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Case Report

Adrenocortical neoplasm in a 2-year-old child: Clinical approach and diagnostic imaging ☆,☆☆

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ABSTRACT

Adrenocortical tumors in children and adolescents are rare and aggressive, accounting for only 0.2% of pediatric cancers, with most cases associated with Li-Fraumeni syndrome. The most common manifestation is virilization due to androgen excess. Imaging techniques are crucial in the diagnosis and management of pediatric adrenocortical carcinoma. CT and MRI are essential for differentiating between benign and malignant lesions and assessing tumor characteristics and extent. Correlating imaging findings with clinical and histopathological data is vital for optimal diagnosis and treatment, underscoring the need for a multidisciplinary approach to managing these rare but aggressive neoplasms. This report presents the case of a previously healthy 2-year-old boy who exhibited virilization symptoms and was diagnosed with adrenocortical carcinoma.

Introduction

Adrenocortical tumors in the pediatric and adolescent population are rare and aggressive [1]. According to the United States National Cancer Institute, pediatric adrenocortical tumors account for 0.2% of all childhood cancer cases, with most being diagnosed in the context of Li-Fraumeni syndrome [2]. The incidence in southern and southeastern Brazil is approximately 15 times higher than in the United States. Pediatric adrenocortical tumors are most frequently diagnosed between the ages of 0 and 4 years [3]. The most common manifestation is typically virilization due to excess androgens, with or without the presence of other adrenal hormones [4].

Accurate visualization of the tumor and potential metastases is crucial, making computed tomography (CT) and magnetic resonance imaging (MRI) effective tools for the differential diagnosis of adrenal masses. Although these methods alone cannot accurately determine the nature of the tumor, a comprehensive clinical approach, informed by an understanding of the clinical manifestations and pathophysiology of adrenal tumors, can help differentiate between high-risk and low-risk neoplastic lesions [2].

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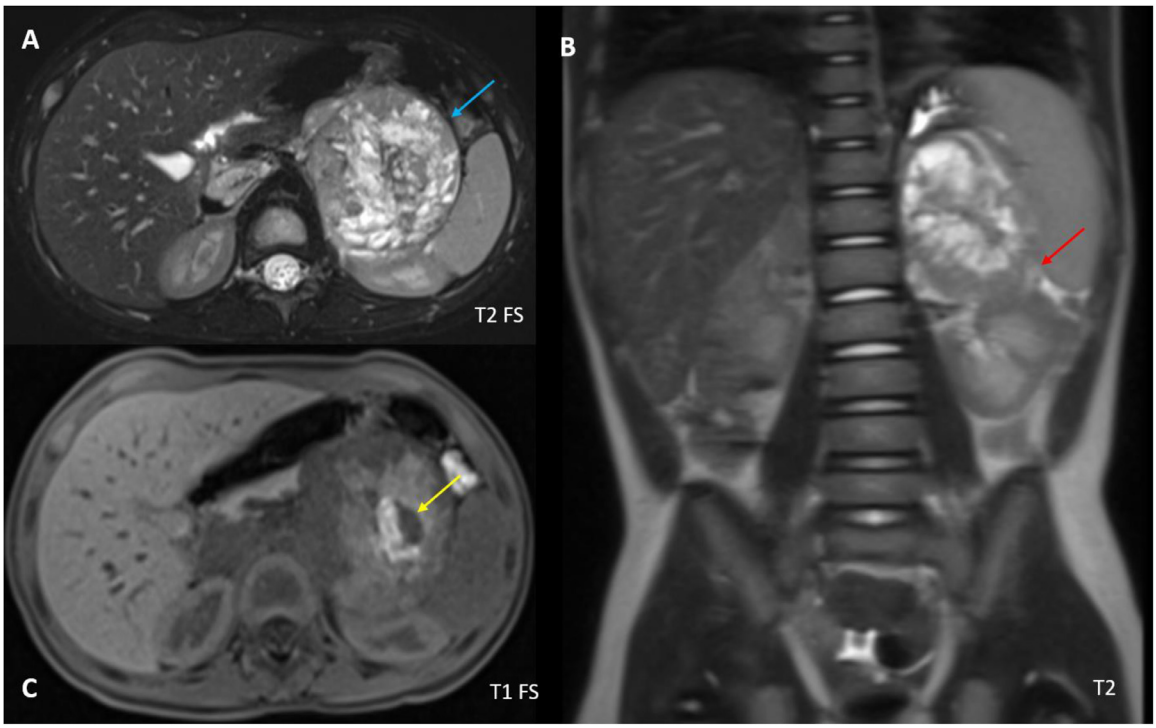

