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CASE REPORT

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Wilms' tumor presenting as Cushing's syndrome

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Abstract We report a 2-year-old boy presenting with Cushing's syndrome caused by a Wilms' tumor. This is the fifth such case reported in the English literature.

Key words Cushing's syndrome · Ectopic adrenocorticotropic hormone (ACTH) · Wilms' tumor

Introduction

Endocrine manifestations of Wilms' tumor (WT) include polycythemia, hypoglycemia, and renin-induced hypertension. Cushing's syndrome (CS) is a very rare presentation of WT, with four such cases having been previously reported in the English literature.

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Case report

A 2-year-8-month-old boy was referred due to the appearance of cushingoid facies and abnormal weight gain for the previous 2 months (Fig. 1). He weighed 15 kg. His blood pressure was 140/80 mm Hg. The serum cortisol and 24-h urinary free cortisol levels were elevated (Table 1). An ultrasound examination showed the left kidney to be compressed and pushed outward by a mass measuring 4.5×5.0 cm that was interpreted as a left adrenocortical tumor in keeping with the clinical suspicion. IV urography showed the left kidney pushed down with distortion of the upper calyx. The chest radiograph did not show any evidence of metastases.

At surgery, a tumor was found in the upper pole of the left kidney. The opposite kidney and both adrenals were normal. A left nephroureterectomy along with removal of the left adrenal gland was done (Fig. 2). The tumor showed unfavorable histology with a predominantly blastemal picture. A focus of tumor was seen outside the kidney capsule while the vascular pedicle, ureteric margin, and left adrenal did not show any tumor (stage II). Consequent to the unexpected findings at laparotomy, the blood samples taken preoperatively for cortisol estimation were retrieved and frozen for adrenocorticotropic hormone (ACTH) assay. Fresh samples were also taken on the 1st and 30th postoperative days for ACTH levels, which were elevated in the preoperative sample and normal in the postoperative specimens (Table 1). Serum cortisol on the 7th postoperative day was in the normal range. Steroid support was tapered and withdrawn by the 5th day. Low- and high-dose dexamethasone suppression tests, which had not been done preoperatively, showed a normal pattern of suppression. An X-ray film of the skull did not show any abnormality of the pituitary fossa.

The child made an uneventful recovery. The blood pressure became normal on the 1st postoperative day. His subsequent treatment included flank irradiation and chemotherapy using actinomycin D, vincristine, and adriamycin following the DD regimen of the National Wilms' Tumor Study III. At 1 year and 4 months after surgery, he had completed chemotherapy and was free of disease. All features of CS had fully regressed.

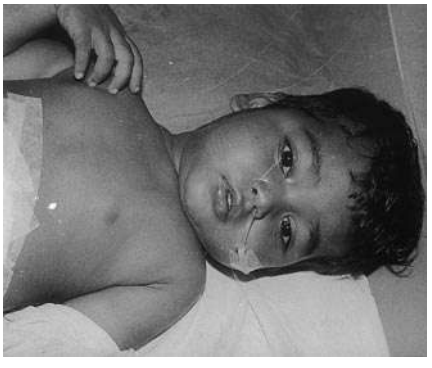

Fig. 1 Immediate postoperative appearance of patient

Discussion

Cushing's syndrome caused by ectopic ACTH-secreting tumors is rare in children [1]. There are only four previous case reports of WT causing CS in the English literature, all associated with raised ACTH levels [2–5]. In the child reported here, a WT of the left kidney was associated with high serum ACTH levels. No

Table 1 Pre- and postoperative cortisol and adrenocorticotropic hormone (ACTH) levels

Assay	Ref range	Preop	Postoperative levels		
			Day 1	Day 30	
Serum ACTH a.m.	0–37 pg/ml	93	27	12	
p.m.	0–37 pg/ml	77	–	–	
			Dexamethasone (Dexa) suppression		
			Basal	Dexa 2 mg	Dexa 8 mg
Plasma cortisol a.m.	5–23 μg/dl	32.3	9.8	2.8	1.4
p.m.	3–15 μg/dl	23.0	4.2	–	–
Urinary free cortisol	2–27 μg/24 h	814.0	–	7.0	8.6

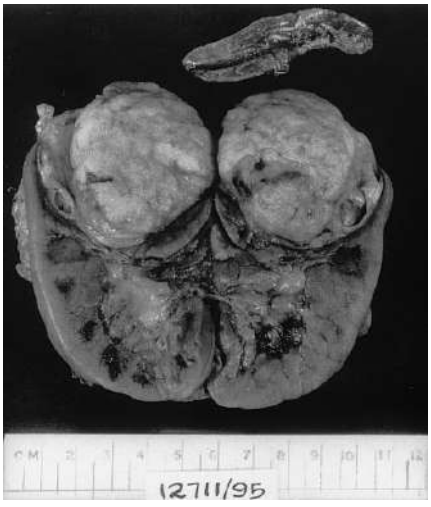

Fig. 2 Bisected left nephroureterectomy specimen. Note that left adrenal was not grossly enlarged

other source of ectopic ACTH was found, and the ACTH and cortisol levels became normal after a left nephroureterectomy. The preoperative ACTH value was high even though the estimation was done on a sample collected 5 days earlier. ACTH is extremely labile, and the levels in the preoperative samples were presumably much higher.

Hypertrophied adrenal glands and loss of the circadian rhythm of serum cortisol levels are characteristic of CD or syndrome secondary to pituitary or ectopic hypersecretion of ACTH. Our patient and one other child reported in the literature had normal adrenal glands [4]. The size of the adrenals was not commented upon in the three other reports. Preservation of the circadian rhythm of serum cortisol, although at a higher level, was noted by us and others. [2, 4, 5]. The observations of Hashimoto et al. suggest the possibility that the hypothalamus-pituitary axis is preserved and stimulated by corticotropin-releasing factor-like activity of Wilms' tumor products [3, 4], rather than being superseded by the ectopic ACTH itself. This, if true, is also consistent with the rapid endocrine recovery in these patients after the tumor is removed.

In addition, in conditions such as Beckwith-Wiedemann syndrome and hemihypertrophy there is an increased propensity for tumors of the adrenal cortex and WT. In WT associated with CS, the possibility of a coexisting tumor should be excluded by serial hormonal assays and preferably also by documenting ACTH in tumor tissue [3]. Serum ACTH should serve as a useful marker in these children.

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