Case Series

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Adrenocortical Tumours in Children: An Emphasis on Histological Scoring System

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Abstract

Adrenocortical carcinoma (ACC) is a rare neoplasm with poor prognosis. Discriminating benign and malignant behaviour is more challenging. We report a case of adrenocortical adenoma (ACA) and two cases of adrenocortical carcinoma (ACC). All three cases were girls and presented with features of virilisation. Tumour weight, size, and Weiss criteria were found to be useful clinicopathological criteria for distinguishing adenoma from carcinoma.

Keywords: Adrenocortical Adenoma; Adrenocortical Carcinoma; Hirsutism.

Introduction

Adrenocortical carcinomas (ACC) are rare tumours with an incidence of approximately one per million per year. They account for 0.05% to 0.2% of all malignancies. There is a bimodal age distribution, with a small peak in the first two decades and a larger peak in the fifth decade [1]. Functioning ACCoften presents with symptoms of steroid hormone over secretion and non-functioning ACC usually present with symptoms related to the local mass effect [2]. We present three cases of adrenocortical neoplasms and a discussion on their clinical findings, histomorphology with special emphasis on various histological scoring systems. The development of advanced imaging techniques has led to earlier diagnosis of malignant adrenocortical tumours, thereby increasing the challenge ofdifferentiating benign from malignant pathology on the basis of histomorphologic features alone [3]. Indications for surgery are adrenal hyper function and size of 4 cm [4].

Case Reports

Case-1

A six year old girl, who was apparently healthy presented with pain abdomen associated with fever, followed by the onset of facial hirsutism, progressive virilisation and clitoromegaly of six months duration. Ultrasonography revealed a mass arising from upper pole of left kidney. With a diagnosis of a virilizing tumour of the adrenal cortex, the mass was excised completely. Intraoperatively an encapsulated mass was noted measuring 15x15x8cm and weighing 900 gms.The cut surface was lobulated with areas of necrosis. Microscopic examination showed tumour cells arranged in trabeculae separated by vascular sinusoids with regressive changes like haemorrhage necrosis and fibrosis. The normal cortical architecture was not preserved. Nuclei were hyperchromatic and showed atypia, with 20-22 mitosis/50 HPF. Vascular invasion was present. On follow-up after a period of six months patient developed hepatic metastasis and succumbed after a period of two months.

Case-2

A fifteen year old girl, presented with pain abdomen vomiting and amenorrhoea of six months. Examination revealed masculine built and body hair distribution, underdeveloped breasts, clitoromegaly and mass in the right hypochondriac region. Buccal smears showed Barrbodies in 15% of cells. With a clinical diagnosis of female pseudohermaphroditism with functioning right adrenocortical tumour, surgical excision of the mass was done. Laparotomy revealed a mass arising from the right adrenal cortex, with a hypoplastic uterus and right ovary, and

absence of left ovary. The tumour was well delineated measuring 16x10x6cm and weighing 480gms. Cut surface showed cystic spaces with haemorrhage and peripheral grey white nodules. Microscopic examination showed tumour cells, with vesicular nuclei, with mild anisonucleosis. Mitotic rate was >5/50HPF with occasional atypical forms. Regressive changes like haemorrhage and necrosis were seen. There was no capsular and vascular invasion. Postoperative period was uneventful, followed up for one year and later lost to follow-up.

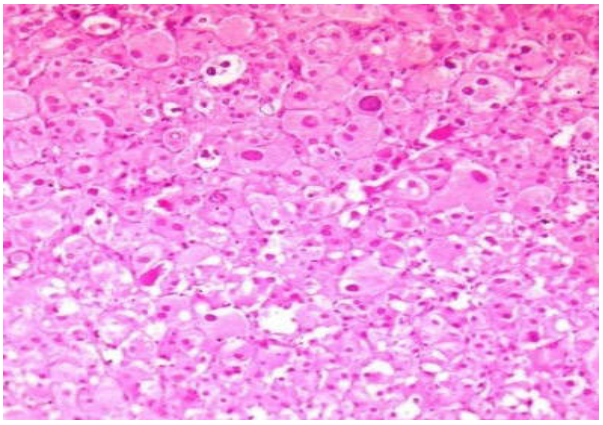

Fig. 1, Case 2: Photomicrograph showing large polygonal cells arranged in form of sheets with moderate degree of pleomorphism (H&E x100)

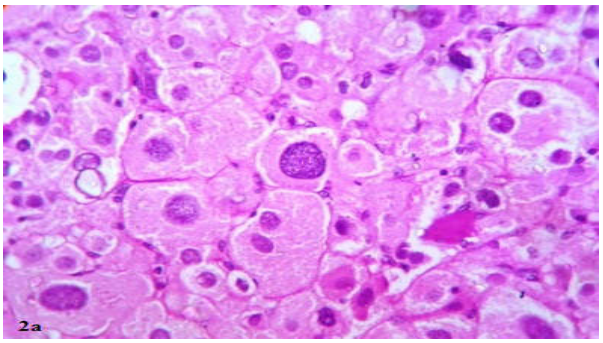

Fig. 2a, Case 2: Photomicrograph showing moderate degree of pleomorphism with mononuclear bizarre and multinuclear giant cells with abundant granular eosinophilic cytoplasm (H&E x400)

