

The effect of aromatase inhibitor in a pubertal patient with aromatase excess syndrome



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Background

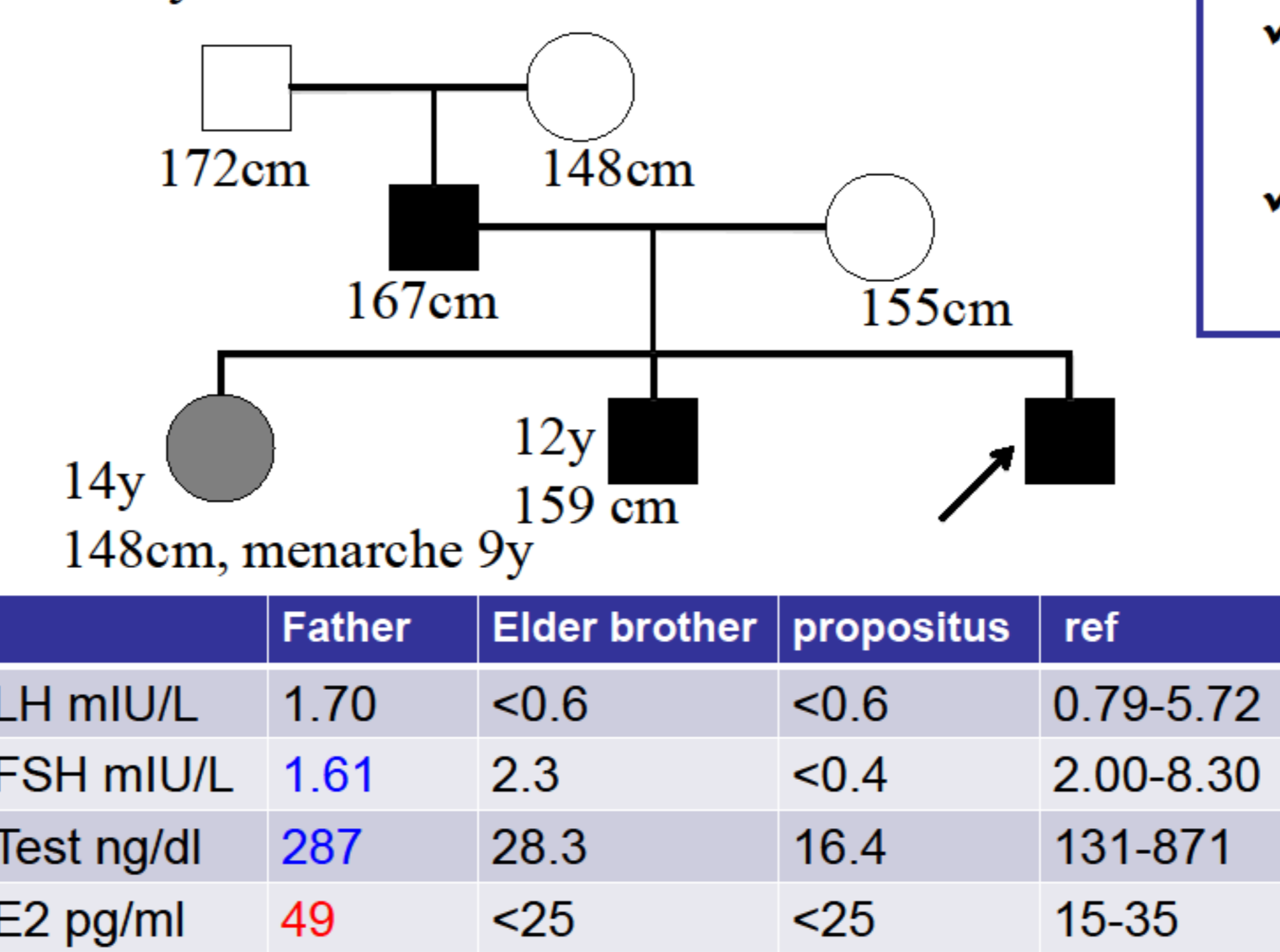
Aromatase excess syndrome (AEXS) is a rare autosomal dominant disorder caused by overexpression of CYP19A1 at 15q21. Patients with AEXS manifest various clinical features associated with estrogen excess; gynecomastia, hypogonadotropic hypogonadism, and advanced bone age are the most salient features in this condition. The primordial treatment of the gynecomastia of the patients with AEXS is surgical mastectomy, however the long-term treatment of aromatase inhibitor for hypogonadotropic hypogonadism and short stature due to advanced bone age was not established in children. We evaluated the effect of aromatase inhibitor for 2 years in a pubertal patient with AEXS.

Case presentation

The propositus was 10-year-old boy. He presented with gynecomastia since 9 years old. The patient's father and elder brother had also exhibited gynecomastia, and undergone mastectomies due to psychological distress. He was consulted for further examinations as familial gynecomastia.

