# Central Precocious Puberty as a Complication of Peripheral Precocious Puberty due to Congenital Adrenal Hyperplasia in a Boy: A Case Report from Iraq

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**(Ann Coll Med Mosul 2025; 47 (1):100-102).**
**Received: 21th Oct. 2024; Accepted: 29th Dec. 2024.**

## ABSTRACT

The transition from peripheral to central precocious puberty may occur from prolonged exposure to sex hormones from gonadotropin-releasing hormone-independent etiologies, including congenital adrenal hyperplasia. Herby, we present a case report in a 6-year-old and 5-month-old boy with congenital adrenal hyperplasia developing into central precocious puberty preceded by peripheral precocious puberty. Early detection and therapy of precocious puberty due to congenital adrenal hyperplasia should begin as soon as feasible because failure to do so may result in short stature and other long-term mental and physical consequences.

***Keywords:*** Adrenal, Central, Hormone, Peripheral, Precocious, Puberty.

# البلوغ المبكر المركزي كمضاعفات للبلوغ المبكر المحيطي بسبب فرط تنسج الغدة الكظرية الخلقي عند طفل ذكر: تقرير حالة من العراق

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## الخلاصة

قد يحدث الانتقال من البلوغ المبكر المحيطي إلى البلوغ المبكر المركزي نتيجة التعرض المطول للهرمونات الجنسية من مسببات مستقلة عن هرمون تحرير الغدد التناسلية بما في ذلك تضخم الغدة الكظرية الخلقي. نقدم في هيربي تقرير حالة لصبي يبلغ من العمر ٦ سنوات و٥ أشهر مصاب بتضخم الغدة الكظرية الخلقي الذي تطور إلى البلوغ المبكر المركزي الذي يسبقه البلوغ المبكر المحيطي. يجب أن يبدأ الاكتشاف المبكر وعلاج البلوغ المبكر بسبب تضخم الغدة الكظرية الخلقي في أقرب وقت ممكن لأن الفشل في القيام بذلك قد يؤدي إلى قصر القامة وغيرها من العواقب العقلية والجسدية طويلة الأمد.

**الكلمات المفتاحية:** الغدة الكظرية، المركزية، الهرمونية، الطرفية، المبكرة، البلوغ.

## INTRODUCTION

Precocious puberty refers to the premature onset of secondary sexual characteristics, happening before the age of eight in girls and nine in boys. In girls, this is typically marked by breast enlargement, and in boys, by testicular growth. Peripheral precocious puberty (PPP) and central precocious puberty (CPP) are the two recognized types [1].

PPP is also known as gonadotropin-releasing hormone (GnRH)-independent precocious puberty. The main genetic causes include congenital adrenal hyperplasia (CAH), Testotoxicosis, and McCune-Albright syndrome[1]. Acquired causes can result from exposure to external androgens, tumors [1], or pseudo-precocious puberty due to severe primary hypothyroidism [2].

The transition from peripheral to central precocious puberty may occur from prolonged exposure to sex hormones from GnRH-independent etiologies, albeit it's not quite obvious how this will happen [3].Children who experience premature puberty may experience mental and physical effects. It's critical to clearly grasp when to intervene to halt pubertal changes.

Herby, we present a case report, up to our knowledge; it is the first case to be reported in Iraq about the occurrence of CPP due to PPP caused by CAH in a boy child.

## Case Presentation

A 6-year and 5-month-old boy had been brought by his parents owing to concerns regarding his ongoing increase in penile length and frequent erections over the past year.

These changes were accompanied by the development of pubic hair over the last 6 months, axillary hair after that, adult body odor, and acne.

The parents also noted a steady increase in his height over the past 2 years.

There was no prior history of headache, blurred vision, altered behavior, head injury, or surgery. The family and perinatal history were reported as insignificant. The family was advised by a private doctor to start with hydrocortisone treatment with a dose that is not remembered by the family associated with on/off treatment days with poor compliance.

Physical examination revealed height was 132 cm above the 95th percentile, height SD score (was + 2.5 SD), weight was 27 kg on the 90$^{th}$ percentile (+ 1.28 SD), BMI of 15.5 Kg/m2 (between 50$^{th}$ and 75$^{th}$ percentile), mid parental height 173 cm. His stretched penile length was 7.5 cm (above the 90$^{th}$ percentile), and testicular volumes were 6 mL on the left and 4 mL on the right; pubic hair was consistent with Tanner stage 4, and there was scant axillary hair. No skin or bone lesions were present. Systemic examinations were unremarkable.

Bone age was 13 -14 years; predicted adult height was nearly 151 cm. Figure 1 shows left wrist and hand x-rays for bone age.

