Testicular adrenal rest tumors in two young patients with congenital adrenal hyperplasia

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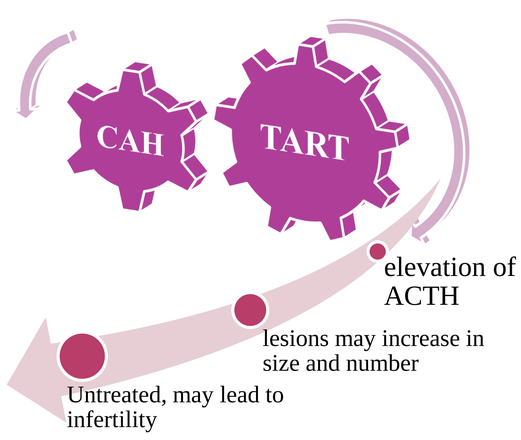
Introduction

Testicular adrenal rest tumours (TART)

- may develop in males with **congenital adrenal hyperplasia** (CAH), due to overstimulation of aberrant adrenal cells (1)
- originate from the adrenal cortex tissue
  - ectopic tissue
  - in the testes-stimulated by ACTH excess
- all pathologies causing an elevation of ACTH levels may be associated with adrenal inclusions (2)
- widely variable prevalence, congenital adrenal hyperplasia by 21-hydroxylase deficiency being by far the most common (3)



Testicular adrenal rest tumours (TART)

- having no malignant features, there seems to be no need to remove them at an early stage (4)
- these lesions may increase in size and number when exogenous hormone therapy is inadequate (4)
- because of the central localization of the tumours, the compression of seminiferous tubules may lead to infertility by obstructive azoospermia and irreversible damage of the surrounding testicular tissue (5)
- untreated, may lead to infertility and irreversible damage of the surrounding testicular tissue (5)

Case reports

First case

- 15 years boy, diagnosed with CAH at the age of 3 weeks due to 21-OH deficiency
- successfully treated with glucocorticoids and salt supplementation until the age of six, then interrupted without consulting a specialist
- gradual increase of testicular size, consults for "testicular tumour"(Figure 1)
- Physical examination:
  - Short stature (147.5 cm, -2DS), puberty P VI, testicles ~ 50 ml, hard
- Imaging:
  - testicular ultrasound: RT 79/46 mm, inhomogeneous hypoechoic; LT 60/33 mm, contains 3 hypoechoic formations, inhomogeneous, of 21/13, 30/15 and 20/12 mm (Figure 2)
  - Adrenal ultrasound (Figure 3): increased dimensions, macronodular aspect
- Replacement therapy with glucocorticoids was given:
  - Prednisone 10 mg/day in 2 divided doses
- The follow-up revealed an improvement of hormonal and imagistic parameters:
  - Clinic – reduction in testicular size of 25% (Figure 4)
  - Biological - improved gonadal axis
  - Morphologic: ultrasound RT 60/50 mm, 58/34 mm LT, normal adrenal ultrasound (Figures 5 and 6).

