PRECOCIOUS PUBERTY IN A GIRL WITH PRADER WILLI SYNDROME (PWS)

Papagianni M, Kosta K, Lialias I, Chatzakis C, Tsiroukidou K, Tsanakas I.

Endocrine Unit, 3rd Pediatric Department, Aristotle University of Thessaloniki, Hippokrateion General Hospital of Thessaloniki

Background

PWS is a rare genetic disorder with a wide range of symptoms and signs. Main characteristics are hypotonia, growth retardation, feeding difficulties in neonatal period, increased appetite and obesity in childhood, delayed puberty or hypogonadism in adolescence. It is also associated with behavioral disturbances and impaired cognitive function. The genetic defect is located on the 15q11-13 chromosome.

Clinical Case

A 7 years old girl with PWS, presented to our unit for the regular follow up due to growth hormone treatment. She was diagnosed at age 2 months. Her genetic test showed deletion of paternal 15q11-13 and presence of one maternal allele on the D15S10, Gabrb3 and D15S113.

Physical examination revealed bilateral thelarche and pubarche (Tanner stage: Breast 2, Axilla Hair 1, Pubic Hair 2, Menarche 0). Her height was 118.7cm (-0.47 SDS), her weight was 27kg (1.7 SDS) and her BMI was 19.16 kg/m^2 (1.68 SDS). GnRH test result was indicative for puberty (peak LH:17.4mIU/ml, peak FSH:13.4mIU/ml) as it is shown below (Table1) and pelvic ultrasound revealed slightly increased volume of uterus and ovaries.

LHRH test (1rst)	LH (mIU/ml)	FSH (mIU/ml)	Estradiol (pg/ml)
0	0.7	3.7	<5
30	17.4	10.1	
60	16.1	13.4	

Table 1. LHRH test at age 7 years

The patient didn't follow puberty suppression treatment as the thelarche was spontaneously regressed. In the next 6 months thelarche relapsed and increased growth velocity was noted. On the physical examination at the age 8.2 years, her height was 127.6cm (0.06 SDS), weight was 36kg (3.4 SDS) and BMI was 22.32kg/m^2 (2.25 SDS) (Table 2). She underwent a new LHRH test which revealed augmented LH, FSH and Estradiol levels (Table 3). She was then put on GnRH analogue treatment.

Age	Height cm	Height SDS	Weight kg	Weight SDS	BMI	BMI SDS
7 yrs old	118.7	-0.47	27	1.7	19.16	1.68
8.2 yrs old	127.6	0.06	36	3.4	22.32	2.25

Table 2. Anthropometric Data

LHRH test (2nd)	LH (mIU/ml)	FSH (mIU/ml)	Estradiol (pg/ml)
0	0.1	2.8	16
30	13.8	8.79	
60	12.7	11.28	

Table 3. LHRH test at age 8.2 years

During suppression treatment, thelarche was regressed and her growth velocity decreased to prepubertal level. Meanwhile, due to increased weight velocity, she had presented with increased sleep apnea episodes and she stopped growth hormone treatment. At her recent follow up, she presented with weight loss, her polysomnography study revealed significant improvement and she is going to be on growth hormone treatment again.

Conclusion

The most common pubertal disorders of the PWS are delayed or incomplete puberty. In our case the patient presented with incomplete precocious puberty but later progressed to complete precocious puberty. There is a very limited amount of information in the literature concerning association of precocious puberty with PWS, probably due to deletion of specific genes on the affected part of the chromosome. Recently MKRN3 gene mutation, which is located on the affected part of the causative chromosome, has been correlated with precocious puberty in patients with PWS.

Bibliography

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MARIA PAPAGIANNI

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