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Pediatric Adrenocortical Carcinoma: Diagnostic Challenges and Therapeutic Approach — A Case Report

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Abstract
Adrenocortical carcinoma (ACC) is a rare tumor. It constitutes 0.2% of malignant tumors in children and it is considered ten times rarer than in adults. Patients with predisposing syndromes like Li-Fraumeni or Beckwith-Wiedemann may develop these tumors.
Clinical symptoms are dominated by endocrine signs, which are present in 90% of cases. The primary cause is virtualization syndrome, which may occur alone or in conjunction with secondary symptoms caused by hypersecretion of adrenal hormones.
Imaging is indispensable in assessing the malignant nature of the adrenal tumor and its extent. Currently, surgical excision of the tumor is the cornerstone of treatment because its quality often depends on the prognosis of the disease. Adrenocortical carcinoma has a poor prognosis despite treatment, with high chances of recurrence and mortality.
Keywords: Adrenocortical Carcinoma, Child, Mortality, Surgical Procedures, Virilism

Introduction

Adrenocortical carcinoma (ACC) is a rare tumor that constitutes 0.2% of malignant tumors in children with an incidence of 0.2 to 0.3 per million people. In children, adrenocortical carcinoma is considered ten times rarer than in adults. In southern Brazil, however, the incidence is very high among children, this is likely due to a mutation of the TP 53 gene (1). The sex ratio is (1.5/ 1 ratio), and it is more common in girls than in boys (2). This predominance is due to signs of hypersecretion which are linked mainly to androgens in females and to cortisol in both sexes.

These tumors can arise in patients who have predisposing syndromes such as Li-Fraumeni or Beckwith-Wiedemann syndromes. These syndromes contribute to ACC development by the existence of germline mutations within the TP53 gene in approximately 70% of cases.

Then loss of function of p53 following a gene mutation can lead to the accumulation of genetic disorders responsible for tumor proliferation, as well as a deregulation of the expression of genes in the chromosomal region 11p15 (3, 4).

The diagnosis is supported by clinical, biological, radiological, and pathological evidence. The clinical manifestations of the tumor can differ depending on its secretory status. The most frequent mode of revelation is the appearance of clinical signs of hyperandrogenism as virilization which is present in over 90% of cases. Hypertension may also be present. Hirsutism, acne, and a deep voice can be seen (5).

The only option for radical treatment is currently surgical. Although management has implemented various therapeutic strategies, the prognosis remains poor (6).

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Case Report

A 15-month-old girl with no previous pathological history. She presented 1-month abdominal distension, the appearance of pubic virilization an enlarged clitoris (**Fig.1**), and cheek acne.

Abdominal ultrasonography (US) showed an encapsulated left adrenal mass of 87x60 mm.

Biological findings included midnight cortisol 17.1 microgram/dl (very high), ACTH 1.1 pg/ml (very low). A brake test of dexamethasone was negative for cortisol 16 microgram/dl (high), aldosterone 1330 pg/dl (high), estradiol 31.7 pg/dl (high), progesterone 1.36 ng/ml (high), FSH < 1.7 IU/L

The remainder of the preoperative evaluation was normal.

An abdominal CT scan revealed a large mass on the left adrenal gland, measuring 93x70 mm encapsulated, with calcifications and areas of necrosis, without signs of local or regional invasion or secondary location (**Fig.2**)

A cerebral MRI and bone scan were performed: in search of a central or bone origin, which were normal.

She had a successful complete surgical resection (**Fig.3**) and was released after 5 days, she was given antihypertensive medication and instructed to follow up with local care every day.

The study of histology revealed stage II adrenal carcinoma with a Weiss score of 6.

The patient had a positive clinical outcome with blood pressure stabilizing during treatment, then she was redirected to pediatrics.

After multidisciplinary consultation. The short-term evolution was marked by death from multiple organ failure due to the negligence of parents who refused to accept the disease, despite repeated explanations from doctors about the risk of the disease.

