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Case Report Open Access

Cushing's Syndrome Secondary to Adrenal Tumor in an 11-month-old Infant: Report of a Case

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Abstract

Cushing's Syndrome (CS) is rare in children and adolescents (10%). It is classified as exogenous and endogenous; dependent ACTH or independent ACTH, the latter with an incidence of 2 to 4 cases per million inhabitants per year; having its origin in tumors of the adrenal gland, which are rare in children.

Clinical case: 11-month-old male infant who attended a medical consultation for 5 days due to obesity, physical examination showed virilization data, high blood pressure, laboratory studies with elevated morning cortisol and normal ACTH, suspecting independent ACTH Cushing's syndrome, a simple abdominal CT was requested with evidence of adrenal gland dependent tumor of approximately 3.3 cm × 4 cm, so surgical management of right suprarenalectomy was decided, with postoperative admission to intensive therapy, being withdrawn on the 13th day of hospital stay. Histopathological report of adrenal adenoma; Follow-up was given to the outpatient clinic at six months with laboratory and cabinet controls without evidence of tumor activity.

Conclusion: There should be a broad diagnostic suspicion of Cushing's syndrome in pediatric patients, to correct the underlying cause that originated it and to reverse possible future complications.

Keywords Cushing's syndrome; Adrenal tumor; Tumor

Introduction

We present the case of an 11-month-old male infant who attended a medical consultation of the Maternal and Infant Institute of the State of Mexico for presenting obesity, high blood pressure, and virilization. He was diagnosed with Cushing's syndrome. Independent ACTH is secondary to adrenal tumor.Obesity had a predominant role in the development of arterial hypertension; both risk factors are part of the metabolic syndrome that is present between 4.2% and 8.4% of the child population [1]. According to The National Health and Nutrition Examination Survey (NHANES), it classifies blood pressure with the 50, 90, 95, and 99 percentiles taking into account gender, age, and height. With the above, the following definitions are recorded: Normal blood pressure: Systolic and diastolic blood pressure lower than the 90th percentile for age, gender and height percentile. High normal blood pressure (prehypertension): Systolic or diastolic figures greater than or equal to the 90th percentile, but lower than the 95th percentile. Hypertension: Pressure greater than the 95th percentile for age, gender, and height percentile in three measurements taken in the course from four to eight weeks.

Severe arterial hypertension: Systolic, diastolic blood pressure or both, greater than or equal to the 99th percentile for age, gender and height percentile. Hypertension of the "white coat": It is the elevated pressure of a patient with figures above the 95th percentile that is recorded in the office or in a clinic, while the average BP is lower than the 90th percentile when the patient is outside the clinical setting. Another form of classification of systemic arterial hypertension is: essential or primary hypertension, when an identifiable cause is not found, and secondary hypertension when a cause is identified (Table 1), which occurs in up to 90% of pediatric patients (Tables 1 and 2), so it is necessary to have a complete clinical history, an adequate physical examination and, above all, a broad diagnostic suspicion (Table 2) [1].

Age	Causes
1 to 6 years	Renal parenchymal disease, renal vascular disease, endocrine causes, coarctation of the aorta, essential hypertension
6 to 12 years	Renal parenchymal disease, essential hypertension, renal vascular disease, endocrine causes, coarctation of the aorta, iatrogenic disease
12 to 18 years	Essential hypertension, iatrogenic disease, renal parenchymal disease, renal vascular disease, endocrine causes, coarctation of the aorta

Table 1: Causes of hypertension in childhood according to the age group [1].

Vital signs	Tachycardia	Hyperthyroidism, pheochromocytoma, neuroblastoma, primary hypertension
	The decrease of pulses in lower extremities	Cortation of the aorta
Eyes	Changes in the retina	Severe hypertension more likely to be associated with secondary hypertension
Ears, nose and throat	Adenotonsillar hypertrophy	Suggests association with sleep disorders
Height and weight	Delay in development	Renal insufficiency
	Obesity (high BMI)	Primary hypertension
	Trunk obesity	Cushing syndrome: Insulin resistance syndrome
Neck and head	Face of moon	Cushing's syndrome
	Face of Elfin	Williams syndrome
	Neck pulled	Turner syndrome
	Tiromegalia	Hyperthyroidism
Skin	Paleness, flushing, diaphoresis	Pheochromocytoma
	Acne, hirsutism, stretch marks	Feocromocitoma
	Brown spots	Neurofibromatosis
	Adenoma sebaceous	Tuberose sclerosis
	Rash Malar	Systemic lupus erythematosus
	Acanthosis Nigricans	Diabetes mellitus type 2
Chest	Apical lifting, It blows on the back	Hypertension, hypertrophy of the ventricle, Coarctation of the aorta
	Pericardial fluid	Lupus Systemic Erythematosus (pericarditis), Renal insufficiency (uremia)
Abdomen	Epigastrium/Flank puff	Wilms tumor, neuroblastoma, pheochromocytoma
		Renal artery stenosis Estenosis de la arteria renal
	Palpable Kidneys	Polycystic kidneys, hydronephrosis

Table 2: Findings of the physical examination that is useful in the diagnosis of hypertension [1].