Fig. 1 – A: A mass (blue arrow) replaces the left adrenal gland. It has an oval shape with well-defined borders, exerts a compressive effect on adjacent structures, and loses the separation plane with the upper pole of the left kidney due to infiltration (B: red arrow). The signal intensity is heterogeneous, predominantly hyperintense on T2 (relative to the liver) with cystic foci. The peripheral region of the mass shows an area of lower signal intensity, which appears hypointense on T1 FS sequence (C) with central hyperintensity, consistent with a hemorrhagic focus (yellow arrow).

We present the case of a previously healthy 2-year-old boy who was admitted to the emergency room after experiencing his first episode of pallor, loss of postural tone, fixed gaze, unresponsiveness to stimuli, and respiratory distress. Physical examination revealed signs of hypervirilization, and imaging confirmed the diagnosis of an adrenocortical neoplasm.

Case presentations

A previously healthy 2-year-old male patient was admitted to the emergency room with a one-hour history of mucocutaneous pallor, fixed gaze, loss of postural tone, unresponsiveness, and signs of respiratory distress, including tachypnea and nasal flaring. Family members reported no relevant medical history. On physical examination, the patient was somnolent, with no meningeal signs, and was noted to have pubic hair, increased muscle mass, and macropenis.

Given these signs of hypervirilization, the patient was evaluated by pediatric endocrinology, who ordered laboratory tests and imaging studies. The results showed normal cortisol levels, negative BHCG, normal LH/FSH, elevated testosterone, and dehydroepiandrosterone levels >1000. A contrast-enhanced abdominal MRI revealed a left adrenal neoplasm measuring $8.3 \times 7 \times 5.7$ cm, highly suggestive of carcinoma, with invasion into the anterior margin of the upper pole of the left kidney, a tumor thrombus extending from the left adrenal vein through the distal renal vein to the retrohepatic inferior vena cava, and precaval lymphadenopathy (Figs. 1, 2, and 3).

Based on these findings, a chest CT scan was ordered, which revealed 4 bilateral metastatic pulmonary nodules and prominent pulmonary arteries with central filling defects in several segmental arteries of the lower lobes, indicative of pulmonary thromboembolism (Figs. 4 and 5). Subsequently, an image-guided biopsy using the ROSE technique was performed, which identified an adrenocortical neoplasm of uncertain malignancy, with p53 overexpression (>5%) and a Ki67 cell proliferation index of 20%.

Given these findings, the oncology team proceeded with chemotherapy, including Mitotane, Cisplatin, Etoposide, and Doxorubicin. Despite this treatment, the patient's condition did not improve; he developed extensive intraparenchymal cerebral bleeding with cerebellar tonsil herniation and ultimately died.

