 \pm 8 14 \pm 5
 Pubertal controls 1306 \pm 576 64 \pm 16 21 \pm 10 (n=6)
 We concluded that the exogenous administration of T or DHT may induce penis growth in mesoaline pseudhermaphroditism caused by 5-alpha-reductase deficiency.

21

LOW IGF-I LEVELS IN PATIENTS WITH HEMOGLOBINOPATHIES. SOURCES AND FOLLOW-UP. Jøesper H.; Abreu S.

Divisions of Endocrinology and Hemato-Oncology, "Ricardo Gutiérrez" Children's Hospital, Buenos Aires, Argentina. Politransfused patients show low IGF-I levels. They could be ascribed to growth hormone (GH) deficit, hypothyroidism, malnutrition or reduced hepatic secretion. To determine their origin and evolution we studied patients politransfused for hemoglobinopathies when entering the study, time I, n=25 (TI) and after 1 year of follow up, time II, n=23 (TII). Both at TI and TII we measured height, weight, total proteins, albumin, gamma globulin, transferrin and IGF-I; at TII we also evaluated T₃, T₄, TSH and the GH response to 2 standard stimuli (normal-GH) 10 ng/ml. Only one patient (at TI) had weight below 85% of normal, and 50% of the whole population had weight percentile > height percentile. Low IGF-I was found in 64% of TI patients and in 73.9% of TII patients. IGF-I logarithmic deviation showed a significant reduction (TI X: -2.55, TII X: -3.34, p 0.01,*). Total proteins and albumin also decreased significantly (TI X: 7.45 vs TII X: 6.93, gr%, p 0.01,*; TI X: 4.22 vs TII X: 3.84, gr%, p 0.02,* respectively). Both at TI and TII IGF-I logarithmic deviation showed a significant correlation with transferrin (TI r: 0.419, TII r: 0.481, p 0.05) and gamma globulin (TI r: -0.489, TII r: -0.416, p 0.05). GH secretion was evaluated in 17 patients; 70.6% (12/17) had low IGF-I levels. One of them (1/12) showed GH deficit and low T₃ and T₄ levels, other five (5/12) showed GH deficit alone. The other six patients (6/12) had a GH response > 10 ng/ml and normal T₃, T₄ and TSH. Conclusions: 1) the low IGF-I levels found in politransfused patients are not due to malnutrition, 2) in 50% of the cases they could be ascribed to GH deficit, either primary or secondary to hypothyroidism, 3) after excluding the above mentioned factors the other 50% could probably be attributed to reduced hepatic secretion (the albumin reduction and the significant correlations between IGF-I and transferrin and gamma globulin could be considered supporting indirect evidences). *paired test

22

RESPONSE TO THE GRF TEST IN PATIENTS WITH GROWTH HORMONE DEFICIT. García H.; Silva R.; Bugueño M.; Youlton R.; Wilhelm V.; Cattani A.; Jara A.; Cortínez A.; Henríquez C.; Torrealba I.; Beas F. and Cassarola F.

Instituto Investigaciones Materno-Infantil. Facultad de Medicina, Universidad de Chile, Hospital Clínico San Borja-Arriarán. The Growth Hormone Releasing Factor (GRF) is a peptide of 44 aminoacids produced in the hypothalamus, which stimulates Gh secretion by the hypophysis. Therapeutical use has been reported in some cases of Gh deficiency (GHD). The GRF was performed in 14 prepubertal children with GHD, 9 men and 5 women, with a mean chronological age of 8.1 years (3.5-11.8) and mean bone age 5.1 years (dif -3), height of 2.5 SD with respect to the mean, and growth rate 4.5 cm/year. The diagnosis of GHD was based on a GH response under 7 ng/ml to 2 stimulation tests and the exclusion of other pathologies. 1 ug/kg iv GRF was administered with measurements of GH at 0-5-10-15-30 minutes. TAC was performed in 9 patients, in 8/9 it was normal and 1 presented empty turkish sella. We used RIA (DFC) with 2nd antibody with 5% intra-assay and 7% inter-assay variation coefficient. The positive response to the test was defined as a GH increase of over 4-fold that of the variation coefficient of the RIA used. RESULTS: There was a positive response in 10/14 patients (71%). The peak GH value was obtained in average at 10 minutes (range 5-30) after the iv GRF injection.

GHD	N	%	Basal GH (ng/ml)	GH peak (ng/dl)
GRF+	10	71	1.3	24.6
GRF-	4	29	0.8	2.1

The positive response to GRF in 71% of the GHD cases, suggests that in most of them, the deficiency lies in the hypothalamus and not in the hypophysis. These patients may benefit from a long-term treatment with GRF.