Clinical Case

An infant of 11 months 25 days, a product of gestational term 2, mother 18 years old, at 39 weeks gestational age, infant birth weight was 3,720 kg and size 56 cm was born via cesarean section because it's large for gestational age presented without significant perinatal history.

Figure 1: Male infant 11 months old with full moon face, abundant peripheral adipose tissue.

During her first months of life, she remained exclusively breastfed. The mother refers the current condition of her son when she notices an accelerated increase in weight after 5 months of age, so she went to a private doctor who recommended restriction in feeding due to obesity without specifying the cause [2]. In the face of the persistence of accelerated weight gain, he decides to go to our institution for evaluation (Figure1).

Physical examination

Irritable, normocephalic, face in full moon, buffalo hump, eyes without alterations, permeable nostrils, oral cavity with normal pharynx, neck without megalias, hypertrophic thorax with good entrance and exit of air, present and normal vesicular murmur, rhythmic precordium, heart sounds of good intensity and frequency, globular abdomen at the expense of adipose panniculus, soft depressible painless, no tumor was palpated, no evidence of peritoneal irritation, normalized peristalsis, virilization, symmetrical integral limbs, with adequate capillary refill, present and normal pulses.

Laboratories

Hb 10.7 g/dL, Hto 37.1%, platelets 375,000/mm^3, leukocytes 10,500/mm^3, lymphocytes 35%, monocytes 7%, segmented 58%, cholesterol 110 mg/dL, creatinine 0.27 mg/dl, glucose 109 mg/dl, LDH 622 mg/dL, total protein 6.2 g/dl, albumin 3.6 g/dl, TGO 49 U/L, TGP 172 U/L, BUN 11 mg/dL, Urea 23.54 mg/dl, Ac. uric 2.3 mg/dL, Ca 9.8 mEq/L, Cl 104 mmol/L, K 3.8 mEq/L, Mg 2.16 mg/dL, Na 140 mEq/L, Phosphorus 3.8 mg/dL.

At admission, it was classified as high-risk obesity and blood pressure was recorded above its 99th percentile for height and age. Therefore, medical treatment with hydralazine was required, maintaining spontaneous uresis at 30 ml, without water retention data. When Cushing's syndrome was suspected due to secondary arterial hypertension and obesity, morning cortisol was requested with a result of 41.4 g/dL (VN 2.5-12.5 g/dL) and ACTH, which was within normal parameters, so it was suspected that Cushing's syndrome ACTH independent, considering as possible causes in childhood, adrenal tumor, so it was requested to perform CT scan of simple and contrasted abdomen with evidence of tumor of homogeneous characteristics, well-defined walls, with regular edges of 3.3 cm × 4 cm, dependent on the adrenal gland (Figure 2), was assessed by the pediatric oncological surgery service where elective surgery, right suprarenalectomy was decided, before surgery 50 mg of hydrocortisone in three doses in continuous infusion was started, with the purpose of preventing and avoiding adrenal crisis after adrenalectomy.

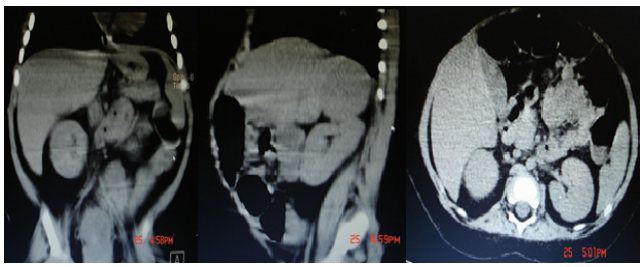

Figure 2: (Left) TAC simple of the abdomen in sagittal section, (in the middle) TAC simple of the abdomen in coronal section, (Right) TAC simple of the abdomen in axial section.- Right suprarenal tumor homogeneous of regular edges without invasion to structures. Adjacent 3.3 × 4 cm, with densities <10 Hounsfield suggestive of bp adrenal adenoma.

