Peripheral precocious puberty due to congenital adrenal hyperplasia with vanishing testis: a rare case in radiology

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ABSTRACT

Background: Genetically, peripheral precocious puberty can be caused by congenital adrenal hyperplasia (CAH). Radiological examination is used for etiology findings and diagnostics. Peripheral precocious puberty of CAH generally affects girls with genitalia disambiguate, less common in boys. Incidence is 1 in 15,000 to 20,000 children with a female to male ratio of about 20:1.

Case Report: A 5-year-old boy with voice change and hair growth in his penis. An immunoserosology, endocrinology, electrolyte laboratory examination had been performed. Besides, some radiological tests of diagnostic bone age, upper abdominal ultrasound, and testicular ultrasound had been determined as confirmation of laboratory findings that support peripheral precocious puberty. In this case, an examination of human skeletal maturity was obtained according to the age of 14. Ultrasound examination showed adrenal enlargement with a size of 4 x 0.6 cm with a V-shaped and cribriform appearance. No testicular was found in the scrotum or the inguinal canal. Both 17-hydroxyprogesterone and testosterone level was increased subsequently.

Conclusion: Bone age examination is needed to determine skeletal maturity. An ultrasound can be used to determine both etiology and concomitant abnormalities of the genital system. However, ultrasound can not detect the location of the testicle intraperitoneally. MRI examination is an imaging technique that is recommended if no testicles are found in the scrotum or inguinal.

Keywords: Peripheral precocious puberty, congenital adrenal hyperplasia, bone age, radiography

INTRODUCTION

Precocious puberty is the development of secondary sexual characteristics in children aged less than 8 years (female) or 9 years (male). The etiology of precocious puberty is divided into two types of puberty – central precocious puberty (true puberty precocious) and peripheral precocious puberty (pseudopuberty precocious). Its incidence rate is 21.4/100,000. Similarly, the incidence of peripheral precocious puberty is about 1 in 15,000 to 20,000 children. The female to male ratio is about 4: 1 to 20: 1. Meanwhile, the incidence of precocious puberty in males with testicular vanishing in Indonesia is 30%.

The hypothalamus produces a gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary to produce and release gonadotropins – luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Central precocious puberty (CPP) is a gonadotropin-dependent mechanism. It occurs due to premature activation of the hypothalamus-pituitary axis, which causes the release of gonadotropin hormone (GnRH), then inducing maturation of the gonads. The increased amount of LH stimulates the production of sex steroid hormones by Leydig cells in the testes or granule cells in the ovaries. Increased androgen or estrogen levels cause physical changes and experience early development, including penis enlargement and the growth of pubic hair in boys and breast enlargement in girls. Increased FSH levels result in the activation of the gonadal glands and ultimately aid in the maturation of follicles in the ovaries and spermatogenesis in the testes. CPP can be caused by harmatoma, astrogliaoma, pineal gland tumor, and arachnoid cyst

Peripheral precocious puberty (PPP), it is a gonadotropin-independent type, whereas the increase in serum steroid levels is not affected by gonadotropin secretion. Related to gonadotropin levels are low, no maturity of the gonads occurs. Based on the etiology, PPP can be divided as acquired or congenital. Congenital or genetic type includes McCune-Albright syndrome (MAS), male precocious puberty (FMPP), and congenital adrenal hyperplasia (CAH). Acquired type includes some tumors that secrete human chorionic gonadotropin (HCG) or steroid tumors in either the adrenal glands, ovaries, testes, or exposure to exogenous sex hormones.

Adrenal gland or suprarenal gland is superior to the right kidney, consisting of the adrenal cortex and adrenal medulla. The cortical layer produces aldosterone in regulating electrolytes and blood pressure, cortisol in balancing sugar levels and metabolism, and androgens in regulating sex hormones. CAH is a recessive thickening or
enlargement of the adrenal glands before birth. CAH is also recognized as its role in the involvement of hormones produced by the cortex. In addition, the adrenal cortex also produces cholesterol. Due to a defect of enzyme 21-hydroxylase, it affects aldosterone and cortisol production to remain low. The brain produces adrenocorticotropic hormone (ACTH) in more generous amounts, which causes adrenal enlargement and increased cholesterol production. Simultaneously, the products cause an increase in the accumulation of 17-OH progesterone, then playing a conversion into testosterone. From this pathophysiology, CAH is divided into both classical types (Salt wasting and non-salt wasting) and non-classical types.