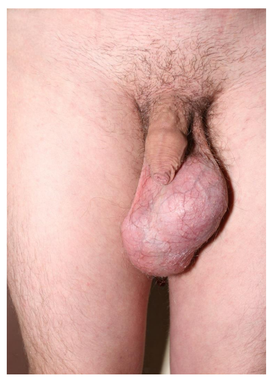


Figure 1. Clinical aspect of testes at diagnosis

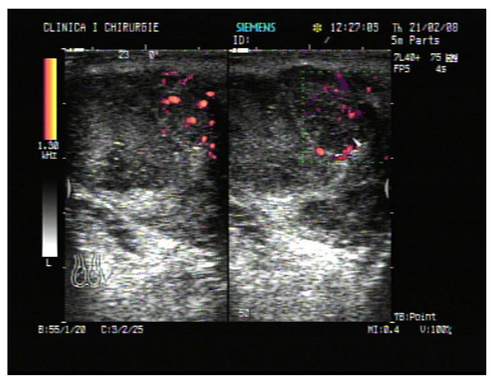


Figure 2. Ultrasound of testes at diagnosis

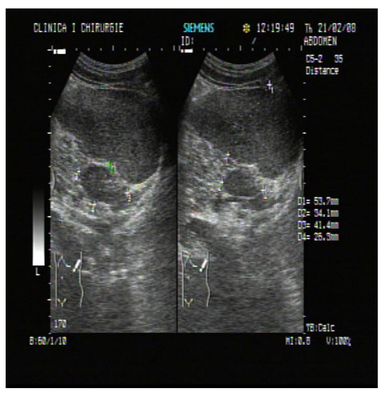


Figure 3. Ultrasound of the left SR at diagnosis

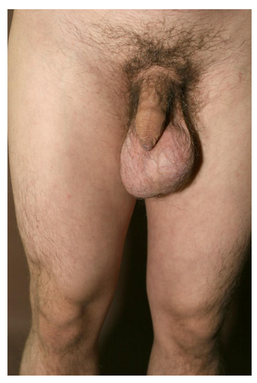


Figure 4. Appearance of testes after treatment

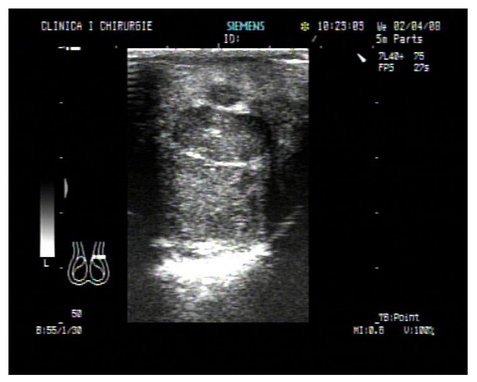


Figure 5. Ultrasound of testes after treatment

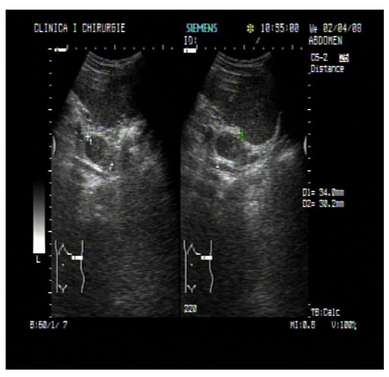


Figure 6. Ultrasound of the left SR after treatment

* All pictures are reproduced with informed consent.

Second case

- 10 years boy, diagnosed with CAH at the age of 3 weeks due to 21-hidroxylase deficiency
- received intermittent steroid supplementation over the course of his life, because of poor compliance
- long-term evolution of adrenal hyperplasia, inconsistent and incomplete therapy resulted in early onset of puberty
  - Puberty stage PIV, G IV
  - Advanced stature (+1,26 SD)
  - Advanced bone age (~ 14 years)
- At the age of 8, the scrotal ultrasound revealed increased size of testes, rich blood supply, with bilateral TRATs (Figure 7)
  - RT: 46/31/26 mm, LT: 51/31/27 mm

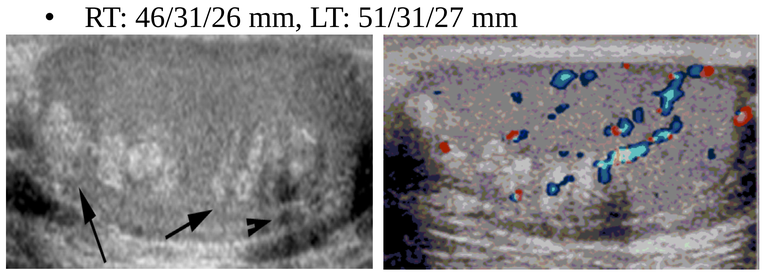


Figure 7. Ultrasound of the left testis showed multiple hyperechoic nodular lesions (arrows) in the mediastinum of the testes

- Given the elevated gonadotropins, advanced bone age and stature, the therapy with GnRH analogues was introduced, with improved evolution.

Parameters	Normal	First case	Second case
FSH (mUI/ml)	2,5-11	**0,1 ↓**	**1.3 ↓**
LH (mUI/ml)	1,2-8,6	**0,3 ↓**	**0,6↓**
TESTOSTERON (ng/ml)	3-10	**16,6 ↑**	**28,5↑**
ESTRADIOL (pg/ml)	< 60	**225 ↑**	**255,9↑**
ACTH (pg/ml)	< 46	**77,8 ↑**	
CORTISOL (ng/ml) - AM - PM	 60-230 30-150	 **440,7 ↑ (?)** **91,7 N**	 **50↓** **35 N**
17OH PROGESTERON (ng/ml)	0,2-2,3	**25,6 ↑**	**11.3↑**
DHEA-S (µg/ml)	0,9-1,8	**7,7 ↑**	**6.5↑**
TEST DEXAMETASONE 1 mg - Cortisol - Testostérone - 17OHProgesterone		 **33,4 (+)** **3,5 (+)** **17,4 (±)**	-
AFP (mUI/ml)	0-8,5	**0,8 N**	**1.2 N**
β HCG (mUI/ml)	0-0,4	**negative**	**negative**

Conclusions and Discussions

- TART is by far the most likely diagnosis in the presence of testicular nodules in the fallowing cases:
  - patient with congenital adrenal hyperplasia
  - bilateral involvement
  - Ultrasound aspect (hilarious location, preserved vascular architecture)
  - anomalies diminishes under well-balanced substitution treatment (5)
- TART is the most important cause of infertility in adult male patients with CAH, representing a diagnostic challenge (1)
- The reported prevalence by sonography varies between 24% and 94% (3)

TART

- Careful microscopic examination suggests that adrenal rests are present in all male patients with CAH (1)
- Untreated nodules of adrenal rests may expand and destroy the testicular parenchyma, resulting in infertility (2)
- The presence of TARTs in these 2 patients is significant, suggestive of suboptimal hormone replacement therapy.
- A future system of regular follow-up and standards in therapeutic concepts is needed to guarantee an improved fertility and good quality of life in male patients with CAH.

References: 1. Jeffrey Dee Olpin, Benjamin Witt. Testicular Adrenal Rest Tumors in a Patient with Congenital Adrenal Hyperplasia. J Radiol Case Rep. 2014 Feb; 8(2): 46–52. 2. Claahsen-van der Grinten HL, Hermus AR, Otten BJ. Testicular adrenal rest tumours in congenital adrenal hyperplasia. International journal of pediatric endocrinology. 2009;2009:624823. 3. Auchus RJ. Management of the adult with congenital adrenal hyperplasia. International journal of pediatric endocrinology. 2010;2010:614107. 4)Rutgers JL et al . Am J Surg Pathol, 1988; 12:503; 5. Claahsen-van der Grinten HL et al, JCEM 2007; 92(2):612

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Adrenal

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