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

Joana Simões Pereira,1) Filipa Marques2), Catarina Limbert1), Lurdes Lopes1)
1)Endocrinology Department, Instituto Português de Oncologia de Lisboa, Francisco Gentil, EPE; 2)Department of Paediatric Endocrinology, Hospital Dona Estefânia, Centro Hospitalar Lisboa Central EPE.

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 Calcifying 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).

Anastrozole 1mg/day

Legends: (1), (2), (3), (4), (5)

Laboratory evaluation:
- FSH <0.20mIU/mL
- LH <0.20mIU/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.

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 conversion 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: