Gynecomastia with precocious onset in Peutz-Jeghers Syndrome: Managing the aromatase overexpression

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INTRODUCTION

- ***Peutz-Jeghers Syndrome (PJS)*** is a rare autosomal dominant disorder caused by mutation in ***LKB1/STK11 gene,*** mainly characterized by multiple hamartomatous polyps in the gastrointestinal tract.
- The mutation in ***LKB1/STK11 gene*** promotes ***aromatase (CYP19A1) overexpression in neoplastic Sertoli-cells***, leading to ***gynecomastia*** and ***Large-Cell Calcyfing Sertoli-Cell Tumor (LCCSCT)***.
- We describe the case of a boy with prepubertal gynecomastia associated with bilateral testicular tumour.

CASE REPORT

Father - ***PJS*** confirmed by molecular diagnosis.

Without any other relevant familiar/personal history

- ***Referred to Paediatric Endocrinology clinics*** **due to:**

Breast enlargement since the age of 2 and a **marked height velocity (HV).**

- ***Physical Examination:***

Hyperpigmented lesions of the lower-lip

Gynecomastia (female Tanner-B4)

Absent pubic/axillary hair, infantile penis and testicular volume of 4mL.

Height 110.5cm (+1.9SDS) and HV was 8.6 cm/year (+2.6SDS).

Laboratory evaluation:

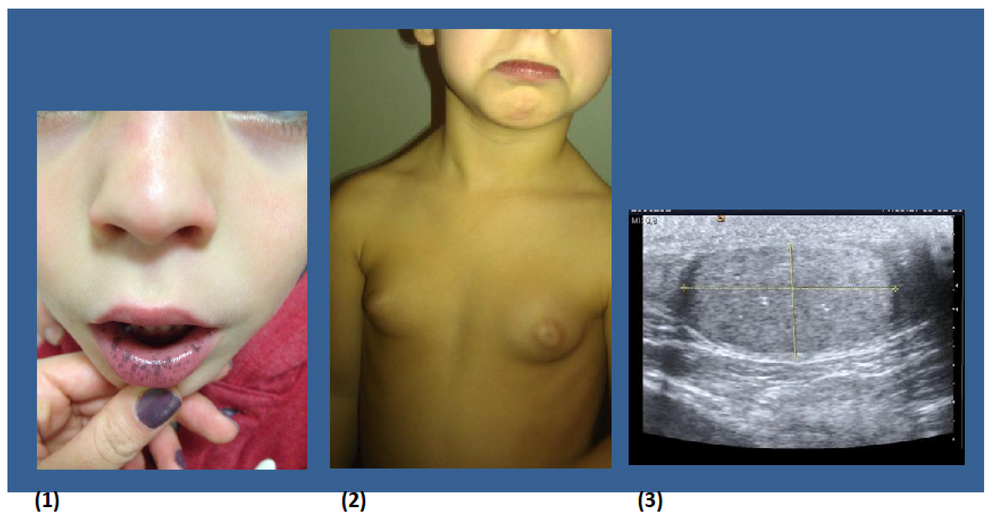
FSH	<0.20mUI/mL
LH	<0.20mUI/mL
Total testosterone	<3.00ng/dL
Estradiol	<20.0pg/mL
Prolactin	5.4ng/mL
Androstenedione	<0.30ng/mL
Inhibin-A	**4.6pg/mL (0.9-1.7)**
LHRH test	Prepubertal response

- ***Radiology exams:***

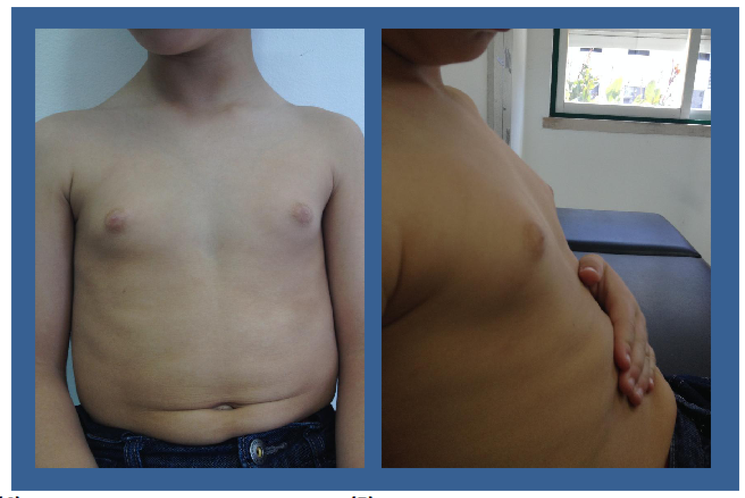
Bone age coincident with chronological age .

Testicular US: Bilateral testes measuring ≈22x10mm and multifocal microcalcifications.

Abdominal MRI excluded adrenal tumours.



Anastrozole 1mg/day



Legends: (1), Mucocutaneous hyperpigmented macules on the vermillion border of the lips, typical of PJS; (2), Gynecomastia (female Tanner B4); (3), Testes ultrasound evidencing microcalcifications; (4) and (5), Reduction of gynecomastia into a Tanner B3 after 1 year of anastrozole.

One year later:

Less tense Tanner-B3
HV of 5.7 cm/year (-0.7SDS)
Serum inhibin-A <0.4 pg/mL
Testicular US: similar to previous

DISCUSSION

- Some authors have described ***Inhibin-A as a marker of Sertoli cell testicular tumors (and in particular LCCSCT) in prepubertal boys.***
- Even though estradiol (E2) levels are undetectable, they can still be sufficient to stimulate breast tissue and growth plates probably due to:
  - > ↑ Tissular sensitivity to E2;
  - > ↑ Bioavailability of E2;
  - > Local convertion to E2.
- Malignancy is found in ≈17% of patients with LCCSCT but *is rare* in young patients with bilateral tumors or in association with a genetic syndrome.
- ***Aromatase inhibitors*** are currently the best option to achieve provide a reduction of the effects of increased estrogens on the breast and growth plates. We used ***Anastrozole***, an effective third generation inhibitor of estrogen synthesis.
- ***In this patient, the aromatase inhibitor has promoted reduction of breast volume, HV and serum inhibin-A, without any significant adverse effects.***

References:
Wit JM et al. Aromatase inhibitors in pediatrics Nat. Rev. Endocrinol 8:135–147 2012.
Gourgari M et al. Large-cell calcifying Sertoli cell tumors of the testes in pediatrics. Curr Opin Pediatr 24(4): 518–522 2012.
Crocker M et al. Use of Aromatase Inhibitors in Large Cell Calcifying Sertoli Cell Tumors: Effects on Gynecomastia, Growth Velocity, and Bone Age. J Clin Endocrinol Metab 99: E2673–E2680, 2014.
Lefevre H et al.Prepubertal gynecomastia in Peutz-Jeghers syndrome: incomplete penetrance in a familial case and management with an aromatase inhibitor. Eur J Endocrinol 154: 221–227 2006.

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