MANAGEMENT OF PREPUBERTAL GYNECOMASTIA IN TWO PATIENTS WITH PEUTZ-JEGHERS SYNDROME: USE OF AROMATASE INHIBITORS

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Background. Peutz-Jeghers Syndrome (PJS) is a rare autosomal-dominant disorder caused by a germline mutation in the serine-threonine-kinase-11(STK11) gene on chromosome 19p13.3 and characterized by hamartomatous polyps throughout the gastrointestinal tract, mucocutaneous hyperpigmentation and predisposition to several malignancies. Not infrequently, PJS may be associated to an estrogen producing large cell calcifying Sertoli cell tumor that may result in gynecomastia, advance skeletal maturation and increased growth velocity. In recent years a conservative medical treatment with aromatase inhibithors was tested as an alternative to orchidectomy.

Objective. We present data of treatment with an aromatase inhibitor in two prepubertal boys presenting with gynecomastia and testicular calcifications associated with STK11 gene deletion.

Patients. Patient 1 (9 years old) and **patient 2** (6 years old) came to our observation for **bilateral gynecomastia**. Physical examination showed **signs of precocious puberty** and **pigmented lesions of the lips** in both patients. **Clinical features** of the patients are reported in **Table 1.** In both patients plasma levels of LH, FSH, 17β-estradiol, testosterone, DHEAS, a-fetoprotein and β-HCG were normal while estrone, anti-mullerian hormone and inhibin-B were elevated. Testicular ultrasound revealed a **benign bilateral multifocal microcalcification pattern**. **Genetic analysis** showed a 1.1 Mb deletion of 19p13.3 incorporating the STK11 gene in P1 who presented atypical clinical features (seizures and learning difficulties) and a deletion of STK11 gene in P2. Both patients started treatment with **anastrozole**:1 mg/daily.

	Age (year)	Pubertal stage (Tanner)	Growth velocity (cm/year)	Bone age (year)
Patient 1	9.0	PH2 Testicular volume: 7.0 mL No penis enlargement	7.5 (> 2.0 DS)	9.0
Patient 2	6.0	PH1 Testicular volume: 4.0 mL No penis enlargement	7.0 (> 1.0 DS)	6.0

Table 1- Clinical features of the patients

Results. We observed a **reduction of growth velocity and gynecomastia** 1 year after treatment initiation in patient 1 and 6 months after treatment initiation in patient 2. Furthermore, **estrone and anti-mullerian-hormone levels decreased** in both patients, while inhibin B levels remain unchanged. No side effects were described (Table 2)

	Pre-treatment					Post -treatment				
	Growth Velocity (cm/y)	Mammary gland diameter (cm)	Estrone (pmol/L) (vn: 42-127)	AMH (ng/mL) (84-141)	Inhibin B (pg/ml) (25-325)	Growth Velocity (cm/y)	Mammary gland diameter (cm)	Estrone (pmol/L) (vn: 42-127)	AMH (ng/mL) (vn 84-141)	Inhibin B (pg/ml) (25-325)
Patient 1 (1 year treatment)	7.5	8.0	250	> 400	332.3	5.7	4.0	31	120	350
Patient 2 (6 months treatment)	7.0	6.0	150	350	300	4.8	4.0	100	190	290

Table 2- Clinical and hormonal data pre and post treatment

Conclusions. Our data confirm that aromatase inhibitors are efficient in treating gynecomastia in PJS prepubertal male patients by controlling estrogen excess and may therefore represent a viable alternative to orchidectomy before the sexual maturation.

References.
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Gonads
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