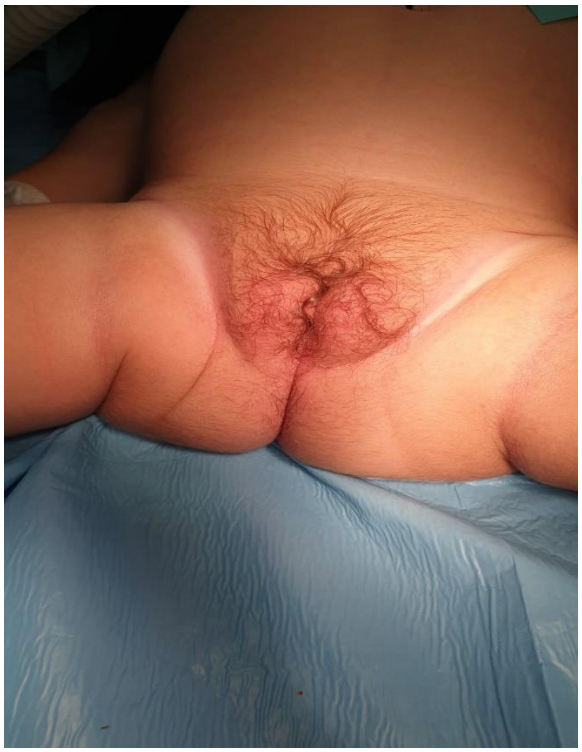


Figure 1. Clinical aspect showing virilism in a female child

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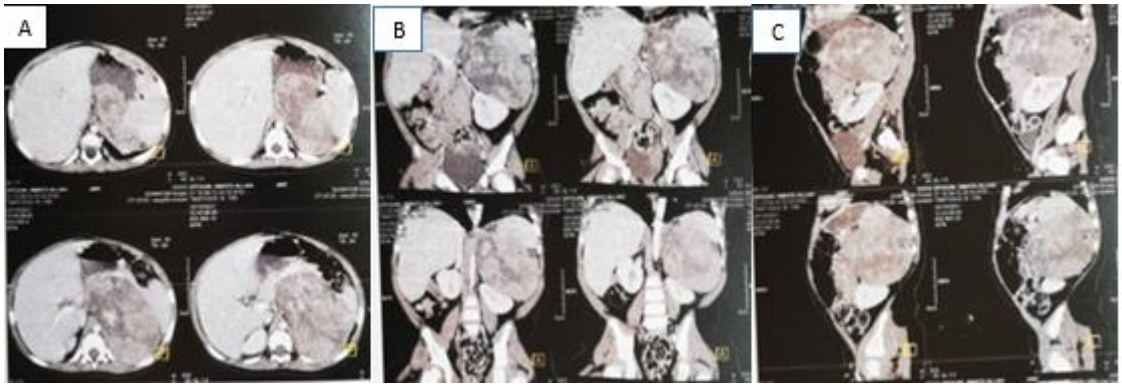


Figure 2. Abdominal contrast-enhanced CT scan in axial (A), coronal (B), and sagittal (C) planes demonstrating a large heterogeneous right adrenal mass with areas of necrosis and calcification, displacing adjacent organs

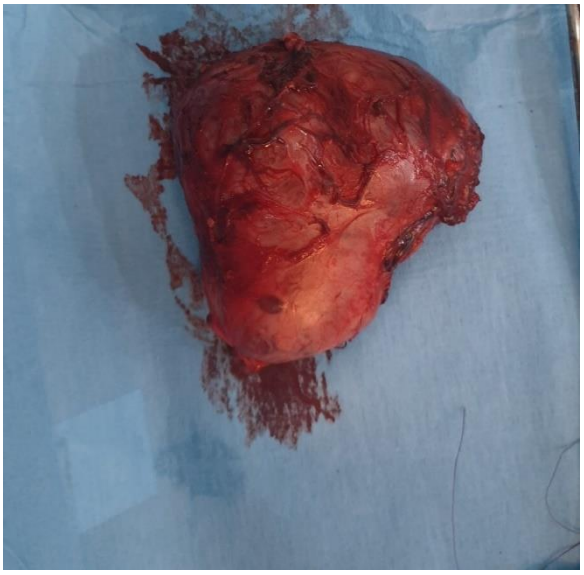


Figure 3. Macroscopic view of the resected adrenal tumor, measuring 90 × 65 mm, with a lobulated surface and areas of hemorrhage

Discussion

The adrenal gland is the origin of three distinct tumors, neuroblastic tumors, Pheochromocytoma, and adrenocortical tumors (ACT), which are present during childhood.

Neuroblastoma and pheochromocytoma are derived from the adrenal marrow, whereas ACT is a result of ACT developing from the adrenal cortex (7).

Adrenocortical carcinoma is rare in children, Since the description of the first pediatric case of adrenal tumor in 1865, only a few cases have been reported (8).

The curve for age-incidence is bimodal, there is a peak around the age of 3 years old, followed by a second peak during adolescence, with female predominance (9).

In general, the pathogenesis is not completely understood (10).

ACC is most frequently associated with endocrine clinical signs, which are present in 90% of cases. The primary cause is virtualization syndrome, which may occur

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alone or in conjunction with secondary symptoms caused by hypersecretion of adrenal hormones. The most common virilization symptoms were: the appearance of pubic hair; facial acne; clitoral hypertrophy; voice changes; hirsutism; acceleration of growth and penile enlargement (4).

Excess glucocorticoids can cause Cushing's syndrome. When the tumor secretes aldosterone or steroid precursors, it may cause arterial hypertension with hypokalemia (1).

In 10% of instances, the ACC was considered non-functional due to the absence of secretion. There was a slight prevalence of involvement in the left gland, accounting for 53.8% of cases (11).