Investigations showed the following: Serum Sodium 140 mmol/L (135-145 mmol/L), Serum Potassium: 4.3 mmol/L (3.5-5.1 mmol/L), Basal Cortisol: 4 nmol / L ( 27.6-718 nmol / L), serum ACTH was 143 pg/mL (7.2-63.3), 17-OH-Progesterone 120 ng/dL ( < 90 ng/dL), LH: 0.7 IU/L (≤ 0.3 IU/L), FSH: 1.1 IU/L, serum Testosterone 5.45 ng/dL (0.2-1.3 ng/dL), Dehydroepiandrosterone Sulfate (DHEA-S): 240 µg/dL (13-83 µg/dL), TSH: 4.2 mIU/L (0.47-5.01mIU/L) and Free T4: 16.04pmol/L (9-22 pmol/L).

Serum Cortisol after stimulation with Synacthen (250 Micrograms) is five nmol / L, 17-OH-Progesterone 2200 ng/dL.

After stimulation with Decapeptyl (GnRH analogue) (0.1mg), serum LH was 69.7 IU/L (< 5 IU/L), and serum testosterone was 8.28 ng/dL.

Abdominal and scrotal ultrasounds were normal, and brain MRI was also normal.

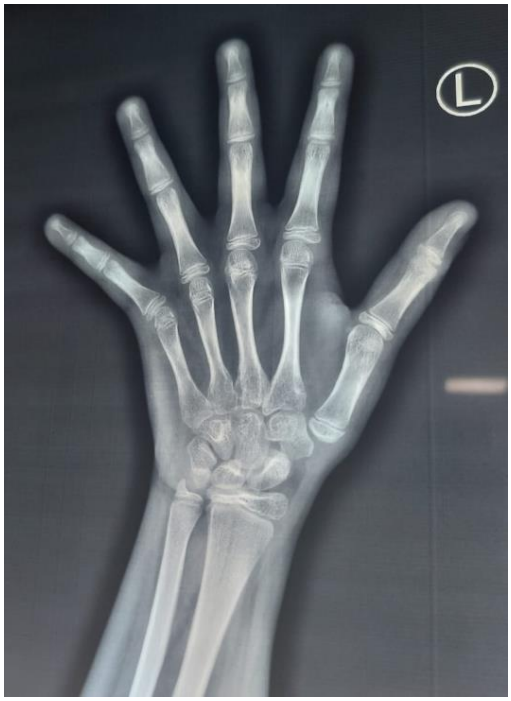


Figure 1 shows left wrist and hand x-rays for bone age.

The patient started treatment with Hydrocortisone 15 mg/m2/day, in addition to Zoladex (Goserelin acetate) 3.6 mg monthly, and growth hormone (GH) 0.035 mg/kg/day.

## DISCUSSION

The most common cause of PPP in boys is CAH, which is rarely present with CPP. Clinical observations suggest several theories about the mechanisms of CPP in CAH: 1) the hypothalamic GnRH pulse generator's early reactivation, 2) advanced bone age, 3) a negative feedback loop resulting from the decrease in testosterone levels following hydrocortisone therapy may lead to an increase in gonadotropin production [4-6], Our case is a six-year and 5 months old boy having CPP with bilateral pubertal sized testes, high stimulated LH, high testosterone level, but at the same time high 17-OH-progesterone level and DHEA-S proposing that it is originally a case of CAH with PPP transformed to CPP due to sustained sex steroid exposure, poor treatment compliance resulted in a rapid increase in bone age, and

inadequate follow-up with the pediatric endocrinologist prevented interfering early, all significantly contributed to the development of CPP.The aim of treatment for CAH with precocity is to restore the lost glucocorticoids, which will suppress ACTH and return adrenal androgen levels to normal. The recommended drug is hydrocortisone because of its decreased potential to restrict growth; the typical starting dose is 10 to 15 mg/m$^2$/day [7].

Growth velocity often decreases in tandem with a slowdown in bone age advancement in children treated with GnRH analog for CAH and CPP. As such, it is doubtful that these children's height deficiency will be corrected by GnRH analog therapy alone [5]. A study by Quintos et al. concluded that in patients with CAH, growth hormone (GH) or GH plus GnRHa treatment improves height prediction and reduces the height deficit for bone age [8]. Our patient was treated with Hydrocortisone, GH, and GnRH analogue.

Our scenario is similar to a case series with three male children who had CAH with CPP [9], another case by Majumdar et al., who described a rare case in which CAH was ultimately discovered in a six-year-old child despite clinical and hormonal signs of CPP 10, and a case reported by Sharmin et al. in an 8-year-old boy with a simple virilizing CAH, causing CPP superimposed on PPP, nearly similar to our indexed patient [6].

## CONCLUSION

Boys who have CAH may develop PPP, which could lead to CPP. Early detection and therapy should begin as soon as feasible because failure to do so may result in short stature and other long-term mental and physical consequences. It should be advised that children with CAH arrange regular follow-up visits to the pediatric endocrine clinic.

## Ethical Approval

The case report was carried out with the patient's and his family's approval.

## Financial Support and Sponsorship

Self-funded.

## Conflicts of Interest

There are no conflicts of interest.

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