17

SEXUAL PRECOCITY OF TESTICULAR ORIGIN IN TWINS: EVOLUTION OF A LEYDIG CELL TUMOR. Madureira G.; Arnhold I.J.P.; Mendonça B.B.; Domenice S.; Matielli J.; Dahia P.L.; Lando V.S.; Barbosa R.F. and Bloise W. Gonadal intersex Unit. Division of Endocrinology, Hospital das Clínicas, University of São Paulo, Brazil.

Twin brothers were evaluated at 6,83 years for precocious appearance of pubic hair at 6.5 years. Parental consanguinity and family history were negative. On the initial physical examination both patients had signs of virilisation (table) without testicular nodules.

	C.A. years	B.A. years	HEIGHT cm s.d.	PUBIC HAIR	PENIS cm	RIGHT TESTIS cm	LEFT TESTIS cm	TESTOS-TERONE ng/dl
CASE 1	6.83	8.5	124.6+0.7	II	8x2.5	2.7x1.2	2.2x1.0	66
	9.08	-	146.2+2.1	IV	12x3.5	3.1x1.6*	2.1x1.2	62
CASE 2	6.83	6.5	122.0+0.2	II	9.5x2.2	2.4x1.3	2.3x1.2	18
	9.08	-	136.3+0.45	II	9.5x2.4	2.6x1.4	2.3x1.3	13

* 1.3 cm nodule

Basal steroid levels in patients 1 and 2 were; respectively: testosterone 66 and 18ng/dl; Δ 4-androstenedione 0.3 and <0.2ng/ml; DHEA 1.3 and 1.2nd/ml, DHEA-S 169 and 153ng/dl; 17-hydroxyprogesterone 0.6 and 0.5ng/ml. Both patients and prepubertal LH response to the LHRH test (ΔLH 4.6 and 7.6mIU/ml). ACTH stimulation did not demonstrate deficiency of adrenal steroidogenesis. Skull X-rays and CT scan and testicular ultrasonography were normal. Pubertal signs progressed only in case 1 and 6 months therapy with LHRH analog was clinically and biochemically ineffective, in fact, testosterone values ranged from 94 to 163 ng/dl. After 18 months, bone age advanced to 12 years in case 1 and remained equal to chronological age in case 2. After 2 years a nodule was palpable in the inferior pole of the right testis in patient 1, confirmed by ultrasonography (table). Right orchidectomy demonstrated a 1.3 cm Leydig cell tumor. Seminiferous tubules showed spermatogenesis up to spermatids and the interstitium contained few partially differentiated Leydig cells. Post-operative serum testosterone values were low (12 ng/dl).
We conclude that this pair of twins with sexual precocity had a different progression: Case 1 had progressive virilisation and appearance of a Leydig cell tumor, whilst case 2 remained clinically and biochemically unchanged. The progression to a Leydig cell tumor not initially demonstrable indicates the need of close observation of patients with sexual precocity of testicular origin.

18

DETECTION OF Y-SPECIFIC DNA SEQUENCES AND H-Y ANTIGEN EXPRESSION IN XY INDIVIDUALS WITH DISGENETIC GONADS DEVELOPMENT.
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We studied four patients with 46,XY karyotype and disgenetic gonads. Two of them (M.F., S.P.) are affected by XY gonadal dysgenesis (Swyer's syndrome) with eunuchoid habitus, female external genitalia and streak gonads. One (R.M.) had mixed gonadal dysgenesis (rudimentary testis on the R and a contralateral streak gonad) and one (M.R.) with perineal hypospadias, had disgenetic gonads (streak on the R. and rudimentary testis in the L, both with gonadoblastoma). All patients had Mullerian duct derivatives. Clinical, endocrine and serologic data, as well as DNA hybridization results using ZFY probe, Page et al. Cell. 51: 1091, 1987) are shown in the Table.

PATIENT	C.A. yrs.	HEIGHT cm.	GENDER	LH mIU/ml	FSH mIU/ml	TESTOSTERONE ng/dl	ZFY	ANTIGEN H-Y
MF	20	157	F	100	80	nd	+	-
SP	18	171	F	51	70	15	+	-
RM	15	164	F	36	103	12	+	+
MR	15	164	M	8	24	110	+	+

The patients with XY gonadal dysgenesis have the Y-specific DNA sequences detected by ZFY probe, which correspond to a region encompassing the, so called, testis determining factor gene(TDF). These cases probably represent the autosomal recessive form of Swyer's syndrome (Two of them belonging to the H-Y negative form). The patient with mixed gonadal dysgenesis expresses H-Y antigen and has the ZFY sequence). Therefore, his condition is probably due to a delay in testicular organogenesis (as indicated by gonadal assymetry, with partial testicular differentiation on the R). The same situation could conceivably occur in the patient with bilateral gonadoblastoma. Altogether, our data suggest the involvement of other loci, besides TDF, in the primary determination of sex in man.