Discussion

Three different types of tumors originate in the adrenal gland during childhood: neuroplastic tumors, pheochromocytoma, and adrenocortical tumors (ACT) [5]. Malignant adrenocortical tumors (ACT), such as adrenocortical carcinoma (ACC), which originate from the adrenal cortex, are rare in childhood, accounting for 0.2% of all pediatric malignancies and 1.3% of all carcinomas in this age group [5,6]. The incidence reported in the literature is 0.2-0.3 cases per million children per year,

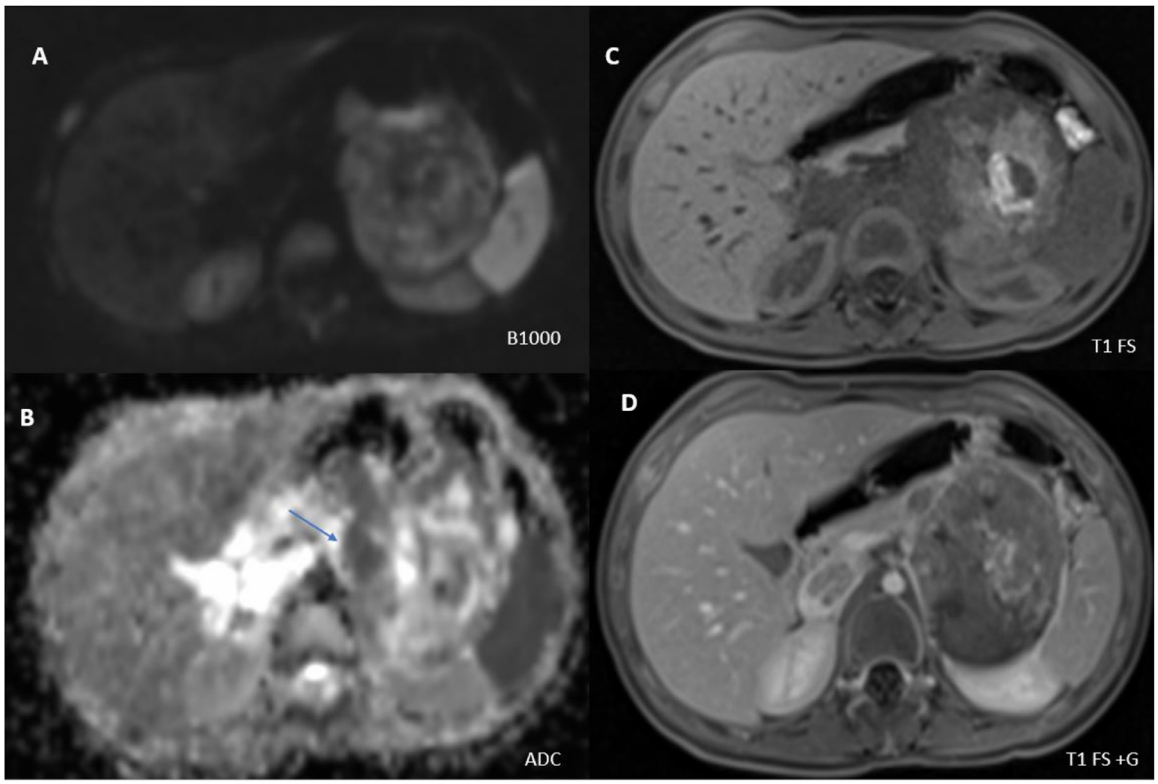

Fig. 2 – A-B: Diffusion sequences show restricted diffusion at the periphery, with marked hypointensity at the anterior and medial margins on the ADC map, corresponding to areas of high cellularity (blue arrow). These areas also demonstrate heterogeneous enhancement on postcontrast sequences (C and D).