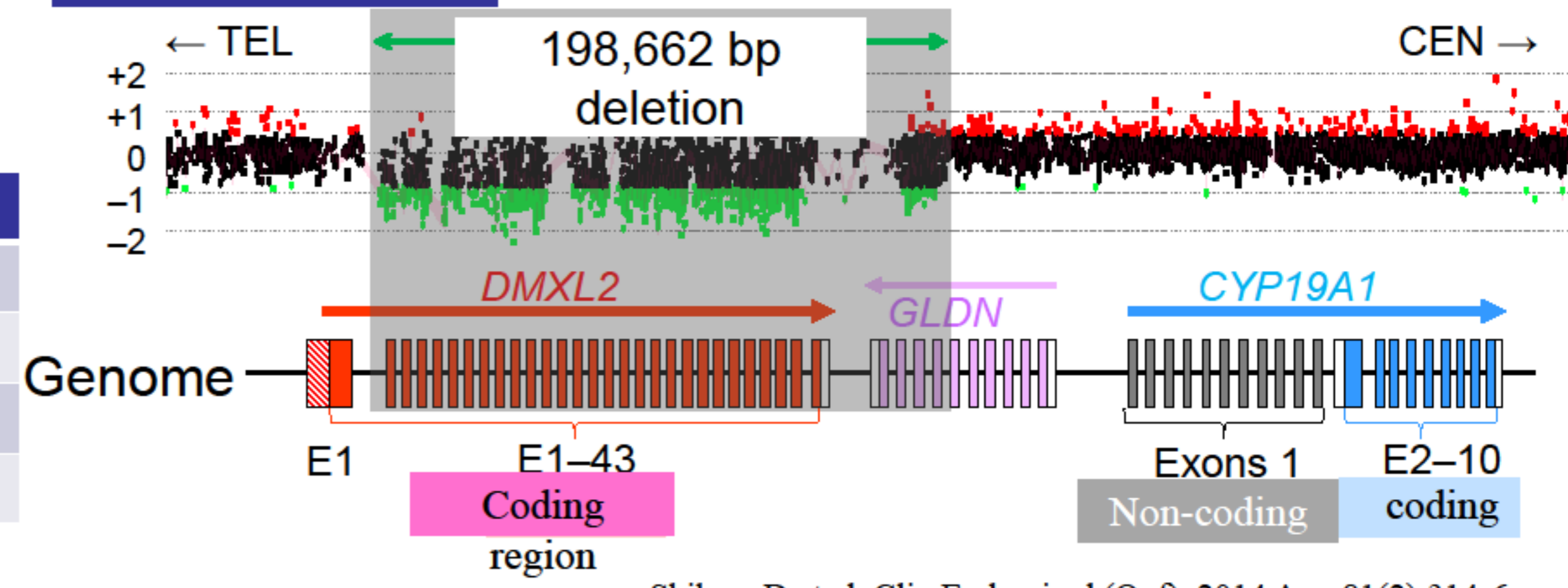
Physical exam: Body height (BH); 145.8 cm (1.34 SD), Body weight (BW); 34.8 kg, %tile BMI; 39.1, Tanner stage: Breast; 4, Pubic hair; 1, Penis; 1, No genital anomaly, bilateral testes; 2-3 ml Bone age; 13y9M, his predicted final height according to the Growth-Potential method was around 151 cm (-3.4 SD).

Family tree



- ✓ The gynecomastia which is not correspond to sexual development
- ✓ Intra-familial accumulation of the gynecomastia (Autosomal dominant)
- ✓ E2 ↑ and FSH ↓ on his father's examination
 - Aromatase excess syndrome suspect.

Microarray CGH



➢ Aromatase excess syndrome due to microdeletion of upstream of CYP19A1.

Methods

Because of his predicted final height, the patient was treated with an aromatase inhibitor (1 mg/day of anastrozole). We have carried out the following examination on 1, 3, 6, 12 and 24 months after anastrozole treatment.

- BH, BW, Blood pressure, Tanner staging, Body composition
- Serum LH, FSH, estradiol (E2), testosterone, AST, ALT, T-chol, HDL-C, LDL-C, Ca, P, 25-OHD, intact PTH levels
- Bone mineral density at L2-L4 by DEXA, Bone age (BA), Spine X-ray