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19

GONADOTROPIN FUNCTION IN PREPUBERTAL BOYS WITH MONORCHIA AND CONTRALATERAL TESTICULAR HYPERTROPHY. Silvia Gottlieb, H.Domené and C. Bergadá. División de Endocrinología. Hospital de Niños R.Gutiérrez. Buenos Aires. Argentina.

Experimental studies have demonstrated that unilateral testicular castration increases FSH blood levels in infantile animals with contralateral testicular hypertrophy. Prepubertal boys with monorchia show also this contralateral gonadal enlargement being the FSH rol on this mechanism a matter of controversies. In order to clarify this mechanism, 12 prepubertal boys with monorchia were studied. Ages were between 3 and 11 years, all were on Tanner Grade 1 of Puberty, right testis was absent in 8 and left in 4. Scrotal testicular volume was 3 ml in 6 and 4 ml in the other 6. i.v. acute test with 25 ug of Gn-RH was performed and blood was drawn at Basal 20'. 30' and 60' post- Gn-RH and serum LH and FSH were measured by RIA. Basal (b) and Maximal increment (Mx) were compared with 9 normal boys, 8 anorchid patients 16 with bilateral cryptorchydism, 4 with unilateral crypt; all were prepubertal, and 21 normal adultmen. Results were as follows ($\bar{x}$±SD):

		LH(b)	LH(Mx)(UI/L)	FSH(b)	FSH(Mx)(UI/L)
Prepub. control	(n=9)	3.4±1.5	15.8±10.3	2.5±1.0	5.9±2.6
Monorchia	(n=12)	2.2±2.8	10.2± 4.9	1.8±1.4	4.7±2.9
Unilat. crypt	(n=4)	7.4±1.4	23.6± 9.0	2.1±0.5	4.2±0.9
Bilat. crypt.	(n=16)	5.8±0.6	20.2± 2.8	2.7±0.2	5.3±0.6
Adults	(n=21)	6.5±3.0	30.3±11.8	4.3±1.6	4.3±1.6
Anorchia	(n=8)	5.8±6.2	47.7±37.0	8.8±6.0	34.0±17.9

In summary: On the basis of experimental data which reports increased FSH values followed by testicular hypertrophy after unilateral castration, and that pubertal patients with monorchia have enlarged scrotal testis and they do not increase further until the onset of puberty, it could be assumed that the mechanism of testicular hypertrophy could be induced by pituitary FSH immediately after the atrophy of the crypt. testis with subsequent reduction to normal values.

20

CRYPTORCHISM IN BOYS UNDER 4 YEARS: TREATMENT WITH hCG + hMG. Longui CA, Arnhold IJP, Mendonca BB, D'Oswaldo AF, Bisi H, Sesso A, Bloise W. Gonadal and Intersex Unit,Hospital das Clinicas,HCFMUSP-Sao Paulo,Brasil.

We analized prospectively 15 boys with cryptorchism: 6 at right side, 6 at left and 3 bilateral, treated with hCG(750 U/m^2/dose; 2x/wk)+hMG (100 U/m^2/dose; 2x/wk) during 6 weeks. Mean follow-up was 8,8 months. We strictly excluded the retractile and the non-palpable testes. In all cases, sexual cromatin was negative and the plasma testosterone peak was normal. Ultrasonographic studies had difficulties to determine the exact testicular position. Side effects: Androgenic signs (15 cases) darker urine (9) increased appetite (8) diuresis increase (6) facial swelling and restless sleep (5). The only side effect that persisted was penile enlargement (mean°1.25cm; range 0.4-2.2 cm). Testicular descent: unilateral cases (12): partial descent in 2; bilateral cases (3): descent in 2 cases. Testicular retraction: Occured in all but one testis. Light microscopy: decrease of tubular volume and spermatogonia number.

