

CASE REPORT

Exaggerated Thelarche - an uncommon presentation of sexual maturation

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ABSTRACT

Isolated premature thelarche commonly affects the girls between 2-6 years (90% <2years). Majority of cases are self limited and are not accompanied by advancement in height or bone age or premature menarche. Since the condition can represent the initial manifestation of a slowly progressive variant of true central precocious puberty, the differentiation of these conditions is important. We present girl who presented with a rare combination of thelarche with advanced bone and skeletal age, without any elevation of sex steroids, and had no other features of the true precocious puberty. The girl on 3½ years follow-up had normal growth pattern and no further progression in the sexual maturation. [IJEM 2007;(3&4):39-40]

Key words: Thelarche, sexual precocity, LHRH stimulation, sexual maturation.

INTRODUCTION

Isolated premature thelarche commonly affects the girls between 2-6 years (90% <2years). Majority of cases are self limited and are not accompanied by advancement in height or bone age or premature menarche(1). Since the condition can represent the initial manifestation of a slowly progressive variant of true central precocious puberty, the differentiation of these conditions is important. Stanhope and Brook encountered cases of sexual maturation whose LHRH responses were intermediate between the above two conditions(2). Subsequently Garibaldi *et al* demonstrated estrogen production in response to GnRHa challenge was increased (commensurate with tissue effects like advanced bone age, height age and firm breast consistency) as compared to isolated thelarche but was lower (50%) than the levels in true precocious puberty(3). We present girl who presented with a rare combination of thelarche with advanced bone and skeletal age, without any elevation of sex steroids, and had no other features of the true precocious puberty. The girl on 3½ years follow-up had normal growth pattern and no further progression in the sexual maturation.

Case Report

K.B. a 6 year female child, first in birth order, born of

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full term uneventful forceps assisted delivery with normal mental and motor development was brought to our clinic with complaints of precocious breast development of one year. Child also had gained a weight of 8 Kgs over a period of four months. Parents gave no history of vaginal bleeding, appearance of any pubic or axillary hair, constipation, cold intolerance, features suggestive of hypothyroidism or any drug intake. Clinical examination revealed an active child, weighing 26 Kgs (>95th percentile by ICMR growth chart), with a height of 118 cms (>95th percentile with target height of 154 cms falling in 75th percentile by ICMR growth chart 4), upper segment /lower segment ratio of 0.98, head circumference of 50 cms and an arm span of 115 cms. Breasts were Tanner stage III. Height age was advanced height (~9.5 years) and corresponding bone ages (10.6 years by TW2 method). Rest of the clinical examination was unremarkable. Investigations revealed normal blood counts, urinalysis, electrocardiography, chest roentgenography, liver and kidney functions. USG abdomen showed uterus measuring 37x11 mm with a faint endometrial lining and normal adrenal and ovarian anatomy. Contrast enhanced CT scan abdomen showed no adrenal or ovarian lesion. MRI brain especially of hypothalamus and pituitary region showed normal anatomy. Hormonal evaluation showed normal thyroid functions, estradiol, basal androgens, and gonadotrophins (Table 1a). ACTH stimulation test was not suggestive of any adrenal steroidogenesis enzyme defects (Table 1b). LHRH stimulation test using 100 µg of Triptorelin revealed a prepubertal response (Table 1c).

Table 1a: Basal hormonal profile of the patient.

Hormone	Value	Normal range (units)
FT3	4.05	2.3-4.20 µg/ml
FT4	1.16	0.89-1.80 ng/dl
TSH	2.48	0.35-5.5 µIU/ml
LH	0.50	0.10-6.0 miu/ml
FSH	4.56	0.10-6.0 miu/ml
Testosterone	0.04	0.22-0.80 ng/ml
DHEAS	63.50	14-266 µg/dl
Estradiol	10.0	10-36 pg/ml

Table 1b: 17-OHP levels after ACTH stimulation (250 µg IV).

0 minutes	0.60 ng/ml
30 minutes	4.0 ng/ml
60 minutes	4.20 ng/ml

Table 1c: LHRH stimulation test results (Triptorelin 100 µg i/v).

Time	-30+	-15+	0	+15	+30	+45	+60	+90	+120
LH	UD	UD	0.2	0.3	UD	UD	UD	UD	UD
FSH	UD	UD	UD	0.4	1.2	1.4	0.8	1.0	1.0

The girl after a follow up of one and a half year showed no evidence of clinical or biochemical advancement in secondary sexual characters and in fact the breast size decreased. In view of the advanced bone and height age but normal basal and dynamic endocrine evaluation, the thelarche was neither isolated nor part of sexual precocity (central or peripheral). Hence a diagnosis of exaggerated thelarche was entertained.

DISCUSSION

Isolated precocious thelarche commonly affects females between 2-6 years (90% <2years) and most of these are self limited. As the name implies it is not accompanied by any menarche or advancement in height or bone age(1, 6). Many a times the initial manifestation of a slowly progressive variant of true central precocious puberty resembles isolated thelarche, the differentiation of these conditions is important. Our case presented as thelarche but on clinical clues of advanced bone age and growth velocity a search for central precocious puberty was started. Contrarily basal and dynamic endocrine evaluation was not suggestive of any sexual precocity. LHRH stimulation test revealed an FSH dominant response with undetectable E2. Hypothalamo-pituitary imaging was normal and follow-up revealed a self limited breast regression with no further skeletal advancement. On LHRH testing LH predominates in cases of true sexual precocity while as FSH predominates in the isolated thelarche subjects(7). Stanhope and Brook encountered cases of sexual maturation whose LHRH

responses were intermediate between the above two conditions(1). Subsequently Garibaldi *et al* demonstrated estrogen production in response to GnRHa challenge was increased (commensurate with tissue effects like advanced bone age, height age and firm breast consistency) as compared to isolated thelarche but was lower (50%) of the levels in true puberty(2). The authors postulated that, in this subset of precocious thelarche patients the substantial estrogen secretion is predominantly FSH driven. As FSH axis is active in utero and during first few years of life the condition may be due to delayed inactivation of the axis(8). The predominance of FSH secretion over LH may account for the self limited nature of the condition, as FSH alone is unable to sustain ovarian maturation despite its known stimulatory effect on ovarian aromatase activity(9). No more cases are documented in the literature subsequently and no data about long term outcomes like height and gonadal status is known in these cases. Our case has clinical and biochemical similar to the described cases and hence it substantiates the existence of the condition and adds to the understanding that sexual maturation also follows a spectrum.

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