Precocious puberty can be isosexual (involving secondary sex characteristics that match the similar sex) or heterosexual (involving the sexual attributes of the opposite sex). CPP is always isosexual, whereas PPP may be heterosexual. Especially if there is no testicle in the scrotum accompanied by hypospadias, then it is necessary to be suspected as a testicular dysgenesis syndrome. In children with precocious puberty, they will experience faster growth than children in their age. However, it will stop at an earlier age (3-6 years). So that children with precocious puberty will have a lower height than their peers. Therefore, radiologists are expected to understand the critical role of radiological examination for diagnostics and determine the etiology.\textsuperscript{1,5,7}

### CASE REPORT

A five-year-old boy was admitted from the regional hospital with complaints of voice changes and hair growth around the penis since one year ago, and a history of hypospadias surgery at 3 years. On physical examination, it was found that the nutritional status was good with a height of 117 cm (standard 100.7-110 cm) – 90th percentile – and the body weight of 22 kgs. Meanwhile, on the genital examination, the penis was measured 4 cm in diameter with a length of 5 cm (normal length 5.2-6 cm for boys aged 5 years) accompanied by the growth of pubic hair around the base of the penis. In addition, there is no palpable testicle on the right and left scrotum and inguinal. Due to these findings, this patient was also suspected of precocious puberty. In these patients, laboratory examinations, including immunoserology (17-OH progesterone) were performed; endocrinology (testosterone); electrolytes and AFP. And also performed a radiological examination.

He was followed by a radiological examination, namely examination of bone age, ultrasound of the

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**Figure 1.** Clinical 5-year-old patient with pubic hair growth at the base of the penis

**Figure 2.** Bone age manus dextra et sinistra of the patient

**Figure 3.** Ultrasound of right adrenal enlargement (RT). There is no enlargement was seen in the left adrenal (LT)

**Figure 4.** There is no picture of the testes on the right and left scrotum
CASE REPORT

On ultrasound examination, he showed an adrenal enlargement with a size of 4 x 0.6 cm with a V-shaped image and a cribriform appearance. And the absence of the testes in the scrotum and also in the inguinal region. Meanwhile, laboratory results that support the diagnosis of PPP were an increase in 17-OH progesterone to 246.77 mg / mL (normal: <0.90 mg / mL) and a testosterone level of 256 mg / dL. Those results of testosterone levels were in accordance with boys aged 7-18 years. AFP levels were 8.69 IU / ml (normal: <5.8 IU / ml). While the results of electrolytes, LH, FSH, and beta-HCG were still within normal limits.

DISCUSSION

In this case, the patient was brought by his family due to voice change and hair growth around the pubic area in the last year. On physical examination, it was found that the penis was 4 cm in diameter with a length of 5 cm (5.2-6 cm for normal boys at 5 years) accompanied by the presence of pubic hair growing at the base of the penis. The absence of an increase in LH, FSH and β-HCG on laboratory studies revealed that the patient had peripheral precocious puberty. An increase in 17-OH progesterone by 246.77 mg / mL causes an increase in testosterone levels 256 mg / dL, leading to the growth of secondary sexual characteristics, including enlarged testicles and pubic hair development, and indicates peripheral precocious puberty caused by congenital adrenal hyperplasia.

As for the examination of skeletal maturity, it was obtained through a radiological examination of the bone age. It was found that the left renal carpalia bone had been completely formed, whereas at 5-years children, the carpalia bone was not entirely growing. It was mainly based on the difference in width between the shorter epiphyses and the wider metaphysis of the distal and middle bars. In this case, we found the width of the epiphyses of the metacarpals, the proximal, middle, and distal bars of the IV digit being the same width as metaphysical, but there is no fusion on the epiphyseal plate. Skeletal maturity can also be affected by hormonal imbalances.

Ultrasound examination showed an enlarged right adrenal when compared to the left adrenal. It obtained the picture of adrenal enlargement about 4 x 0.6 cm with a V-shaped image and cerebriform appearance. Also, there were no testes found in the scrotum or the right and left inguinal tract. On ultrasound, if there is a testicle in the scrotum, we will get a picture of the echogenicity that increases mild to moderate. Refer to no testis observed within the scrotum, then testicular dysgenesis syndrome.
is dominantly suspected. It is characterized by increased AFP and a history of hypospadias. PPP caused by CAH generally affects girls with genital ambiguities and is less common in boys.\(^4\)

Currently, the patient is also planned for an MRI examination to ascertain the position and presence of the testis intraperitoneally and a chromosome examination to determine the patient’s gender. In patients with \textit{undesensus} testis accompanied by secondary physical changes, bone maturity should be considered with the age of the human bone, ultrasound, and MRI to confirm the position of the testes as well as to determine whether there is an adrenal enlargement or not.

**CONCLUSION**

Patients with precocious puberty are cases that we often encounter but have different etiologies, especially for PPP that occurs in boys. Apart from physical and laboratory examinations, radiological examinations also have an essential role in precocious puberty. Bone age examination is required to determine skeletal mortality. At the same time, ultrasound can be used to determine the etiology and delivery of the genital system. However, ultrasound is not easy to detect testicular location intraperitoneally. In this case, further examination using MRI is the recommended imaging technique to see whether the testicle is in the peritoneal cavity or not, so that the patient can determine the gender.

**REFERENCES**