Case Report

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ADRENOCORTICAL CARCINOMA IN A 2 YEAR OLD CHILD, A RARE ENTITY

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ABSTRACT

Adrenocortical carcinomas are a rare type of malignancy, particularly in children. There is no such gender predilection with both male and female preponderance in different studies. Early diagnosis and treatment are necessary for better prognosis as well as its differentiation from entities like adrenocortical adenoma and phaeochromocytoma. Here, we describe a case of adrenocortical cancer in a 2-year-old child who had virilistic symptoms, hirsutism and weight gain. Her tanner stage was II. On histomorphology Weiss score was 8 and Wieneke AFIP score was 6. Patient received timely chemotherapy after surgery.

KEYWORDS: Pediatric, Cancer, Childhood, Adrenal, Adrenocortical.

INTRODUCTION

One to two cases of adrenocortical carcinoma occur annually per million persons, making it a rare kind of tumor. They make up between 0.05% and 0.2% of all cancers. With a smaller peak in the first two decades and a greater peak in the fifth decade, the age distribution is bimodal (1). Adrenocortical carcinoma (ACC) makes up just 6% of pediatric adrenal tumors and less than 0.2% of all pediatric neoplasms in children (2). In 1865 (3), the first instance of childhood ACC was documented. The majority of children under five are 65% of cases of ACC(4). In most large clinical series, adrenocortical cancer develops slightly in women more often than in men, despite certain studies showing a small male predominance. Up to 30% of patients who initially appear with stomach pain may also have a palpable abdominal tumor. Hyperaldosteronism is less common, but this tumor may be linked to Cushing syndrome or show signs of virilization (excessive sex steroid production). Adrenocortical carcinoma may develop in children randomly or as part of certain hereditary tumor syndromes, including , Congenital adrenal hyperplasia, Beckwith- Li-Fraumeni syndrome, Wiedemann syndrome, multiple endocrine neoplasia type 1, and Carney complex, (6,7) are a few examples of endocrine disorders.

CASE PRESENTATION

A 2 years old female presented to Pediatrics OPD with complaints of weight gain, increased appetite, excessive hair growth on face and pubic region and breast enlargement for past 6 weeks as stated by her mother. Excessive hair growth was first noticed in the pubic region followed by lower limb, upper limb and subsequently face and neck with sparing of axillary region, abdomen and back. In last 2 months size of both breasts has increased rapidly with no nipple discharge. There was no history of seizures, prior hospitalization, altered sensorium, lethargies, swelling in any other part of body part, vision loss, polydipsia, excessive swelling, polyuria and irradiation in past. There is no prior evidence between trauma with voice change. She was delivered via single vaginal birth at 38 weeks' gestation without any antenatal maternal medication use or radiation exposure, and had a straightforward postpartum phase. She has attained all developmental milestones for age and had been immunised as per schedule. Her height and weight were found to be higher than normal for his age upon physical evaluation. Her vitals remained steady. Respiratory, cardiovascular and central nervous systems were within normal limits. On per abdomen, a mass was palpable in left hypochondrial and lumbar region, firm in consistency and non-tender. Stage II of Tanner.

Laboratory tests on the patient's serum and urine were performed. While serum VMA was normal, random serum cortisol levels were increased. Low amounts of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were observed. Serum estradiol (E2) was elevated, but serum dehydroepiandrosterone sulphate was normal. No chromosomal abnormalities were found on Karyotyping, and the results of the lipid profile, serum ionized calcium ,thyroid function test, kidney, liver, and hemogram were all within normal

ranges.A 6.9*6.9 cm heterogenous mass lesion was seen on abdominal ultrasonography at the upper pole of the left kidney. Contrast-enhanced computed tomography of the abdomen revealed a sizable, well-defined soft tissue lesion that was heterogeneously enhancing. in left suprarenal fossa measuring 8.3*7.7*8.4 cm with maintained fat planes with left kidney (Fig1a). Multiple subcentrimetric, mesenteric and paraaortic lymph nodes were also noted.

Open adrenalectomy was done. Histopathology revealed Adrenocortical carcinoma with extensive necrosis.

On gross examination findings, a single cystic pale brown tissue piece measuring 10.5x6.5x6.5 cms was received. Outer surface was irregular and on cut showed multiple papillary like projection and at places haemorrhagic areas were present measuring 2.5x2.5 cms.