CONCLUSION: This dosage of hCG+hMG was sufficient to elicit androgenic effects in all boys, and the testosterone peak was in the normal range. With careful exclusion of retractile testes,testicular descent was obtained in 4 boys (26%), however in all but one, retraction occured on the average 8 weeks follow-up. Preliminary data on testicular histology, suggest that testicular anomalies are present already in the second year of life.

21

ADRENOCORTICAL FUNCTION IN ADEQUATE AND SMALL FOR GESTATIONAL AGE PREMATURE NEONATES DURING THE FIRST TWO WEEKS OF LIFE. Belgorosky A., Warman M., Nizzo D., Chaler E., Maceiras M., Sola A., Rivarola M.. Serv.de Endocrinología y Neonatología. Hospital de Pediatría "Prof.Dr.J.P.Garrahan", Buenos Aires, Argentina.

The function of the definitive and fetal zones of the adrenal cortex were studied in 8 pre-term(PT) neonates with adequate weight for gestational age (AGA) and in 10 small for gestational age (SGA) PTs during the first 14 days of post-natal life, as well as in 9 full-term (FT)AGA newborns during the first 7 days of post-natal life. Peripheral vein serum cortisol and 17α-hydroxyprogesterone (17-OH-P) were used as parameters of the function of the definitive zone, while serum dehydroepiandrosterone sulphate (DS) was taken as indicator of the function of the fetal zone of the adrenal cortex. Cord vein blood (CVB) serum 17-OH-P was used as a marker of the function of the fetoplacental unit. There was a significant negative correlation between 1-day-old and 5-day-old serum 17-OH-P, cortisol or DS and gestational age in the 27 subjects studied. On the other hand, there was a significative negative correlation between serum 17-OH-P and days of postnatal life in the 3 groups of neonates, and between serum cortisol and days of postnatal life in PT AGA neonates but not in PT SGA newborns. During the first week of life, mean ± SD serum cortisol was 267±143 and 273±136 mol/l in PT AGA and PT SGA neonates respectively, significantly higher ($p<0.05$ and $p<0.02$) than in FT newborns (118±81), while serum 17-OH-P was higher ($p<0.05$) in PT AGA neonates only (8,77±6.6 vs 3.60 ±2.81 nmol/l in FT). Serum 17-OH-P was lower in cord vein blood of PT, as well as in mother's blood during delivery, compared to that of FT (67±86 vs 341±182 nmol/l, $p<0.01$). Our data showing higher levels of cortisol and 17-OH-P in PT newborns suggests that the stress of the extra uterine adaptation in prematurity resutls in an adequate response of the definitive zone of the adrenal cortex. On the other hand, higher serum 17-OH-P levels present in PT neonates should be taken into account for the differential diagnosis of 21-hydroxylase deficiency.

22

SERUM 17-OH PROGESTERONE LEVELS IN PREMATURES BY DIRECT AND POST EXTRACTION ASSAYS DURING THE FIRST SEVEN DAYS OF LIFE. Warman M, Nizzo D, Chaler E, Maceiras M, Sola no A, Rivarola MA, Belgorosky A. Servicio de Endocrinología y Neonatología. Hospital de Pediatría "Garrahan". Buenos Aires. Argentina.

Elevated levels of serum 17-hydroxyprogesterone (17-OH-P), either by direct assay (DRIA), which includes an interference substance, or after diethyl either extraction (E), have been described in premature babies (PT). However the nature of the interference substance remains unknown. Serum 17-OH-P by DRIA were determined in 8 full term newborns with adequate weight for gestational age. Mean values during the first 7 days of life were 24.75±15.19, 62.85±25.25 and 74.78±37.09 nmol/l respectively. These values were significantly higher than those determined after E (3.60±2.81, 8.77±6.6 and 6.14 ±4.34 nmol/L, $p<0.01$). A significant negative correlation was found between 17-OH-P DRIA and gestational age, $r=0.53$, $p<0.01$ and $r=0.61$ $p<0.01$, on days 1 and 5 of life respectively. The negative slope was found between 17-OH-P DRIA and cortisol ($r=0.81$, $p<0.01$) or dehydroepiandrosterone sulfate (DS) ($r=0.56$, $p<0.01$) on day 1 but not on day 5. It is concluded that 17-OH-P DRIA is higher than 17-PH-P DRIA and that lack of correlation on day 5 between 17-OH-P DRIA is higher than 17-OH-P DRIA and cortisol or DS suggests that the interference has an extraadrenal origin. It could be a product of the hepatic metabolism of adrenal steroids.