In this case, the patient's symptoms were comparable to those reported in the literature, highlighting the manifestations of excessive corticosteroid secretion. Pathologies associated with ACC include Beckwith-Wiedemann, multiple endocrine neoplasia type 1, Li-Fraumeni syndrome, hamartomatous defects, and congenital defects of the genitourinary tract (9).

The laboratory workup for ACC typically involves measuring urinary steroid levels. This is done through a 24-hour urine collection to assess the levels of 17-ketosteroids (particularly dehydroepiandrosterone, or DHEA) and 17-hydroxysteroids. Also the measurements of serum cortisol, dehydroepiandrosterone sulfate (DHEA-S), androstenedione, 17-hydroxyprogesterone, aldosterone, and testosterone (12).

Imaging is indispensable in assessing the malignant nature of the adrenal tumor and its extent. Staging should include CT or MRI imaging. The typical appearance on computed tomography (CT) is that of a unilateral lesion, large, heterogeneous. These tumors tend to have a diameter of 8 to 10 cm or more, with the maximum diameter rarely being less than 3 or 4 cm as is the situation for our patient (13).

Imaging of the pelvis, chest, and abdomen, helps identify metastases, which commonly occur in the regional lymph nodes, kidneys, lungs, liver, and peritoneum.

The criteria for determining malignancy in pediatric adrenal cortical neoplasms are still unclear and are currently under discussion. The Weiss score was developed to establish the diagnosis of malignancy of adrenocortical tumors. The tumor is classified as malignant or suspicious for malignancy when the Weiss score is equal to or greater than 3 (1). Our patient had a Weiss score of 6 and the pathologist confirmed the malignancy.

Several methods, particularly molecular biology, are currently under study and some of them may be very useful in the future. Better molecular understanding may identify new druggable targets, which will be a step towards more personalized therapy to enhance our understanding of the molecular basis of pediatric ACC and its treatment in an international context (7). These therapies allow to predict the prognosis and provide additional therapies after surgery.

Currently, surgical excision of the tumor is the cornerstone of treatment because its quality often depends on the prognosis of the disease. This surgery should be performed by an experienced surgical team. Laparoscopy is recommended for small lesions, while larger tumors that invade neighboring tissues require laparotomy with wide excision with sacrifice procedures (14).

In stage 4, surgery can reduce tumor volume and sometimes be used on accessible metastases, especially in the liver.

The majority of authors reported using chemotherapy and surgery for patients in advanced stages, specifically stages III and IV. There are several chemotherapy options available for the treatment of ACC. These include drugs such as vincristine, ifosfamide, adriamycin, carboplatin, etoposide, and mitotane. Although there is

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no consensus on the effectiveness of mitotane in pediatric patients, it is still prescribed in cases where tumor resection is not possible or there is metastatic disease (11).

For patients with tumors that cannot be completely removed, neoadjuvant therapy should be considered. Adjuvant therapy is recommended if there is any tumor spillage during surgery, while salvage chemotherapy is used for local relapse and secondary metastases.

In pediatrics, local radiotherapy has been shown to enhance both overall survival and disease-free survival rates, for several tumors, including neuroblastoma. In addition to surgical therapy, radiotherapy's impact on local recurrence in pediatric patients needs further evaluation (7).

Our patient did not benefit from chemotherapy or radiotherapy because she has no metastasis and her tumor was completely removed (stage II).

The most commonly reported risk factors are age over 4 years, extension of primary disease to adjacent structures, presence of metastases, a high tumor pathology score, and advanced disease stages are associated with a poor prognosis (11).

Despite the treatment efforts by the various multidisciplinary medical teams, the prognosis for adrenocortical cancer is poor with recurrence and death.

Although our patient presents a tumor located at (stage 1) which should have a much better prognosis, the patient died of a multiorgan failure given that the parents did not accept the disease.

Conclusion

Adrenocortical tumors in children have a very low incidence, which partly explains why pediatric oncologists sometimes have little knowledge about them. This tumor is aggressive due to its large size at diagnosis and already has metastases. The most clinical manifestation is virilisation which orientates the diagnosis more rapidly. Imaging is indispensable in the management of these tumors. Treatment is primarily surgical with total resection of the tumor.

A collaborative approach among pediatrics, pediatric surgery, anesthesiology, and pathology enhances diagnosis and expedites treatment.

The information of the parents about the risk and prognosis of the disease remains essential and a real challenge.

This case report contributes to the existing literature and emphasizes the importance of timely intervention by clinicians.

Ethical Considerations

Informed written consent was obtained from the parents of the patient for publication of this report.

Acknowledgments

During the preparation of this work the author(s) did not use AI.

Author’s Contributions

Assia Haif analyzed and interpreted the patient data regarding adrenocortical carcinoma and carried out the surgery. Djelloul Achouri proposed the design of the case report. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare that they have no competing interests.

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