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Pediatric adrenocortical tumor in a 17-month-old girl: Diagnostic and therapeutic challenges in a rare case of virilization

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Case Report

Abstract

BACKGROUND: Adrenocortical tumors (ACTs) are extremely uncommon in children. These tumors predominantly secrete hormones, leading to significant clinical manifestations, including peripheral precocious puberty and virilization. The diagnostic approach, which includes clinical assessment, laboratory tests, imaging, and histopathological evaluation, presents challenges in differentiating benign from malignant ACTs.

CASE REPORT: We describe a 17-month-old girl who underwent pubic hair growth over a four-month period. Imaging tests revealed a solid-cystic mass in the right adrenal gland, which raised suspicion of malignancy. Histopathological analysis confirmed an ACT with moderate to high nuclear atypia and lymphovascular invasion following the patient's right adrenalectomy. Adjuvant treatment with doxorubicin, etoposide, and cisplatin was started because of the tumor's intermediate malignancy score and lymphovascular invasion.

CONCLUSION: This case report emphasizes how difficult it is to diagnose and treat pediatric ACTs, underscoring the significance of early identification, thorough evaluation, and individualized care. Optimizing results requires a multidisciplinary approach and continuous follow-up due to the tumor's rarity and potential malignancy.

KEYWORDS: Adrenocortical Carcinoma; Virilization; Adrenal Neoplasm

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Introduction

Adrenocortical tumors (ACTs) are rare neoplasms that arise from the adrenal cortex, which is responsible for producing hormones. ACTs, such as adenomas and carcinomas, are uncommon in children. The tumors display unusual clinical and biological characteristics that distinguish them from other pediatric carcinomas and similar neoplasms in adults. In the pediatric population, the majority of ACTs are hormone-secreting lesions. Excessive production of adrenocortical hormones can result in symptoms such as virilization and Cushing's syndrome, with hyperaldosteronism occurring in rare cases. Nonfunctional tumors, defined as neoplasms that do not secrete adrenocortical hormones, represent approximately 10% of pediatric cases.[1]

At an incidence of 0.3 to 0.38 per million, ACT is more prevalent in female children under the age of five, and data from Iran suggest a similar trend. Clinical symptoms, laboratory tests, imaging scans, and histopathologic review are key components of the diagnostic process; however, distinguishing

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benign adrenocortical adenomas from carcinomas remains challenging.[2]

ACT is difficult to diagnose and depends on the physical and histological features of tissue samples taken after surgery. Hormonal activity is a hallmark of ACT, evident in more than 90% of cases.[1] The clinical manifestations arise from the tumor's overproduction of steroids and their precursors. Common abnormalities include elevated levels of testosterone, androstenedione, dehydroepiandrosterone sulfate (DHEAS), and 11-deoxycorticosterone. Surgery is the essential operation in the effective treatment of ACT. The efficacy of chemotherapy in the treatment of childhood ACT is unverified.[3] This report aims to describe the case of a 17-month-old girl with an ACT, outlining her clinical presentation, diagnostic process, surgical intervention, and histopathological findings to elucidate the challenges in diagnosing and managing pediatric ACTs.

Case Report

A 17-month-old girl was admitted in October 2024 with a chief complaint of pubic hair growth observed over the preceding four months. The patient's medical history was unremarkable, with no significant past medical issues or family history of similar symptoms or endocrine disorders. Physical examination revealed stable vital signs, and the abdominal examination was normal, showing no palpable masses or tenderness. No other areas of abnormal hair growth were noted. Routine laboratory tests, including complete blood count (CBC), electrolytes, liver, and renal function tests, were within normal limits.