Step to the operating room (Figure 3) In which right suprarenalectomy was performed, finding the following: Adrenal tumor of 4 × 4 × 3 cm with well-defined edges, pale yellow color, no hemorrhages (Figure 4) with subsequent admission to the intensive therapy service for postsurgical management with the following vital signs fc 100 bpm, fr 26, temperature 36.5, hemodynamically stable TA 100/50 mmHg and with the requirement of invasive mechanical ventilation, with an approximate stay of 6 days in intensive care, and subsequently floor in charge of surgery, internal medicine, nutrition and pediatric endocrinology studying with satisfactory recovery so he was discharged, being hospitalized a total of 21 days. Histopathological report of adenoma-like adrenal cortex tumor (Figure 5). Follow-up was given in the outpatient consultation to the sixth month with laboratory and cabinet controls without evidence of tumor activity.

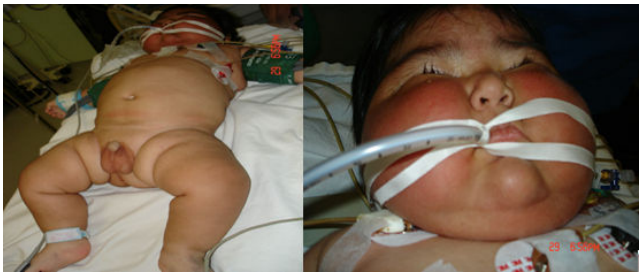

Figure 3: Infant of 11 months in dorsal decubitus, face in full moon, abundant peripheral adipose tissue, virilization, with cardiorespiratory monitoring and anesthetic protocol (general anesthesia), in the operating room.

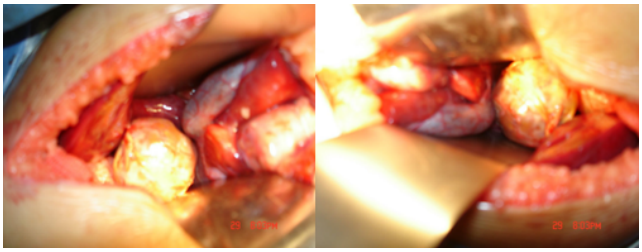

Figure 4: Right subcostal incision up to midline, liver, gallbladder, omentum with no evidence of tumor activity, no adenopathies, 4 × 4 × 4 cm tumor with rounded edges, right adrenal gland dependent of fat characteristics which do not invade adjacent structures.

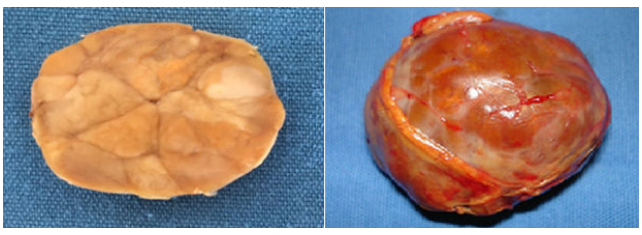

Figure 5: Adrenal adenoma Right 4 × 4 × 4 cm in cross-section, with regular edges, yellow coloration.

Results and Discussion

Cushing's Syndrome (CS) is rare in children and adolescents (10% of the general incidence of the disease), which constitutes an important diagnostic and therapeutic challenge. Regarding the distribution by sex, unlike the female preponderance of the disease in the adult population, in the prepubertal age, it is more frequent in males, with equal distribution during puberty and predominance in girls in postpubertal ages [3].

The SC is classified as exogenous or iatrogenic and endogenous [4]; and this one in dependent ACTH if it is more than 15 pg/mL of this hormone, or independent ACTH if there is less than 5 pg/mL [5], the latter being a very rare entity; with an incidence of 2 to 4 cases per million inhabitants per year [6]. From the clinical point of view, patients with SC can have a similar phenotype, which makes the diagnosis more probable (Table 3). The most sensitive indicator of hypercortisolism in children is growth retardation. Within the tumors originating in the adrenal gland are divided into a) Adrenal cortical or corticosuprenal tumors (TCS); and b) pheochromocytomas and paragangliomas [7].

Sign or symptom	Published incidence (%)
Central obesity	79-97
Facial plethora	50-94
Impaired glucose tolerance	39-90
Weakness, proximal myopathy	29-90
Arterial hypertension	74-87
Psychological changes	31-86
Fragile capillary	23-84
Hirsutism	64-81
Oligomenorrhea or amenorrhea	55-80
Impotence	55-80
Acne or seborrhoea	26-80
Abdominal stretch marks	51-71
Maleolar Edema	28-60
Back pain, vertebral collapse or fracture	40-50
Polydipsia, polyuria	25-44
Kidney stones	15-19
Hyperpigmentation	4-16
Headache	0-47
Exophthalmos	0-33
Tinea versicolor	0-30
Abdominal pain	0-21

Table 3: Signs and symptoms of Cushing's syndrome.