Microscopic findings: Multiple sections examined showed markedly necrotic (Fig 1f) partly encapsulated tumour present in sheets and nests surrounded by thin fibrovascular septae. The tumour cells were medium sized with central round to oval highly pleomorphic hyperchromatic nucleus and moderate deeply eosinophilic to clear cytoplasm (Fig 1b). There was presence of many atypical mitotic figures (16 mf/20hpf) (Fig 1c) along with calcific foci. Tiny islands of residual dysplastic adrenal tissue were also present. Lymphovascular invasion and focal capsular breach was noted (Fig 1d and e). Weiss score was 8. Wieneke et al, AFIP score was 6.

Immunohistochemistery was done for vimentin and inhibin which were positive (Fig 1g and 1h).

Genetic testing for TP53 mutation for Li Fraumeni and CDKN1C for Beckwith-Weidemann syndrome were not done due to unavailability of test at our centre.

Patient is presently on four drug chemotherapy (Vincristine, cisplatin, etoposide and cyclophosphamide).

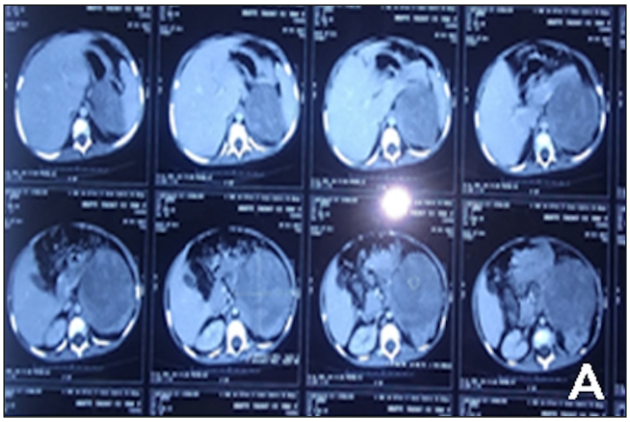

Fig. 1A: Computed Tomography Showing Presence of Lesion in Left Suprarenal Fossa

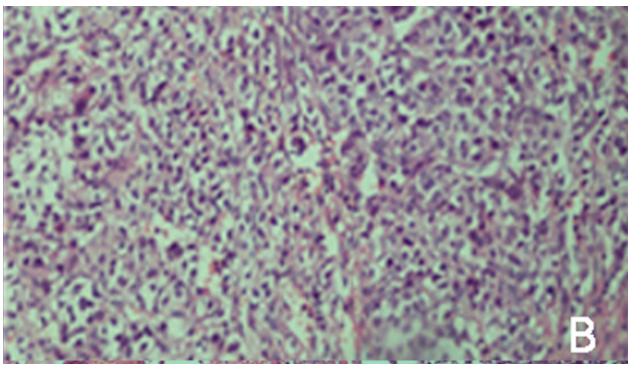

Fig. 1B: Hematoxylin and Eosin Stain Showing Presence of Pleomorphic Cells (X10)

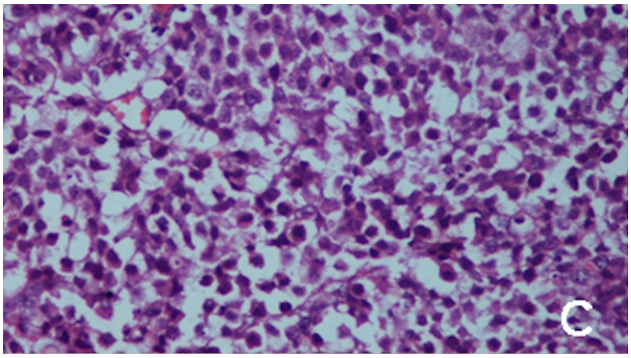

Fig. 1C: Hematoxylin and Eosin Stain Showing Presence of Mitotic Figures (X40)

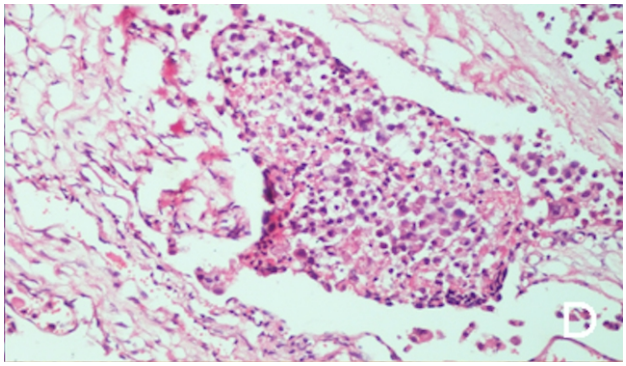

Figure 1D: Hematoxylin and Eosin Stain Showing Presence of Lymphovascular Invasion (X40)

