

Coincidental Central Precocious Puberty and Wilms Tumor in a 5-year-old Girl

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INTRODUCTION

Wilms tumor is the most frequent pediatric renal malignancy and its usual presentation is an abdominal mass or hematuria. Unusual presentations have also been reported, such as paraneoplastic syndromes (acquired von Willebrand disease, sudden death due to pulmonary embolism and Cushing syndrome). These conditions can precede, occur concomitantly or present in a later phase of tumor development. Precocious puberty, as paraneoplastic endocrine syndrome, has already been described in children with malignant tumors (brain, gonadal, adrenal tumors and hepatoblastoma). However, little is known about central precocious puberty, as paraneoplastic manifestation of nephroblastoma or secondary to its specific chemotherapy.

CASE PRESENTATION

A 5-year-old girl presented with macroscopic hematuria and abdominal pain.

Her personal and familial medical history were unremarkable.

On physical examination a mass in the right upper quadrant was palpated. She had bilateral breast buds, corresponding to **stage 2** of the Tanner classification and no other pubertal signs.

The first diagnosis was **nephroblastoma stage I** and simultaneous **premature telarche (PT)**, confirmed by the pre pubertal levels of luteinizing (LH) and follicular stimulating hormone (FSH), and estradiol.

The oncological protocol was commenced, with complete excision of the tumor and chemotherapy cycles over 3 months.

A second endocrine assessment was performed at the end of chemotherapy. An accelerated linear growth (**a gain of 3 cm in 4 months**) and a **rapid breast development** (passage from stage 2 to stage 3) with no axillary or pubic hair were noted. The hormonal work-up found an **activated pituitary-gonadal axis** along with **advanced skeletal maturation and ultrasound signs of uterine hormonal impregnation**. The human chorionic gonadotropin (hCG) levels were normal. Brain magnetic resonance imaging showed a **morphologically normal pituitary, but of pubertal size and no congenital or acquired lesions in the pineal or hypothalamic-optic region**. The definitive diagnosis of idiopathic central precocious puberty (CPP) was made and the treatment with GnRH agonist was started.

An interesting point to consider was whether the CPP in our case represented a coincidental finding.

We performed a full review of the published literature indexed in PubMed up to January 2019 regarding Wilms tumor and puberty. Search terms included 'Wilms tumor', 'paraneoplastic syndrome' and 'precocious puberty'. Our search failed to identify existing reports relating to the coexistence of Wilms tumor and CPP.

| | At admission | 4 months later | 10 months later |
|--|--|---|--------------------------------------|
| Clinical data | Weight 21 kg Height 117 cm Tanner stage II - breast development | Weight 21 kg Height 120 cm (+ 3 cm/4 months) Tanner stage III - breast development | Tanner stage II - breast development |
| Hormonal data | LH < 0.3 IU/L (normal range < 0.5) FSH 0.9 IU/L (normal range < 1) Estradiol < 20 ng/L (normal range < 25) | LH 1.4 IU/L FSH 3.8 IU/L Estradiol 54 ng/L hCG < 2 U/L (normal range < 2) LH (40 min post 100 µg triptorelin injection, sc) 13 IU/L FSH ((40 min post 100 µg triptorelin injection, sc) 6.3 IU/L | LH 3.4 IU/L |
| Radiological data | Abdominal US - well-circumscribed heterogeneous echogenic mass of 9.2 x 9.5 cm in right renal fossa | Bone age - 8 years Pelvic US - normal ovary size and morphology, enlarged uterus with maximum length of 45 mm Brain MRI - Pituitary height of 6 mm and marked convexity of the upper surface. No lesions in the pineal or hypothalamic-optic region | |
| Oncological diagnosis and treatment | Wilms tumor (nephroblastoma) SIOP WT01 protocol Right nephrectomy | End chemotherapy | |
| Endocrine diagnosis and treatment | PT No treatment | CPP GnRHa 11.25 mg intramuscularly every 3 months | Same treatment |

CONCLUSIONS

Our observation (PT with rapid progression to CPP in a 5-year-old girl with a concomitant Wilms tumor) may shed light on the necessity to diagnose precocious puberty (PP) early in every child irrespective of the presenting illness. A complete clinical examination, and prompt referral to a pediatric endocrinologist for specific work-up and treatment, are helpful in limiting early and late long-term health implications (short stature, psychosocial outcomes, metabolic and cardiac events, and the risk of breast cancer development).

We therefore recommend that when faced with PP in a child with a concomitant tumor, the diagnosis of paraneoplastic or neoplasia-associated PP should be discussed.

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