A CASE OF CENTRAL PRECOCIOUS PUBERTY IN A PATIENT WITH PRADER-WILLI SYNDROME

Pellegrin MC[1], Tornese G[2], Faleschini E[2], Ventura A[1,2]
1. University of Trieste, Trieste, Italy
2. IRCCS Burlo Garofolo, Trieste, Italy
Authors have no financial support nor conflict of interest to declare

Address: ***Pellegrin Maria Chiara***
University of Trieste - IRCCS Burlo Garofolo,
Via dell'Istria 65, 34137 Trieste, Italy
Email: mariachiara.pellegrin@gmail.com

Background

Hypogonadism is one of the major diagnostic criteria of Prader-Willi syndrome (PWS). A hypogonadotropic hypogonadism is often present as a result of hypothalamic dysfunction (together with other hormonal disorders, such as growth hormone deficiency and hypothyroidism).

Presentation

A 8.5-year-old boy with genetically-confirmed PWS (maternal uniparental disomy) presented in our Endocrinology Unit for routinely follow-up.

He was born preterm with low birth weight. Posthemorrhagic ventricular dilation was treated by ventriculoperitoneal shunting. Diagnosis was made because of persistent hypotonia and failure to thrive after shunt removing. Therapy with rhGH was started at 1.5 years old without provocative diagnostic testing at a daily dosage of 25 mcg/kg, with good clinical response on growth and motor performance. Therapy with L-thyroxine (1 mcg/kg/day) was started at 2 years because of silent central hypothyroidism discovered at routine exams. At 3 years, congenital abdominal cryptorchidism was surgically corrected with bilateral orchidopexia, which resulted in asymmetric testis (hypotrophy of the left one).

The physical examination revealed precocious pubertal development: volume of the right testis 5 ml, Tanner stage 2 for pubic hair and genitalia. BMI was in normal range. Growth rate was accelerated (9.4 cm/year, +4.83 SDS) with advanced bone age (10.5 years according to the Greulich and Pyle method). A GnRH test revealed premature activation of the hypothalamic-pituitary-gonadal axis (LH>FSH) with pubertal testosterone levels (Table 1). Serum IGF-1 level, ACTH and thyroid function test were normal.

A brain MRI showed mild hydrocephalus and a normal pituitary gland (Figure 1). Gonadal ultrasound demonstrated testicular microlithiasis (Figure 2). Tumour markers were negative (alfa-fetoprotein 0.7 ng/mL, beta-HCG 0.1 mUI/mL).

With a final diagnosis of central precocious puberty (CPP), LHRH analogue therapy was started (Leuprorelin 3.75 mg every 28 days), obtaining good clinical and hormonal response. After 1 year of treatment Tanner stage is stable, growth in decelerated, weight and BMI are worsened (Table 2).