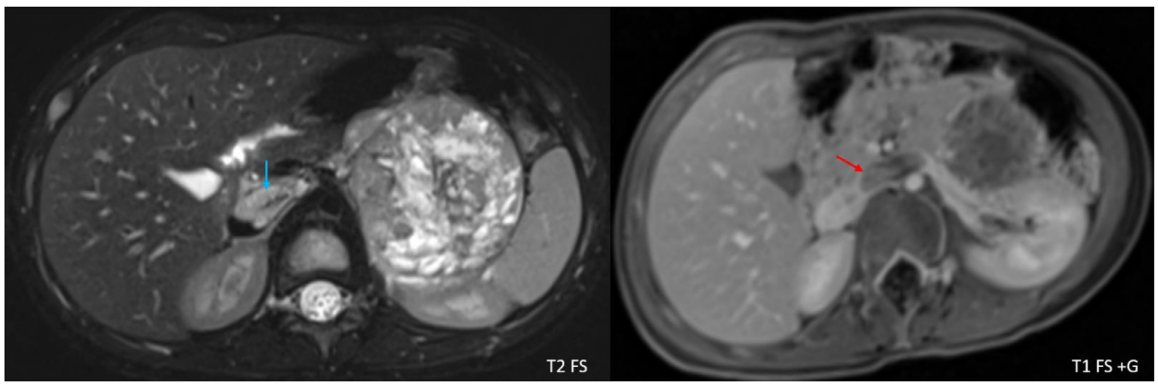

Fig. 3 – In image A, loss of signal void of the inferior vena cava (blue arrow) is observed, secondary to a hyperintense solid mass with heterogeneous enhancement, as seen in image B, originating from the left renal vein (red arrow) and adrenal vein, consistent with a tumor thrombus.

with the highest incidence observed in children under 5 [7]. Notably, the incidence rate of pediatric ACC in southern and southeastern Brazil is nearly 15 times higher compared to the global incidence. This elevated incidence is likely attributable to the high prevalence of the TP53 p.R337H founder mutation in this region [3].

Regarding the pathophysiology of ACC, tumorigenesis is mediated by β-catenin, insulin-like growth factors, p53/Rb signaling, and chromatin remodeling processes. The early onset of the disease and hormone-mediated virilization may be due to its origin in the fetal zone of the adrenal gland [5].

Most adrenocortical carcinomas (ACC) are hormone-producing, leading to an excess of glucocorticoids or androgens. However, about 15% of ACC cases are diagnosed incidentally [8], with venous invasion—often involving the inferior vena cava—being the most frequent complication

