Case Report

Precocious puberty in a child: A rare cause and review of literature

Thulasiraj Saminathan[1], Dhivyalakshmi J[1], Latha M. Sneha[2], Leena D. Joseph[3]

Departments of [1]Pediatrics, [2]Division of Pediatric Hematology and Oncology and [3]Department of Pathology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India

Abstract

Precocious puberty (PP) in pediatric office practice is challenging as the cause varies from benign to malignant conditions. Adrenocortical tumors are rare in childhood and pseudo-precocious puberty is the most common clinical presentation in children. We report a case of a 5-year-old boy who presented with features of abdominal distention and virilization, and his abdominal magnetic resonance imaging (MRI) revealed an adrenal tumor which was confirmed as adrenocortical carcinoma by biopsy. This case report highlights the importance of the awareness among general practioners and pediatricians to rule out adrenocortical tumors while evaluating a child with PP.

Keywords: Adrenal tumors, children, precocious puberty

Introduction

Precocious puberty (PP) is the onset of secondary sexual characteristics before 8 years of age in females and 9 years in males. It can be either "true" or central PP (gonadotropin-dependent, with premature activation of the hypothalamic–pituitary–gonadal axis) or precocious pseudopuberty, also called peripheral PP (independent of gonadotropin and axis maturation) and is due to the excess secretion of sex hormones from the gonads or adrenal glands.[1] Evaluation of the causes of PP in a child is complex, and malignant conditions are not usually thought of. We report a case of a 5-year-old boy who presented with progressive abdominal distention and features of virilization and his MRI abdomen revealed an adrenal tumor which was finally confirmed as adrenocortical carcinoma.

Address for correspondence: Dr. Latha M. Sneha, No. 1, Ramachandra Nagar, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai - 600 116, Tamil Nadu, India.
E-mail: drmslatha@yahoo.com

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Case Report

A 5-year-old boy, second born to non-consanguineous parents was brought with complaints of progressive abdominal distension, acne, hirsutism, appearance of pubic hair along with increased penile length for the past 3 years. His natal and post natal history was uneventful. There was no family history suggestive of endocrine tumors or familial disorders. He has been consulting multiple practitioners for the above complaints, but was never evaluated thoroughly.

On examination, he had acne over forehead and cheeks with a large café a lait spot over abdomen in the right side and fat hump in shoulder. He was obese, hypertensive and had cushingoid features. Anthropometry showed height 110 cm (between fiftieth and seventy fifth centile), weight – 25.7 kg, BMI 21.1 kg/m^2. Pubic hair and genitalia Tanner staging was stage IV, bilateral testes volume – 6 mL and his stretched penile length (SPL) was 7.5 cm. Abdomen showed a well-defined, firm oval mass in the left lumbar region of size (8 × 6 cm).

Complete blood count and bio chemistry parameters were normal. His serum hormonal assays showed low basal

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levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and elevated levels of serum cortisol, testosterone, 17-hydroxyprogesterone and dehydroepiandrosterone sulfate (DHEA-S). HbA1c and thyroid function profile were normal. Gonadotropin releasing hormone (GnRH) stimulation test showed a negative response. The bone age was advanced by 3 years, confirming the diagnosis of pseudo-precocious puberty. CECT abdomen showed a lesion of size 19 × 12.7 × 11.6 cm, which was not separately visualized from the left adrenal gland [Figure 1]. Multiple central hypo enhancing areas suggestive of necrosis, with multiple coarse calcific foci were noted within lesion. CECT chest showed multiple lung nodules (upto ~8 mm) in bilateral lung fields suggestive of pulmonary metastasis [Figure 2].

Histopathology of the adrenal mass showed predominantly necrotic tissue with a small fragment of tumor cells with nuclear pleomorphism, moderate eosinophilic granular cytoplasm, and occasional mitosis [Figure 3]. By immunohistochemistry the tumor cells are positive for vimentin and inhibin, suggestive of adrenocortical carcinoma [Figure 4a and b]. Final diagnosis of malignant adreno cortical carcinoma (ACC) stage IV with peripheral precocious puberty progressing to central precocious puberty was made. He was started on chemotherapy, mitotane, and antihypertensives after discussing in multidisciplinary tumor board. The tumor was refractory to chemotherapy and he succumbed to disease 4 months after diagnosis.

Discussion

Adrenocortical tumors are very rare in children, accounting for about 0.2% of all tumors and approximately 6% of all adrenal tumors.[2] About 65% of adrenocortical tumors occurs in <5 years of age.[3] Pseudo-precocious puberty is the most common clinical presentation, seen in 50–84% cases.[3] ACT can be functional (hormone secreting) or non-functional (silent). Functional tumors are more commonly seen in children and adolescents. Some of the common causes of pseudo-precocious puberty are long-standing untreated primary hypothyroidism, McCune Albright syndrome, congenital or secondary adrenal hyperplasia causing excessive production of androgens[4-6] and exogenous sex steroids. The other rarer causes are adrenal tumors, non-classical congenital adrenal hyperplasia, germ cell tumors, testicular tumors, familial male-limited PP.