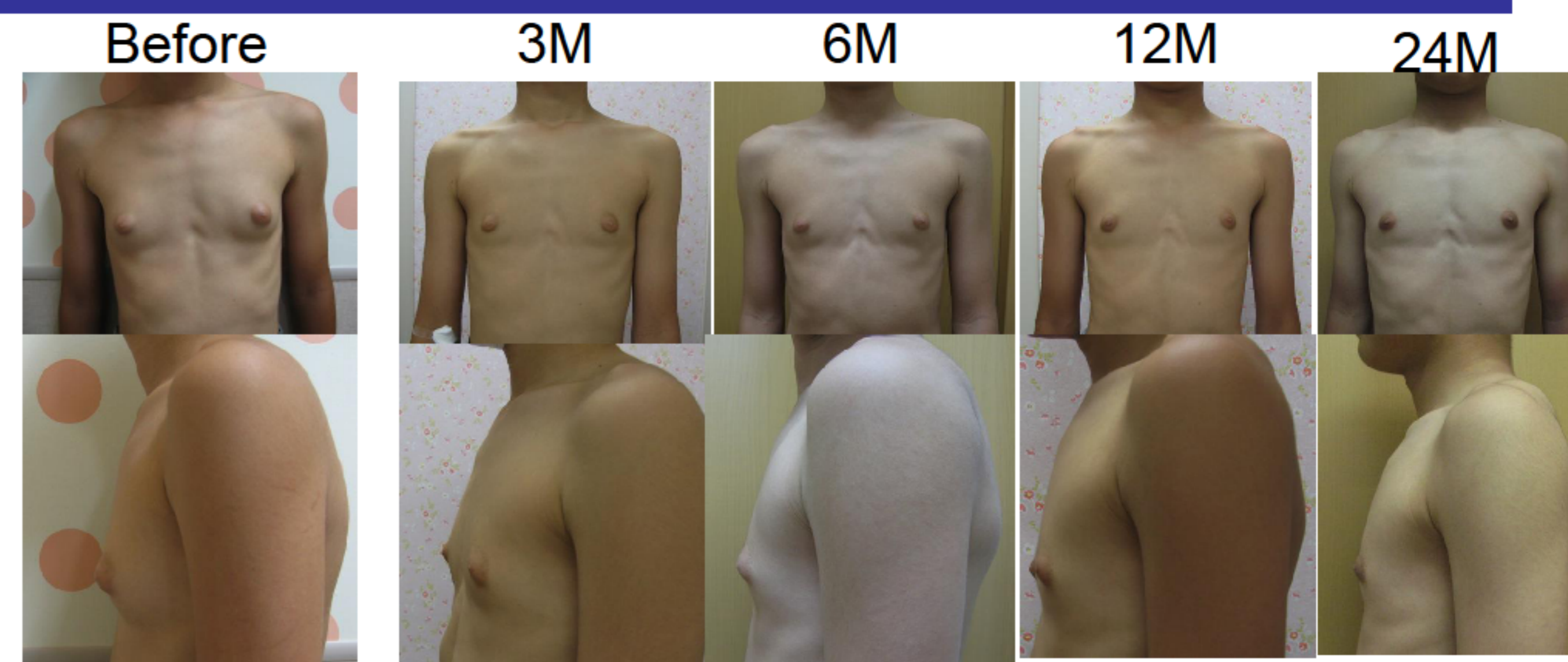
Evaluation:

- Gynecomastia: Change of Tanner staging
- Bone age: BH SDS for BA, Predicted final height according to the Growth-Potential methods
- Hypogonadism: Change of serum LH, FSH and testosterone levels, Change of the muscle mass, fat mass and body fat percentage.
- Adverse events

This research obtained the approval of the Niigata University School of Medicine Ethical Review Board.

There were no significant adverse events of anastrozole.

RESULTS



	Before	1 M	3 M	6 M	12 M	24 M
Chronological age	10y9m	10y10m	11y	11y3m	11y9m	12y9m
BH cm (SD)	148.8 (+1.3)	150.6 (+1.4)	151.4 (+1.4)	152.2 (+1.3)	156.4 (+1.3)	162.0 (+0.9)
BW kg	37.3	38.5	40.3	42.3	45.4	52.4
%BMI	43.4		53.4	61.2	59.5	68.6
Tanner stage; Breast	4	3	3	2	2	2
BA	13.9			13.9	14.2	15.8
BH SDS for BA	-1.8			-1.3	-1.1	-1.2
Predicted final height	152.2			155.6	160.2	164.5*
Size of testes (ml)	4	6	8	10	12	15
BMD (L2-L4) g/cm ² (SD)	0.73 (+0.6)					0.93 (+2.3)
body fat percentage (%)	16.3		14.1	14.4	13.4	13.3
Fat mass (kg)	6.1		5.5	5.7	6.0	6.8
Muscle mass (kg)	29.3		31.7	32.7	36.4	41.9
Testosterone ng/dL	19.5	389.6	167	436.3	197.5	728.3
LH mIU/mL	<0.6	2.9	2.9	2.9	1.2	2.2
FSH mIU/mL	1.9	2.8	3.2	3.6	2.8	2.6
E2 pg/mL	<25	<25	<25	<25	<25	27
Anastrozole (mg/day)	0	1.0	0.5	0.5	0.5	0.5

CONCLUSIONS

2 years of anastrozole treatment for pubertal AEXS patient with a poor predicted final height was safe and effective for the improvement of gynecomastia and predicted final height.

References

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