

Exaggerated Thelarche: An Unusal Variant of Premature Thelarche

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A girl of a 6 years old was reported by her parents with the complaints of gradual enlargement of breasts from her 3 years of age, but no vaginal bleeding, or growth of axillary or pubic hair. Her mother did not use any hormonal products during her pregnancy period. There is no history of early pubertal development, sexual ambiguity or neonatal death in the family. On examination revealed height -122 cm (>75th centile), weight -19 kg (<25th centile), BMI-12.7 kg/M² (<5th centile), breasts in Tanner stage -III, axillary and pubic hair not grown, and genitalia normal. Ultrasound showed prepubertal uterus. Hormone assays showed serum estradiol in lower pubertal level (32 pg/ml), serum LH in prepubertal level (0.11 mIU/ml), and serum FSH in lower pubertal level (4.48 mIU/ml). But X-rays showed bone age advanced (corresponds to 9 years). So this taller girl with isolated breast development with FSH predominant mild estrogen secretion and advanced bone age was diagnosed as a case of exaggerated thelarche, which is a rare variant of premature thelarche. The parents were assured that it is a self limited benign disorder. On follow up after 3 months, serum estradiol, FSH and LH all mildly increased, but LH still in borderline pubertal. So the patient is progressing towards normal puberty. The patient needs regular follow up to see if rapid progression to puberty develops leading to central precocious puberty which is a rare possibility.

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Introduction

Isolated breast enlargement without other signs of sexual maturation is termed as premature thelarche^{1,2}. The breast enlargement usually regresses after a few months,^{3,4} but occasionally persists for years or lasts until the onset of normal puberty¹.

The disorder usually occurs by age 2 (in over 80%) and rarely after age 4.^{3,4} In a retrospective study in Minnesota, the incidence of premature thelarche was 21.2 per 100,000 patient-years, 60% of cases were noted between 6 months and 2 years of age, and most regressed in 6 months to 6 years after diagnosis, although a few persisted until puberty. When 10- to 35-year follow-up was available, no untoward effects on later health, growth, or fertility were evident.⁵

Garibaldi described a variant of premature thelarche and coined the term exaggerated thelarche for this disorder. Exaggerated thelarche is defined as early breast development to Tanner stage-III or greater with mildly accelerated skeletal maturation and/or increased growth velocity but no adrenarchal hair development or biochemical sign of precocious puberty.⁶

Although few cases are reported, we don't know its prevalence. We are reporting a girl who presented with thelarche with advanced bone age, but no other features of the true precocious puberty. As a rare disorder, we want to report this unusual case for academic interest.

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Case Report

A 6 years old girl, was brought to Endocrine OPD of Dhaka Medical College by her parents with the complaints of gradual enlargement of breasts from her 3 years of age. At first it appeared as a small mound. Then it gradually increased in size, with remarkable enlargement for the last 1½ years. Parents gave no history of vaginal bleeding, growth of axillary or pubic hair, convulsion, headache, visual disturbance, constipation, cold intolerance, polyuria or polydipsia. The child was born in a hospital by NVD without any perinatal abnormality or injuries. Her mother is diabetic for the last 3 years, but she was not aware whether she was diabetic at her pregnancy. Her mother did not suffer from any significant maternal sickness or used any hormonal products during her pregnancy period. There is no history of early pubertal development, sexual ambiguity or neonatal death in the family.

Clinical examination revealed an active girl with normal vital signs, height -122 cm (>75th centile by NCSHS growth chart), weight -19 kg (<25th centile), BMI-12.7 kg/M² (<5th centile), breasts in Tanner stage-III (Fig.1), axillary and pubic hair not grown, and genitalia (clitoris, labia minora and vagina) normal. There was no skin patch or bony deformity. Systemic examination including fundoscopy was normal.

Investigations revealed complete blood count-normal, serum creatinine-54 µmol/l, SGPT-36 IU/l and blood glucose (fasting)-5.1 mmol/l. In ultrasound examination, uterus measured 3.6x1.5 x0.6 cm³ with a volume of about 1.69 ml (prepubertal), and tubo-ovarian area was normal with a small ovary (prepubertal). Hormone assays showed serum FSH - 4.48 mIU/ml (lower pubertal), serum LH -0.11 mIU/ml (prepubertal) and serum estradiol-32 pg/ml (lower pubertal). Other relevant hormones were S TSH - 2.3 µIU/ml (0.5-4.7),

S FT4 - 1.17 ng/dl (0.7-1.9), 17 OH Progesterone - 0.47 ng/ml (0.2-0.5) and S prolactin - 7.28 ng/ml (1.4-24.2), all were in the normal range. X-rays to determine bone age- showed bone age corresponds to 9 years (advanced). On follow up after 3 month, serum FSH, LH and estradiol were repeated and found serum FSH raised to 8.22 mIU/ml (in pubertal range but increased), serum LH to 0.43 mIU/ml (increased to borderline pubertal range) and serum estradiol-47.9 pg/ml (raised but in lower pubertal range)



Figure1. Bilateral Tanner Stage-III breast development

Discussion

Sexual precocity may be considered as the appearance of any sign of secondary sexual maturation below 7 years for Caucasian girls, and 6 years for African-American girls.¹ But there is no data for the Asians, especially for

Bangladeshi population. In our patient, breast enlargement started at 3 years of age.

In premature thelarche breast development typically occurs below 3 years of age. Plasma estradiol levels are slightly higher for age in premature thelarche.⁷ The concentration of serum FSH may be in the pubertal range.^{3,8-11} But serum LH concentration is prepubertal.¹¹ Uterus is rarely enlarged on ultrasonogram.² In our patient only breasts are enlarged, but axillary and pubic hair not grown, genitalia normal, menstruation not started, no history of use of exogenous estrogen, serum FSH in lower pubertal level, S LH in prepubertal range, S Estradiol in lower pubertal level and uterus is prepubertal on ultrasonogram. Growth in stature is normal in premature thelarche.^{3,12-15} Skeletal maturation is also normal in premature thelarche.¹¹ But in our patient bone age is advanced and the patient is relatively taller with height >75th centile. So our patient of isolated breast development with FSH predominant mild estrogen secretion and advanced bone age is the rare variant of premature thelarche, called exaggerated thelarche.

But it should be mentioned that bone age is also advanced (alone with premature breast development, without sexual hair development and with prepubertal serum LH) in precocious pseudopuberty due to ovarian tumor/cyst or hypothyroidism. In our patient ultrasonogram did not reveal any abnormality in the ovaries, thyroid function tests were normal, and no skin or bony abnormality was detected clinically. So causes of precocious pseudopuberty were excluded.

Follow up after 3 months showed recent marked enlargement of breasts, S LH-borderline pubertal, but increasing, S FSH – increasing in pubertal range, and S estradiol – increasing in lower pubertal range. So our

patient of exaggerated thelarche is leading towards normal puberty, but still there is a chance that it may progress to true precocious puberty. Parents were reassured regarding the benign self-limited nature of the disease. We planned to follow the patient every 3 months for assessment of growth velocity, breast development, vaginal mucosal change, sexual hair growth and sex hormone (estradiol, FSH, and LH), every 6 months for ultrasonogram to see uterus and ovary, and every 1-2 years to see bone age. If rapid progress of pubertal development or CNS symptoms appear, MRI of brain may be needed to exclude central precocious puberty.

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