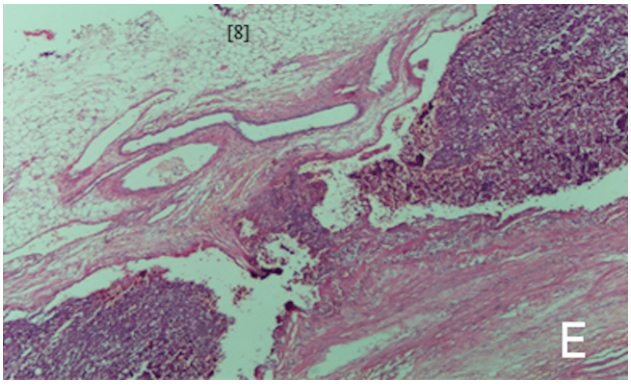

Figure 1E: Hematoxylin and Eosin Stain Showing Presence of Capsular Invasion (X10)

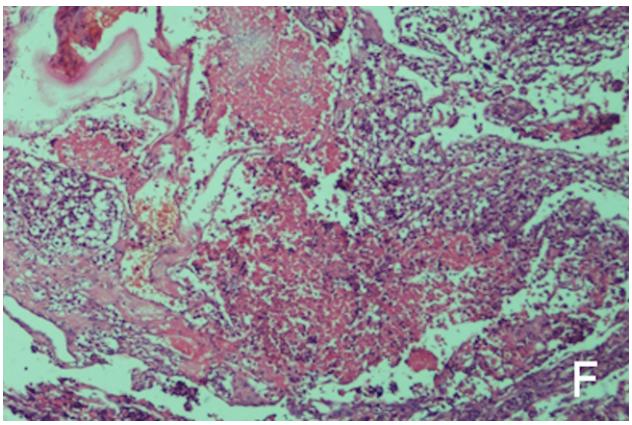

Figure 1F: Hematoxylin and Eosin Stain Showing Presence of Necrosis (X10)

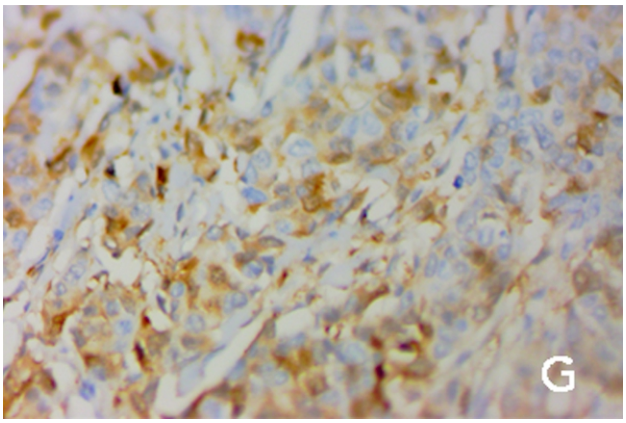

Figure 1G: Immunohistochemistery Stain Showing Vimentin Positivity (X40)

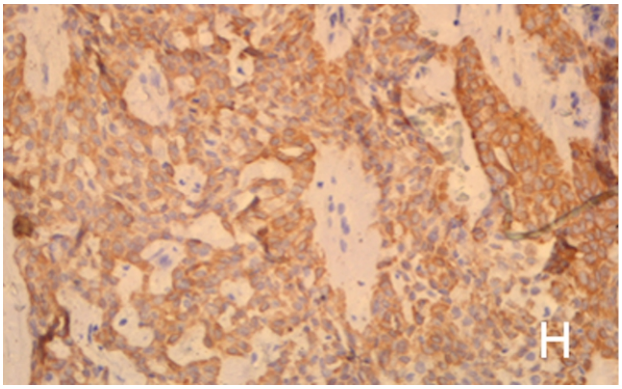

Figure 1D: Hematoxylin and Eosin Stain Showing Presence of Lymphovascular Invasion (X40)

DISCUSSION

Adrenocortical carcinoma, with the first occurrence being documented in the 19th century (1865), is uncommon in youngsters. Bimodally, the first five years of life are when 65% of childhood ACCs manifest. Since the majority of kids with ACC seem healthy and typically develop normally, the non-functioning small tumors make the diagnosis more complex. With no specific data available for Paediatric ACCs in India, ICMR states that childhood cancers account for 2.69% of all cancers in both males and females. The incidence in United States amounts to up to 25 cases on annual basis according to the SEER program (Surveillance, Epidemiology and End Results).