We conducted imaging studies based on the clinical presentation. According to an abdominal ultrasound, there was a solid-cystic heteroechoic mass in the right adrenal gland. The mass had clear edges and measured 78 × 50 × 55 mm, giving it a volume of 115 cc. A contrast-enhanced abdominopelvic computed tomography (CT) scan was conducted to further characterize the lesion, which identified a large, heterogeneous mass in the right suprarenal region involving the right adrenal gland. The tumor exhibited trans-axial dimensions of 51 × 63 mm and a craniocaudal measurement of 73 mm. The mass was in direct contact with the inferior vena cava (IVC) and the right lobe of the liver. There was no fat around these structures to help identify the tumor. We noted mild luminal narrowing of the IVC, likely due to the mass effect and displacement of the right kidney's superior pole.

The differential diagnosis suggested a potentially malignant ACT, warranting surgical intervention. The patient received a right adrenalectomy for conclusive treatment and pathological assessment. The resected specimen was an encapsulated lobular mass, surrounded by adipose tissue, with dimensions of 8.3 × 7.6 × 4.5 cm and a weight of 130 grams. Upon sectioning, the mass displayed a homogeneous orange-yellow cut surface featuring a cystic region measuring approximately 3 × 2.2 cm, which contained bloody fluid.

The histopathological analysis of the specimen confirmed the diagnosis of adrenocortical neoplasm. The tumor exhibited polygonal cells with eosinophilic-to-clear cytoplasm, demonstrating moderate to high nuclear atypia at the microscopic level. Some cells displayed prominent nucleoli, arranged in sheets and nests. There was an increase in the mitotic rate, surpassing 15 mitoses per 20 high-power fields, along with numerous atypical mitotic figures. A solitary instance of lymphatic invasion was observed with no indications of necrosis present. The tumor received an intermediate malignancy score of 3 according to Armed Forces Institute of Pathology (AFIP) criteria for pediatric patients, categorizing it as low risk per the guidelines of the International Pediatric Adrenocortical

Tumor Registry (IPACTR). Despite the absence of capsular invasion, we noted lymphovascular invasion and found no necrosis or regional lymph node involvement. The staging criteria for pediatric adrenal cortical neoplasms classified the tumor as stage I.

Postoperatively, the patient recovered well and commenced chemotherapy with doxorubicin 20 mg/m^2 on days 1 and 8, etoposide 100 mg/m^2 on days 5-7, and cisplatin 40 mg/m^2 on days 1 and 9 to address the tumor's malignant potential. Her intermediate malignancy score and the occurrence of lymphovascular invasion informed the decision to commence chemotherapy.

Discussion

This study aimed to describe a rare case of a hormone-secreting ACT in a 17-month-old girl, highlighting the clinical presentation, diagnostic process, surgical intervention, and histopathological findings. ACTs originate from the adrenal cortex and are traditionally classified as epithelial tumors, either carcinoma or adenoma. In the pediatric population, these tumors are uncommon. They account for less than 0.5% of all childhood neoplasms and 6% of all pediatric adrenal tumors. Most ACTs happen randomly, but people with genetic syndromes like multiple endocrine neoplasia type 1 (MEN-1), Beckwith-Wiedemann syndrome (BWS), Li-Fraumeni syndrome (LFS), and other genetic cancers are more likely to develop a tumor.[2] Therefore, conducting genetic analyses in children diagnosed with ACT is crucial, especially for individuals who have a positive family history. Previous research has shown how ACTs and environmental variables, including fetal alcohol syndrome or prenatal exposure to toxins, are related; however, verification is challenging due to the potential association of these factors with other neoplasms.[2,4]

Virilization, characterized by early pubic or axillary hair start, acne, penile or clitoral enlargement, hirsutism, accelerated growth velocity, and voice changes, is the most common clinical manifestation of ACT in children. Cushing's syndrome is the second most prevalent manifestation, characterized by symptoms including central obesity, moon facies, and hypertension (HTN).[1] Central precocious puberty may develop from persistently high sex steroids that trigger the gonadotropin-releasing hormone (GnRH) pulse generator. Conn's syndrome, or primary aldosteronism, is frequently associated with bilateral cortical hyperplasia. Aldosterone-producing adenoma is infrequently observed in pediatric populations. Excessive levels of androgens and estrogens typically lead to accelerated growth rates and early closure of the epiphyses. The impact of abnormal exposure to adrenal hormones on final adult height remains uncertain.[1,5] The case findings align with prior studies reporting that most pediatric ACTs are hormone-secreting and present with symptoms such as virilization. This case's tumor met the criteria for intermediate malignancy, which necessitated the administration of adjuvant chemotherapy.