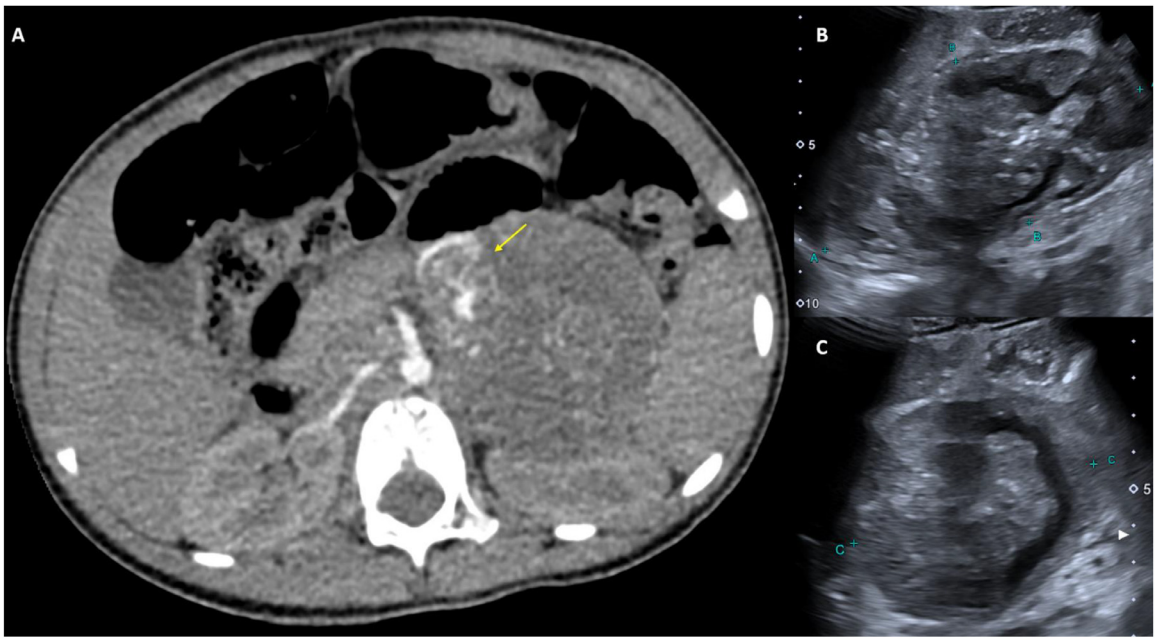

Fig. 4 – A: Image from chest CT scan showing the appearance of the lesion with this modality: Left adrenal mass, heterogeneous, predominantly hypodense with multiple tortuous arterial structures towards its medial margin (yellow arrow). B-C: On ultrasound, this mass appears highly heterogeneous, representing its different solid, cystic-necrotic, and hemorrhagic components.

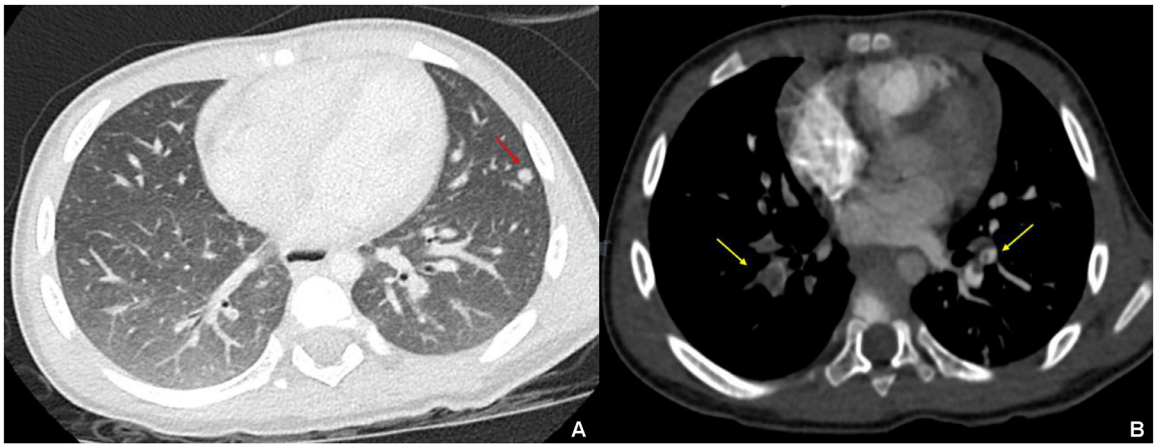

Fig. 5 – Chest CT scan: lung window (A) shows a solid, round nodule with spiculated margins located in the inferior lingular segment (red arrow). In the vascular structures evaluation window (B), multiple central filling defects are observed in the segmental arteries of both lower lobes (yellow arrows), consistent with pulmonary thromboembolism.

[9]. Diagnosis can be made through pathological features, immunohistochemical markers, reticulin histochemical staining, and imaging findings [10].

The Modified Weiss criteria and angioinvasion have demonstrated diagnostic value for adrenocortical carcinoma (ACC), while the utility of immunohistochemistry and histochemistry is limited [10]. In pediatric adrenal cortical neoplasms, the definitive criteria for malignancy remain uncertain and are subject to debate, as these neoplasms can behave differently in children compared to adults. Although the criteria used in adults are useful, they are not directly applicable to the pediatric population [10].

Other criteria that have been studied include the Wieneke criteria (WC), modified Wieneke criteria (WCm), and the modified reticulin algorithm (RA). The WC is highly predictive of clinical outcomes; additionally, invasion of the vena cava and peri-adrenal extension is 100% specific for diagnosing adrenal cortical neoplasia [11]. The RA is comparable to WC and WCm, easier to apply, and a more sensitive histopathologic approach to identifying aggressive behavior in pediatric adrenal cortical neoplasms. Therefore, integrating RA with WC may be useful for assessing pediatric adrenocortical neoplasms of uncertain malignancy and warrants further investigation [5].

