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Short Communication

Premature pubarche in an infant: nonclassical congenital adrenal hyperplasia or mini-puberty variant?

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Introduction

Premature pubarche (PP) is defined as the appearance of pubic hair before 8 yr of age in girls and 9 yr in boys, without other signs of puberty. The appearance of pubarche before one year of life is rare, with few reports in the literature. We present a case of PP in a 7-mo-old infant that was found to be in mini-puberty and also had non-classical congenital adrenal hyperplasia (CAH).

Case Report

A previously healthy, 7-mo-old male infant presented with a 3-mo history of pubic hair. He was a healthy, term newborn who was born to nonconsanguineous parents, and had appropriate weight and length. Physical examination revealed thick and long pubic hair on the scrotum, without hyperpigmentation or enlargement of the penis (Fig. 1a). No other signs of virilization or secondary sexual development were noted. His height (–0.08 SDS) and weight (–0.11 SDS) were normal for his age and appropriate for midparental height, with no apparent acceleration in growth rate.

Laboratory data obtained the same day showed normal dehydroepiandrosterone sulfate (DHEA-S) and androstenedione levels, as well as negative results for ß-subunit of human chorionic gonadotropin (ßhCG), alpha-fetoprotein (AFP), and carcinoembryonic antigen (CEA). Basal plasma LH concentration was 1.5 mIU/ml (Reference value [RV]: 0.02–0.3 mIU/ml), testosterone was 25.2 ng/dl (RV: < 2.5 ng/dl), and 17-OH-progesterone was 2.48 ng/ml (RV: < 1.1 ng/ml) (gas chromatography/mass spectrometry). Bone age was equal to his chronological age. Abdominal ultrasound did not show any masses, and demonstrated normal adrenal glands. Due to his elevated 17-OH-progesterone concentration, analysis of the *CYP21A2* gene was performed and showed a homozygous variant of p.Val281Leu. Genetic studies of the parents were not done. After an observation period of 6 months, pubarche spontaneously resolved (Fig. 1b), with no other signs of virilization, and growth velocity remained normal.

Discussion

As noted, PP is defined as the appearance of pubic hair before 8 yr of age in girls and 9 yr in boys, without other signs of puberty. It more frequently occurs between the ages of 6 to 8 yr,

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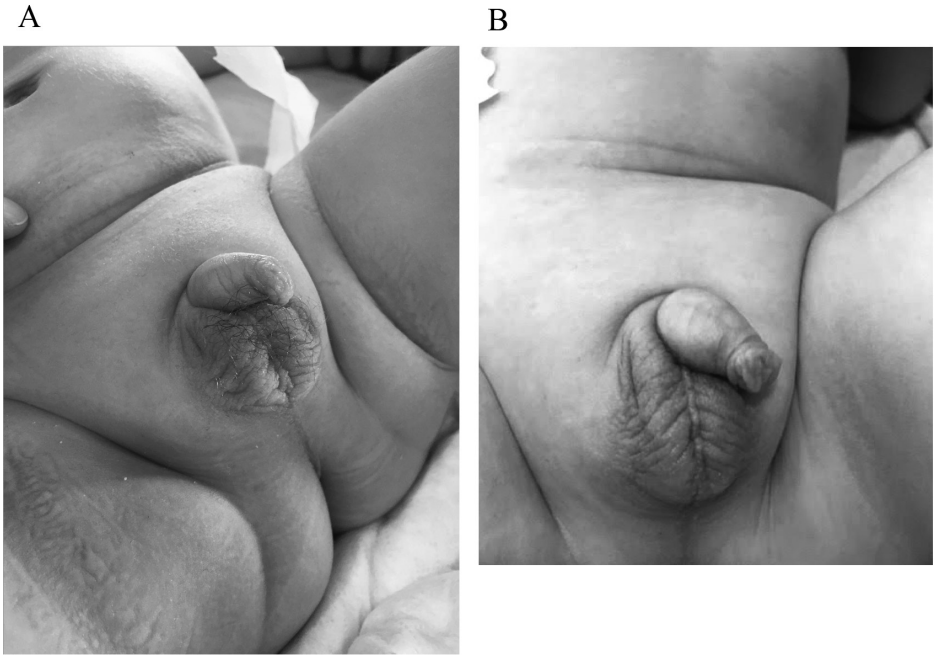

Fig. 1. A: Pubic hair confined to the scrotum. B: Six months later, pubic hair resolved.

with a clear predominance in girls (1). Pubarche in the first year of life is rare, with few reports and little description in the literature. It is thought to be benign because most cases resolve spontaneously; however, long-term follow-up is necessary to determine the etiology. When clinical signs of pubarche are noted, careful physical examination and analysis of the growth chart should be performed. The initial biochemical evaluation must include the determination of sex steroids and 17-OH-progesterone levels. If testosterone concentrations are elevated, ßhCG and an abdominal and pelvic ultrasound should be evaluated (2). The diagnosis of premature pubarche is based on the exclusion of other causes of prepubertal hyperandrogenism (3), and the etiology in infants remains unknown. A possible explanation might be the early physiological rise of testosterone in mini-puberty (4), which is not accompanied by other signs of secondary sexual development (axillary hair or odor, advanced bone age, and/or acceleration of the growth rate) and resolves spontaneously. Among the pathological causes that may initially present as premature pubarche, classic or non-classical CAH, precocious puberty, virilizing tumors, and exogenous exposure must be excluded. Classically, these conditions present with other findings such as clitoromegaly, increased penile length, advanced bone age, and growth acceleration. Despite the fact that this case did not present with other clinical findings of CAH, elevated 17-OH-progesterone concentration suggested non-classical CAH. Molecular study showed a homozygous variant of p.Val281Leu. This pathogenic variant has been described in patients with non-classical CAH (5); however, to our knowledge, this variant has not been described in infants that present with premature pubarche. As this boy's phenotype resolved in time and did not present other features of CAH, the clinical significance of this genotype is not clear.

Treatment is not always indicated in patients with non-classical CAH, unless they are symptomatic. Symptomatic hyperandrogenism

can be reduced with low-dose glucocorticoids, as in children with early onset and rapid progression of pubic and body hair, rapid growth, and/or skeletal advancement.

Conflict of Interest: The authors have no relevant conflict of interest.

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