In children, the most prevalent tumor of adrenal origin is neuroblastoma, whereas TCS as a whole is extraordinarily infrequent, being rare in children and adolescents, so practically no pediatric endocrinological or oncological center has experience in its diagnosis and follow-up. They appear with a bimodal distribution, with a maximum in the first decade of life and another at 52 years for adenomas and 39 years for adrenal carcinomas. Among the most common chromosomal alterations observed in children with TCS are found in chromosomes 9q34 and 10p21; Among the oncogenes involved are RAS (aldosterone-producing adenomas), β-catenin, IGF-II genes involved in tumor suppression TP53 and MEN1. Adrenal cortical tumors can be associated with the Li-Fraumeni syndrome, multiple endocrine neoplasia type 1, Beckwith-Wiedemann syndrome, Carney complex [7].

In childhood, half of the cases of Cushing's syndrome are due to adrenal carcinoma, while the sixth part is due to benign adrenal disease, and they are usually more frequent in females. The case we presented was that of an 11-month-old male infant, with a histopathological report of adrenal adenoma. Among the suprarenal masses that produce cortisol, half of the cases are due to adenoma in most series. 20% of benign and malignant adrenal tumors share virilizing or feminizing effects [8]; the virilizing form is the most common form of presentation in children (50%-84% depending on the series) secondary to the existence, in most cases, of carcinoma [9]. In this case, it was presented with data of early virucidal pseudopuberty, which is defined as the onset of puberty before the age of eight in girls and the age of nine in boys. It is very important to identify the cause since untreated patients show height loss of approximately 20 cm for boys and 10 cm for girls and a reduction in growth potential even after treatment of the disease [10]. Since the inhibitory effect of hypercortisolemia on GH secretion continues for at least 1 or 2 years. It is likely that the age of onset and the duration of hypercortisolemia before healing are factors that determine the severity of the delay and the final height reached.

Once the clinical suspicion of SC is established, the existence of hypercortisolism should be confirmed by means of biochemical tests. The examinations recommended in the latest guidelines of clinical practice of the American Society of Endocrinology (Endocrine Society) are Free cortisol in urine 24 hours (CLU), suppression test with 1 mg dexamethasone at 23 h (Nugent test) and nocturnal salivary cortisol. However, the determination of urinary free cortisol in screening and testing with low doses of dexamethasone raises the difficulty of inadequate collection, especially in younger children. The measurement of urinary cortisol should be corrected by the body surface area; normal values <70 μg/m^2/day (198.7 nmol/m^2/day) are considered. There are authors who affirm that the most effective screening test is the measurement of plasma cortisol at 24:00 hours, despite the difficulty of its ambulatory performance. The combination of nocturnal determination of salivary cortisol with the response after 1 mg of dexamethasone at night has high sensitivity (100%) and specificity (93%).

You can also find alterations in laboratory tests such as: Aneosinophilia, lymphopenia, hyperglycemia, hypertriglyceridemia. Before virilizing TCS, the levels of 17 urinary ketosteroids and/or dehydroepiandrosterone (DHEA), DHEA sulfate (DHEA-S, exclusive adrenal production), circulating androstenedione and testosterone will be determined. In the presence of feminizing tumors, estrogen levels in plasma will be determined, including estradiol and estrone, as well as sodium, potassium, and cortisol.

Ultrasonography, which is easily accessible, easily performed and has no radiation, has little sensitivity for the evaluation of the adrenal glands, beyond the first months of life, so it is not the first choice, although it may determine the presence of In adrenal masses, computerized axial tomography (CT) with intravenous contrast medium and Magnetic Resonance Imaging (MRI) is considered to be of choice for evaluation of the adrenal glands. In recent years, the progressive use of increasingly better diagnostic imaging methods has provided a better anatomical detail, which has increased the number of adrenal lesions detected incidentally [11]. When the mass is unilateral,

the diagnosis of cortical adrenal adenoma is firm. If the mass is bilateral, it is useful to perform an adrenal scan to know if the activity is unilateral (and the contralateral mass is a formation not related to the syndrome) or bilateral, in which case the study protocol of aberrant or illegitimate recipients may be considered.

Treatment

The initial treatment in the endogenous CS of any etiology is surgical. Most adrenal tumors are benign and in these cases, unilateral adrenalectomy is indicated, the complexity of this type of surgery derives from its difficult surgical approach, so it is suggested that it be performed by specialized surgeons in the case.

Conclusion

A broad clinical history and an adequate physical examination should be performed in the presence of suspected hypercortisolism data in pediatric patients such as obesity, growth retardation, typical fascies, hypertension, and in some cases, virilization or feminization. Given the suspected diagnosis, request laboratory and cabinet studies since, as it is a rare disease in children, it is very difficult to diagnose it. The treatment of endogenous Cushing's syndrome will always be surgical and not treating this disease not only increases the risk of osteoporosis at early ages but also increases the delay in bone growth before and in a lower percentage after surgical treatment.

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