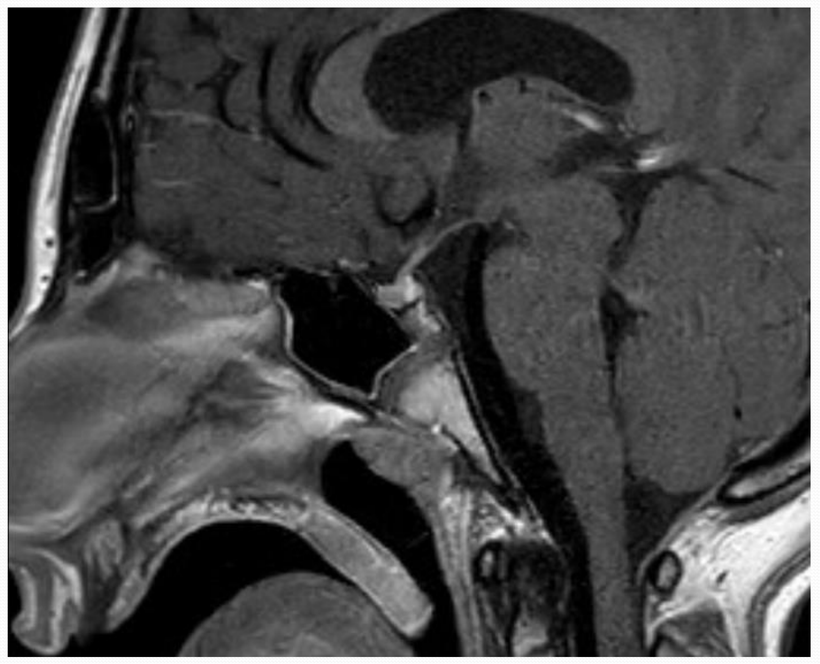

Figure 1. T1-weighted sagittal MRI through the pituitary fossa shows a normal, isointense anterior pituitary and a hyperintense posterior pituitary gland. Hypothalamic area was unremarkable. Mild ventricular enlargement was found as sign of previous hydrocephalus.

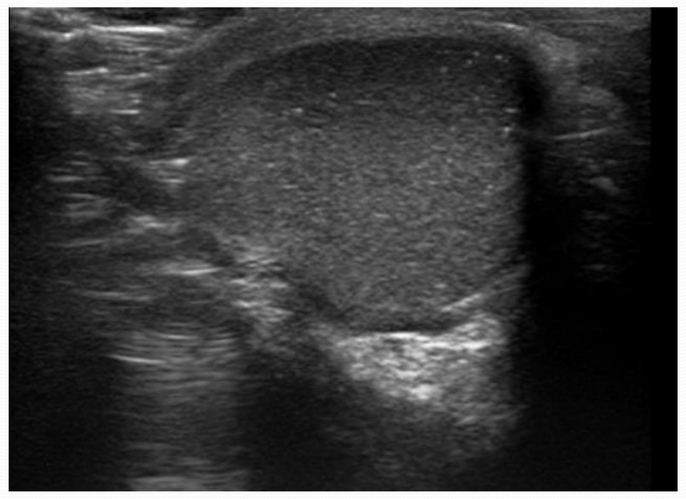

Figure 2 Ultrasonographic image of the right testis showing multiple hyperechoic foci consistent with testicular microlithiasis

	First examination	6 months after GnRH analog treatment	1 year after GnRH analog treatment
Age, years	8.5	9.1	9.6
Tanner stage	II	II	II
Bone age, year	10.5	11	11
Height SDS	1.14	1.23	1.02
Weight SDS	0.86	0.90	1.28
BMI SDS	0.59	0.61	1.2

Table 2: Clinical findings at onset of precocious puberty and during follow-up

	Basal	30° min	45° min	60° min	90° min	120° min
LH, mUI/ml	0.6	10.4	11.6	11.0	8.3	6.8
FSH, mUI/ml	4.5	7.9	9.4	10.4	10.5	10.8
Testosterone, ng/ml (nv 0.03-0.3)	1.07					1.15
Free testosterone, pg/ml (nv 8.7-54.7)	2.14					1.66

Table 1: Laboratory findings consistent with true precocious puberty

Conclusions

Fourteen cases of CPP in PWS have been reported so far. The aetiology remains largely unknown (except for few cases with pituitary anomalies or brain ischemic damage). Our patient presented CPP with only one functioning microlithiasic testis. We hypothesize that perinatal brain damage could have contributed to premature activation of the axis.

Reference list

1. *Lee HS, Hwang JS. Central precocious puberty in a girl with Prader-Willi syndrome. J Pediatr Endocrinol Metab. 2013;26:1201-4.*
2. *Crinò A, Schiaffini R, Ciampalini P, et al.; Genetic Obesity Study Group of Italian Society of Pediatric endocrinology and diabetology (SIEDP). Hypogonadism and pubertal development in Prader-Willi syndrome. Eur J Pediatr. 2003;162:327-33.*

DOI: 10.3252/pso.eu.55ESPE.2016