Partial androgen insensitivity syndrome: An infrequent cause of pubertal gynecomastia

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Sir,

Gynecomastia refers to an enlargement of the breast tissue in males, caused by the proliferation of glandular breast tissue [1]. Pubertal gynecomastia is a common condition seen in around 60% of adolescent boys and in most cases, it resolves spontaneously over 1–2 years [1]. Persistent pubertal gynecomastia is less frequent and can be associated with underlying pathological conditions. We report a case of persistent pubertal gynecomastia with micropenis and bifid scrotum due to partial androgen insensitivity syndrome (PAIS).

A 16 year 4 month old male presented to the endocrinology clinic with bilateral breast enlargement for 2 years, without bleeding or nipple discharge (Fig. 1a). The patient denied consumption of any medications causing gynecomastia. There was no history of gynecomastia in family members. On physical examination, height was 161 cm, weight was 58.1 kg with a body mass index (BMI) of 22.4 kg/m^2, and blood pressure was 110/70 mm Hg. General examination revealed a lack of facial hair, sparse axillary hair, and very little body hair. Sexual maturity ratings (SMRs) revealed bilateral breast tanner stage 3, pubic hair Tanner stage 3, the testicular volume 12 cc, a micropenis [stretched penile length 3.5 cm (<−2.5 sd)], and a bifid scrotum (Fig. 1b). Hormone profile of the patient was as follows: T3–122 (82–179 ng/dl), T4–8.0 (5.2–12.5 ug/dl), thyroid-stimulating hormone (TSH)–2.11 (0.4–4 µIU/ml), Testosterone > 1500 (241–827 ng/dl), Estradiol-21.72 (11.6–41.2 pg/ml), luteinizing hormone (LH)-31.1 (1.1–9.3 mIU/ml), and follicle-stimulating hormone (FSH)-22.65 (2.8–11.3 mIU/ml). Renal [Creatinine-0.7 (0.7–1.4 mg/dl)] and liver function tests were within normal limits. The urine beta-human chorionic gonadotropin (HCG) test was negative. Physical examination and blood tests ruled out systemic diseases such as hyperthyroidism, liver dysfunction, renal insufficiency, and tumors secreting human chorionic gonadotropin. PAIS was suspected on account of elevated total testosterone level, raised LH level, and raised estradiol level along with the lack of adequate virilization.

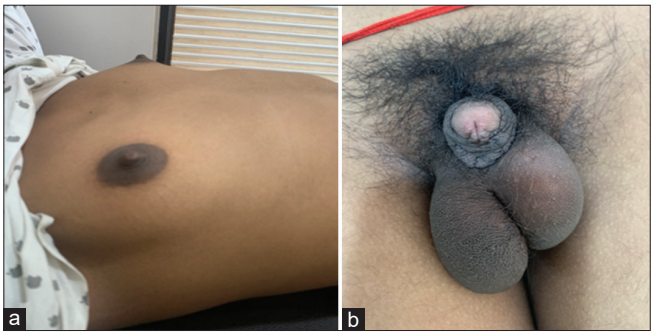

Figure 1: (a) Gynecomastia lateral view (b) external genitalia and bifid scrotum with micropenis

Further genetic testing revealed a hemizygous missense variation in exon 7 of the *AR* gene (chrX: g.67722898C>T) that results in amino acid substitution of Cysteine for Arginine at codon 841 (p.Arg841Cys). This variation has previously been reported in a patient affected with androgen insensitivity syndrome and has been classified as pathogenic by the ClinVar database [2,3]. The *in silico* predictions of the above variant are probably damaged by PolyPhen-2 (HumDiv) and Sorting intolerant from tolerant (SIFT), Likelihood Ratio Test (LRT), and Mutation Taster 2. PAIS patients generally have normal FSH levels. The elevated FSH level, in this case, may be due to the recent use of tamoxifen by the patient [4]. Surgery for breast reduction is recommended for esthetic reasons in PAIS. Hence, the patient was referred to the surgery department for a bilateral mastectomy. Priya Vaidyanathan *et al*. reported a case of persistent pubertal gynecomastia due to PAIS with a novel mutation in the androgen receptor (AR) gene [5]. Lee *et al*. described a similar case of PAIS presenting with gynecomastia in a 16-year-old male who avoided outdoor and social activities subsequently requiring mammoplasty [6].

We conclude that a careful diagnostic evaluation should be pursued in patients with persistent pubertal gynecomastia with varying degrees of under virilization. High testosterone along with elevated LH and E2 levels in a patient with persistent pubertal gynecomastia is suggestive of PAIS.

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CONSENT

Written informed consent was taken from the patient for the publication of this report.

REFERENCES

1. Carlson HE. Approach to the patient with gynecomastia. J Clin Endocrinol Metab 2011;96:15-21.
2. Gottlieb B, Beitel LK, Nadarajah A, Paliouras M, Trifiro M. The androgen receptor gene mutations database: 2012 update. Hum Mutat 2012;33:887-94.
3. The Clin Var Variation Report. National Library of Medicine. Available from: https://www.ncbi.nlm.nih.gov/clinvar/variation/9830/?new_evidence=false [Last accessed on 2022 June 23].
4. Vermeulen A, Comhaire F. Hormonal effects of an antiestrogen, tamoxifen, in normal and oligospermic men. Fertil and Steril 1978;29:320-7.
5. Vaidyanathan P, Kaplowitz P. Partial androgen insensitivity syndrome presenting as pubertal gynecomastia: Clinical and hormonal findings and a novel mutation in the androgen receptor gene. Endocrinol Diabetes Metab Case Rep 2018;2018:18-0128.
6. Lee SW, Kwak DS, Jung IS, Kwak JH, Park JH, Hong SM, *et al*. Partial androgen insensitivity syndrome presenting with gynecomastia. Endocrinol Metab 2015;30:226-30.

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