The prognosis for these patients is heterogeneous and challenging to predict, leading to the investigation of various biomarkers, including TCD8+ lymphocytes, Ki-67, and p53, among others. It has been observed that the presence of symptoms combined with a Ki-67 level ≥ 30% predicts shorter survival [10]. However, other research indicates that Ki-67 lacks reliable prognostic value in pediatric ACC, limiting its usefulness to the adult population with this tumor. There is also evidence suggesting an association between TCD8+ lymphocyte infiltration and improved prognosis, though further studies are needed to confirm this [12]. Additionally, several risk factors are linked to a poor prognosis, such as a high mitotic rate, overexpression of GATA4, a high percentage of necrosis, larger tumor size, metastasis, and advanced age at diagnosis [5,13].

The role of imaging techniques in diagnosing adrenal lesions is crucial for distinguishing between benign and malignant lesions, as well as between metastatic and non-metastatic conditions. These techniques aim to provide a conclusive diagnosis, thereby reducing the need for additional invasive procedures [14].

Contrast-enhanced computed tomography (CT) is the preferred imaging method for identifying adrenal lesions due to its wide availability and high spatial and temporal resolution [15]. In CT images, adrenocortical carcinoma is often characterized by heterogeneous enhancement, either peripheral or rim-shaped, resulting from areas of hemorrhage or necrosis within the tumor. Occasionally, particularly in children, these tumors may be smaller (less than 5 cm) and have a regular shape, which can lead to confusion with adenomas [15].

Magnetic resonance imaging (MRI) is highly effective in characterizing adrenal lesions due to its superior contrast resolution and ability to differentiate tissues. This capability is particularly useful for identifying various tissue components within heterogeneous lesions [15]. The accuracy of MRI can be further enhanced with the use of contrast agents such as gadolinium. After administration, 90% of adenomas show homogeneous enhancement, whereas 60% of malignant lesions exhibit heterogeneous enhancement [16]. Additionally, diffusion-weighted MRI (DW-MRI) has shown promising results using apparent diffusion coefficient (ADC) maps, as ADC can differentiate between benign and malignant solid tumors [17].

MRI has specific features useful for diagnosing adrenal carcinoma (ACC), including signals that vary from isointense to hypointense on T1-weighted images, a hyperintense signal on T2-weighted images, and a heterogeneous signal decrease on chemical shift imaging [18]. Consequently, MRI has become increasingly important in the diagnosis, staging, and treatment of solid tumors in pediatric patients, thanks to its high resolution and lack of ionizing radiation [19]. This highlights the importance of correlating MRI findings with clinical manifestations and histological analysis of the lesions, as noninvasive discrimination of different tumor types can be of great clinical value [17].

Currently, management options for pediatric adrenocortical neoplasms include surgery, radiotherapy, and chemotherapy. In most patients, the first line of treatment is surgery to respect the tumor and perform a lymphadenectomy, as many relapses are due to local recurrence or metastasis to lymph nodes [5]. Chemotherapy is administered to pediatric patients in advanced stages of the disease, typically using a combination of mitotane, cisplatin, etoposide, and doxorubicin, which has been primarily studied in the adult population [20]. Radiotherapy has been shown to decrease local recurrence in adults, but more studies are needed in the pediatric population to determine its positive effects on disease-free survival, as has been observed with its use in tumors such as neuroblastoma [21].

Conclusion

In the diagnosis and management of pediatric adrenocortical carcinoma, imaging techniques play a crucial role. Contrast-enhanced computed tomography and magnetic resonance imaging are essential methods for differentiating between benign and malignant lesions and assessing the tumor's extent and characteristics. These techniques not only enable accurate characterization of adrenal lesions but also help avoid unnecessary invasive procedures. Magnetic resonance imaging offers additional advantages due to its high resolution and absence of radiation, which is particularly important in the pediatric population. Correlating imaging findings with clinical and histopathological data is vital for optimal diagnosis and treatment, emphasizing the importance of a multidisciplinary approach in managing these rare but aggressive neoplasms.

Patient consent

The reported case was reviewed and approved, and individual patient consent was obtained following institutional guidelines.

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