Increasing testicular size due to bilateral Large Cell Calcifying Sertoli Cell tumours (LCCSTs) in a peri-pubertal child with Carney Complex.

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Case Report:

Background: 11 year old boy. Diagnosis: Carney Complex; Heterozygous for a known nonsense mutation of the PPKAR1A gene (p.R42)

Presentation: Referred for Endocrine follow-up. Short stature; height 131.6. SDS -1.64; height velocity 5.63 SDS + 0.86

Pubertal Assessment: Testicular volume increased in 6 months from 4 to 8 cc and appeared bulky. No axillary or pubic hair.

Investigations: Testicular Ultrasound, Testosterone, DHEAS. Testicular biopsy. Bone age.

Results: Biochemistry was consistent with a pre pubertal status. Bone age equivalent to chronological age.

Testicular ultrasound showed bilateral multiple small echogenic foci not typical for microlithiasis irregularly spread throughout testes (FIG 1)

Testicular Biopsy : Consistent with Large cell calcifying sertoli cell tumour. Also showed pubertal spermatogenesis (FIG 2)

Management: Conservative with close clinical and radiological follow up.

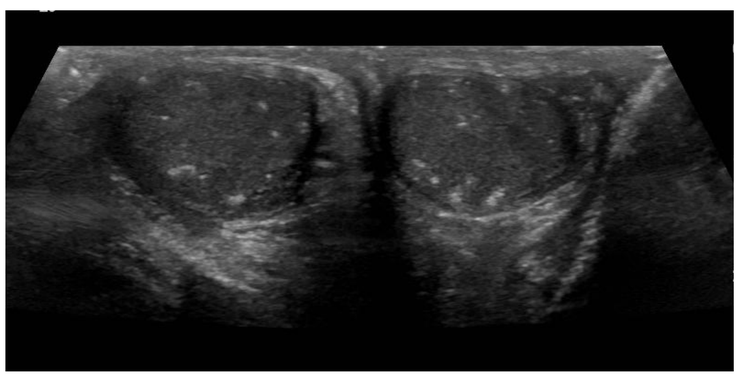

Figure 1. Testicular Ultrasound. Transverse view of both testes; showing multiple irregular echogenic foci throughout the testes bilaterally consistent with coarsened calcified lesions, most consistent with multiple large cell calcifying Sertoli cell tumours.

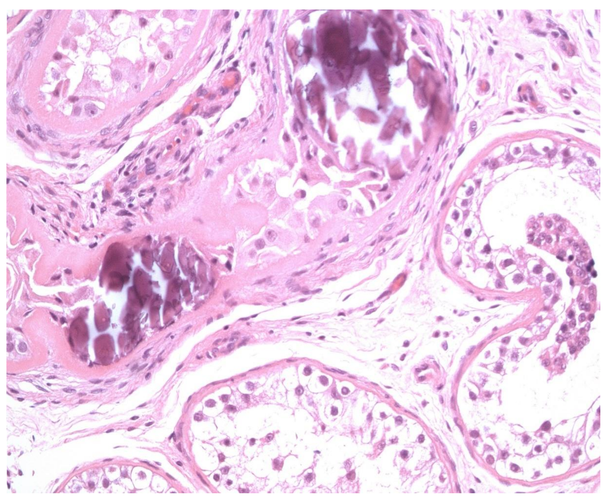

Figure 2. Testicular biopsy showing polygonal cells with central calcification. The cells have abundant eosinophilic and finely granular cytoplasm.

Diagnostic criteria of Carney complex [a] [1.]

1. Spotty skin pigmentation with a typical distribution (lips, conjunctiva and inner or outer canthi, vaginal and penile mucosa)
2. Myxoma (cutaneous and mucosal) [b]
3. Cardiac myxoma [b]
4. Breast myxomatosis [b] *or fat-suppressed magnetic resonance imaging findings suggestive of this diagnosisc*
5. PPNAD*b or paradoxical positive response of urinary glucocorticosteroids to dexamethasone administration during Liddle's test*
6. Acromegaly due to GH-producing adenoma [b]
7. LCCSCT*b or characteristic calcification on testicular ultrasonography*
8.Thyroid carcinoma*b or multiple, hypoechoic nodules on thyroid ultrasonography, in a young patient*
9. Psammomatous melanotic schwannoma [b]
10. Blue nevus, epithelioid blue nevus (multiple)[b]
11. Breast ductal adenoma (multiple)[b]
12. Osteochondromyxoma [b]

Supplemental criteria:
1. Affected first-degree relative
2. Inactivating mutation of the *PRKAR1A gene*

a ***To make a diagnosis of CNC, a patient must either: 1) exhibit two of the manifestations of the disease listed, or 2) exhibit***
one of these manifestations and meet one of the supplemental criteria (an affected first-degree relative or an inactivating mutation of the PRKAR1A gene).
b With histologic confirmation.

Discussion:

- Carney Complex (CNC) is a rare multi endocrine neoplasia syndrome associated with endocrine and non-endocrine tumours. [1]
- Three types of testicular tumour have been described; Large cell calcifying Sertoli Tumours (LCCST), Leydig cell tumours and testicular tumours of adrenal origin.
- LCCST is a rare benign stromal tumour. That had been observed in 33-41% of males affected with Carney Complex, usually appearing in the first decade of life.
- It can be hormonally active, presenting with gynaecomastia or gonadotropin-independent precocious puberty. [2,3]
- It is generally benign although malignant transformation has been described.
- In pre-pubertal patients conservative management is preferred, with anti sex steroid therapy as needed, to manage secondary sexual characteristics. [3]
- LCCST can cause replacement obstruction of seminiferous tubules leading to reduce fertility. CNC patients have morphologically reduced sperm and abnormal sperm number. [4]
- Testicular sparing surgery is often not suitable due to the multifocal nature of the tumour.

Conclusion:

Assessment of boys with CNC in the peri-pubertal age group can be complex. The clinical evaluation of growth and puberty must be balanced with known complications of this multi-system condition, with a high index of suspicion for the associated endocrine features. This case illustrates the challenges in monitoring pubertal progress and growth in adolescent boys with this condition.

References:

1. Constantine A. Stratakis , Lawrence S. Kirshner and J.Aidan Carney Clinical and Molecular Features of the Carney Complex: Diagnostic Criteria and Recommendations for Patient Evaluation The Journal of Clinical Endocrinology & Metabolism 86(9):4041–4046.
2. Esperanza Berensztein, Alicia Belgorosky, Maria T.G. de Ddvila, and Marco A. Rivarola Testicular steroid biosynthesis in a boy with a large cell calcifying Sertoli cell tumor producing prepubertal gynecomastia; Steroids 1995 60 Feb.
3. B. Brown, A. Ram, P. Clayton, G. Humphrey Conservative management of bilateral Sertoli cell tumors of the testicle in association with the Carney complex a case report. Journal of Pediatric Surgery (2007) 42, E13–E15.
4. P. Wieacker, C. A. Stratakis, A. Horvath, S. Klose, I. Nickel & P. Muschke. Male infertility as a component of Carney complex. Andrologia 39, 196–197.