The two predisposing syndromes associated with ACT are Li–Fraumeni syndrome and Beckwith–Wiedermann syndrome.[7] Central PP usually presents with gonadal enlargement of ovaries in females or testicles in males, whereas pseudo-precocious puberty presents mainly with the early development of pubic and/or axillary hair.[8] The excess secretion of androgenic hormones resulting in virilization and pseudo-precocious puberty is the most common symptom of ACTs. But, a late presentation of ACT can be seen with CPP secondary to the maturation of the hypothalamic–pituitary–gonadal axis.[3] Virilization in young children should raise the suspicion of adrenal tumor. Razavi had

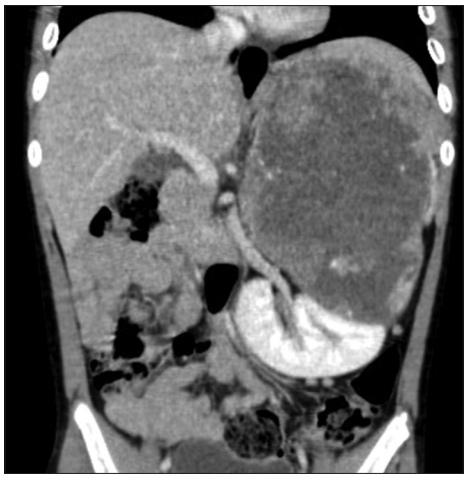

Figure 1: CECT abdomen coronal view showing a large well-defined heterogeneously enhancing lesion, with lobulated margins and multiple central hypo enhancing areas suggestive of necrosis, with multiple coarse calcific foci noted within lesion

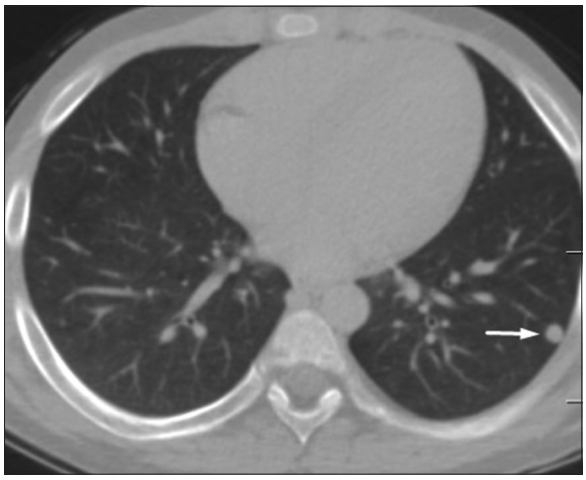

Figure 2: CECT chest axial view showing bilateral lung nodules suggestive of pulmonary metastasis

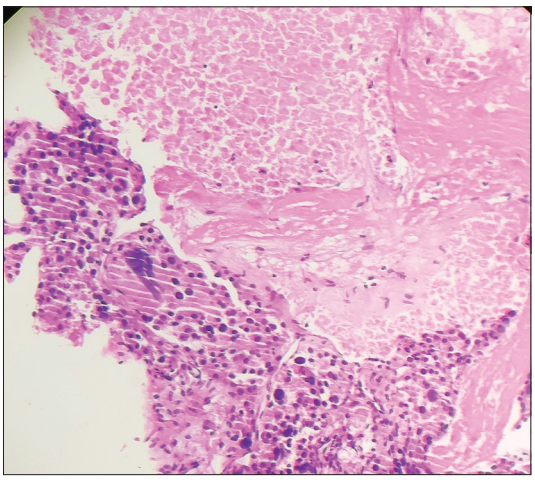

Figure 3: Histopathology showing predominantly necrotic tissue with a small fragment of tumor cells with nuclear pleomorphism, moderate eosinophilic granular cytoplasm and occasional mitosis

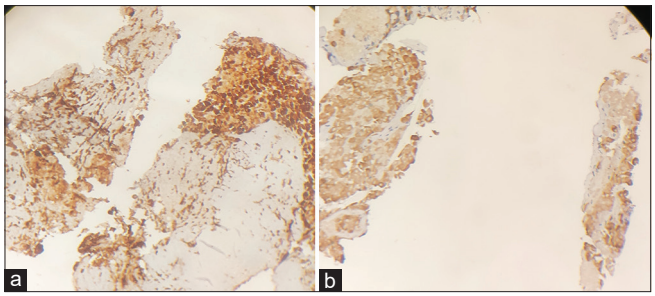

Figure 4: (a) and (b) Immunohistochemistry showing the tumor cells which are positive for vimentin and inhibin

reported ACT in a 10-month-old infant, who presented with facial hair, acne, and increased penile length[2] Ghazizade *et al.*[9] had reported a 2-year-old girl who had virilization since birth.

Surgical resection is the treatment of choice. Surgery is the only definitive therapeutic modality in localized disease, which can be curative only if adrenocortical carcinoma is diagnosed early. Advanced disease or metastasis has poor prognosis with only 10% survival rates.[7] Adjuvant chemotherapy with cisplatin-based regimens and mitotane are recommended for metastatic or recurrent disease, but paucity of large studies makes consensus to be framed on the benefit.

Conclusion

Malignancy is a rare but important cause of PP in children. Any child >4 years with pubarche should be considered to have ACT until proven otherwise. As Cushing syndrome is very rare in children, a child <10 years with cushing's syndrome should be evaluated for ACT.

Key messages

Virilization symptoms in children warrants an extensive evaluation and could be the initial manifestation of malignant tumor.

Acne in children <6 years of age, needs endocrine evaluation to rule out hormone secreting tumors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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