Li-Fraumeni and Beckwith-Weidemann syndromes, which are constitutional genetic variables, are clearly associated with the majority of children with ACC. It has been established that environmental factors, specifically prenatal exposure to carcinogens, are a cause of the early development of ACC. Less than 10% of patients were older than 15 when they first presented, with a median age of about 3 years. The condition has a female preponderance, according to research. The exact tumour's ability to secrete adrenocortical hormones greatly influences how the ACC presents. Hormone-secreting tumors and the associated classical endocrine syndromes (Conn's and virilizing, feminizing, Cushing's, syndrome) are the most common presentation in this age range. The virilizing syndrome represented 80% of all cases in this age group, according to a review by Ribiero et al. (4), and it was also the most common presentation. Amenorrhea, clitoral enlargement, pubic and facial hair with a male escutcheon, pubic hair, and, occasionally, temporal baldness are the most common symptoms, especially in women.

Any child with pubarche younger than 4 years old should be diagnosed with ACT as a differential diagnosis until it is determined that there is another cause. Additionally, the occurrence of acne in a baby can be used to diagnose an adrenocortical lesion.

It is problematic that ACT in children is classified as pathogenic. Diagnosing cancer from adenoma can be challenging, even for a pathologist with experience. The classification systems created by Weiss et al. and Hough et al. were based on microscopic, macroscopic, and clinical criteria present at diagnosis. By applying a modified Weiss and colleagues' classification system, Bugg et al. (8) divided pediatric ACTs into three categories: adrenocortical adenomas, high-grade carcinomas, and low-grade carcinomas. (8) definition. Confluent necrosis, atypical mitoses, the nuclear grade, and the mitotic index were used to classify the samples. The most accurate indicators of prognosis were stated to be tumor size and high-grade cancer. Another scoring the system was created by Wieneke et al, AFIP for scoring and grading adrenal tumor into benign, intermediate for malignancy and malignant tumor (9). It is based of tumor size, weight and invasion of tumor into capsule, venous system along with presence of necrosis and mitotic figures.

The key biochemical clue to a diagnosis in the majority

of ACT is typically found in tests a comparison of urine and plasma levels of 17-ketosteroids (DHEA-S, dehydroepiandrosterone sulfate). For persons with ACT, typical laboratory testing includes measuring their urine levels of 17-KS, 17-OH, DHEAS free cortisol, androstenedione , testosterone, renin activity, aldosterone, DOC, and other 17 deoxysteroid precursors. In addition to assisting in the diagnosis, this wide panel of tests provides helpful indicators for the identification of tumor recurrence. Utilizing MRI and CT for assessment is a part of radiological studies. Recent research suggests that MRI may be able to distinguish between benign and malignant tumors. It is yet to be seen whether MRI will displace CT scanning as the primary and most beneficial imaging technique or offer the practitioner prognostic data.

There are case reports and case series elaborating presence of adrenocortical carcinoma in children like in our case. Gundgurthi et al, 2012 described ACC in a 2-year-old girl like in our case (10). Li et al, 2021 (11) and Hanna et al, 2008 (12) described 8 cases and 23 cases of ACC in children with median age of 6 years and 9 years respectively. Both the studied showed female predominance with female to male ratio of 3:1 and 1.9:1. Female predominance was also showed in a study by Gupta et al, 2018 (13) with female to male ratio of 3.6:1.

Differentials include adrenal cortical adenoma, phaeochromocytoma, renal cell carcinoma and metastatic adenocarcinoma. Adenomas can be differentiated on basis of their benign morphology with absence of mitosis, pleomorphism and necrosis. Phaeochromocytoma shows polygonal cells with eosinophilic granular cytoplasm are present. with salt-and-pepper chromatin arranged in nesting pattern. These cells are synaptophysin and chromogranin positive. Renal cell carcinomas generally show clear cells and are EMA positive. Metastatic carcinoma will have primary at another site and will be EMA positive while ACC are generally EMA negative.

Chemotherapy's role in healing is comparatively limited. of pediatric ACC, and open adrenalectomy rather than laparoscopic surgery is the single most crucial technique (14,15). Prognostic indicators include age greater than 3.5 years, the time between the onset of symptoms and the diagnosis, tumor volume higher than 200 cm3, weight greater than 80 g, and urine output of 17-OH in excess of 4 mg m-2 day-1. Multivariate analysis revealed that only tumor size was independently linked with disease-free survival.

CONCLUSION

Adrenocortical carcinoma in children is a rare entity. It should be differentiated from other adrenal tumours like high grade phaeochromocytoma. Timely diagnosis helps in proper surgical resection and further chemotherapeutical treatment.

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