Imaging constitutes the next critical step in the evaluation process. Imaging is crucial for tumor localization, surgical planning, evaluation of distant metastases, and disease staging. Abdominal ultrasonography serves as the initial imaging modality for patients exhibiting symptoms of adrenocortical disease. CT represents a critical advancement in the diagnostic process, serving as the predominant imaging modality for the identification of adrenal tumors due to its optimal cost-benefit ratio. A CT scan of the abdomen allows for a more accurate assessment of the tumor compared to ultrasonography, particularly regarding size, capsule, calcifications, necrosis, and bleeding. CT facilitates the early detection of ACT and aids in preoperative staging for surgical planning; however, it has limitations and is unable to differentiate between benign

and malignant tumors.[5] Positron emission tomography (PET) effectively assesses the functional characteristics of lesions, and it is increasingly utilized in the initial assessment of ACT and in post-operative monitoring.[3]

Surgery is the most critical intervention for the effective treatment of ACT. Open surgery should take precedence over laparoscopic approaches in cases of malignant adrenal tumors. Hydrocortisone replacement therapy is very important before and after surgery for people whose adrenocorticotropic hormone (ACTH) levels are very low because their tumors are making too many steroids and stopping their pituitary glands from releasing ACTH.[6] The effectiveness of chemotherapy in managing childhood ACT remains uncertain. Adult patients with ACT frequently utilize mitotane, an adrenal cortex inhibitor, but its effectiveness in pediatric populations remains uncertain. When someone has aggressive ACT with metastases, cytostatics, primarily doxorubicin, cisplatin, and etoposide, are used to treat them. The investigation of immunotherapy's role in the treatment of adult patients with ACT is ongoing. Immune checkpoint inhibitors, such as pembrolizumab, could potentially be used.[1,4,7] In this patient, the primary treatment involved a right adrenalectomy, followed by chemotherapy with doxorubicin, etoposide, and cisplatin to address the tumor's malignant potential. Postoperatively, the patient showed satisfactory recovery, with no immediate complications noted. While chemotherapy's efficacy in pediatric ACTs remains uncertain, its use in this case was informed by the tumor's malignant characteristics and lymphovascular invasion, consistent with management strategies outlined in the IPACTR.

The heterogeneity of ACT has complicated the establishment of prognostic factors. There are four stages of ACT. Localized tumors that are ≤ 5 cm in size are classified as stage I, while those that are > 5 cm are classified as stage II. The presence of a tumor thrombus in the vena cava and/or renal vein, positive regional lymph nodes, or invasion of surrounding tissues characterizes stage III. When distant metastases arise, it is a sign of stage IV. A favorable prognosis is linked to stage I and II, age under 4 years, lower tumor size, and virilization as the only sign of children's adrenal cortical cancer. ACT size appears to be strongly associated with the likelihood of recurrence.[2,4]

Limitations of this study include its single-case design, which limits generalizability. Additionally, the lack of long-term follow-up data restricts the ability to assess recurrence and survival outcomes definitively. Future studies should focus on larger cohorts and longer follow-up durations to better evaluate the role of chemotherapy in pediatric ACTs and to identify prognostic factors more robustly.

Conclusion

This case highlights the difficulty in identifying and treating pediatric ACTs, which demand detailed clinical and histological assessment. Since they are uncommon and may be malignant, early identification and customized care are crucial. Tailoring therapeutic approaches, multidisciplinary management, and further research are essential for improving outcomes in affected children.

Conflict of Interests

Authors have no conflict of interests.

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