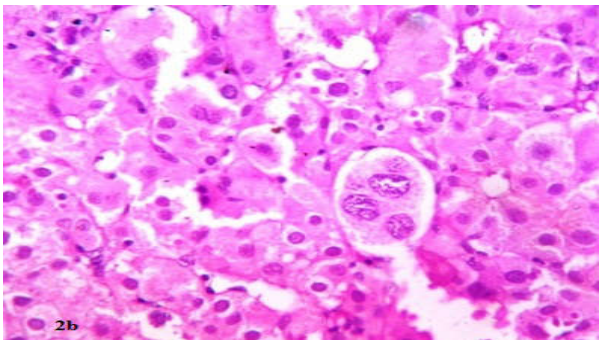

Fig. 2b, Case 2: Photomicrograph showing moderate degree of pleomorphism with mononuclear bizarre and multinuclear giant cells with abundant granular eosinophilic cytoplasm (H&E x400)

Case-3

A 14 months old girl child who was apparently normal presented with complaints of growth of pubic and axillary hair of 4 months duration. On examination – Breast engorgement, axillary and pubic hairs, clitoromegaly, moustache and central obesity were noted. CT scan revealed a mass in right suprarenal region measuring 6.7x5.8x6cm with a diagnosis of Functioning Right Adrenal Adenoma. Hormonal assays showed testosterone 13.92 ng/ml (Normal - 0.002-0.008ng/ml), Cortisol 31.65 µg/dl (5-23 µg/dl), DHEA-S 48492 ng/ml (50-550 ng/ml) and 17-OH Progesterone 13.92 ng/ml(< 0.99 ng/ml). Surgical excision of the mass was done. The mass was well-circumscribed measuring 5x5x2cm and weighing 200g. Microscopic examination revealed a well-encapsulated lesion comprised of moderately pleomorphic cells in sheets. Cells have moderate granular eosinophilic cytoplasm and prominent nucleoli, spironolactone bodies +, few giant cells and bizarre forms were noted. Mitosis was infrequent and no atypical forms were seen. No necrosis, haemorrhage, fibrosis, calcification. No capsular/vascular/sinusoidal invasion. Diagnosis of Adrenocortical Adenoma was made. During post-operative period child developed electrolyte abnormalities like hypernatremia and hypokalemia leading to ventricular fibrillation and child expired after 15 days.

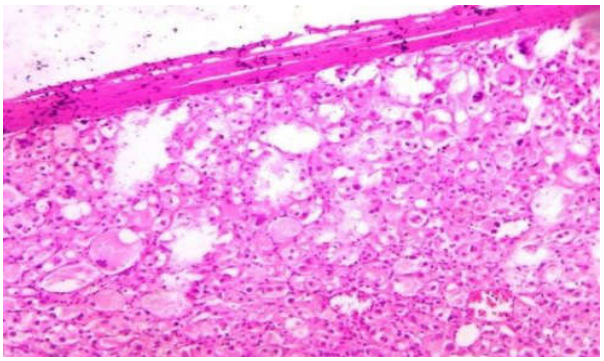

Fig. 3, Case 3: Photomicrograph showing an encapsulated lesion with an intact capsule (H&E x100)

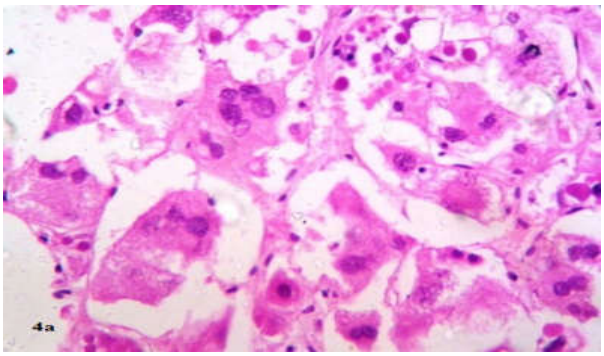

Fig. 4a, Case 3: Photomicrograph showing intracellular and extracellular spironolactone bodies (H&E x400)

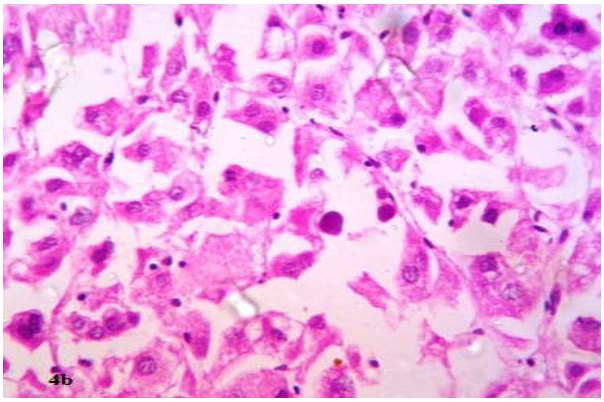

Fig. 4b, Case 3: Photomicrograph showing intracellular and extracellular spironolactone bodies (H&E x400)

Discussion

Clinical presentation of ACC is variable. Paediatric ACCs have several important differences compared to adult ACCs. The incidence for children is greatest in the first year of life. ACC is more common than adrenocortical adenoma in children. Most of the paediatric patients present with symptoms of adrenal hormone hyper secretion. The most common presentation in children is virilization, followed by Cushing's syndrome [5]. All three cases in our study presented with features of virilisation.

The most critical point in adrenocortical pathology is the differential diagnosis between ACA and ACC; there is no single histological criterion which can reliably differentiate between the two and distinguishing them represents a great challenge for both clinicians and pathologists.

In a retrospective analysis of 49 adrenal masses Aubert et al. determined that a tumour weight greater than 50 g predicted malignancy with 100% sensitivity and 90.9% specificity and also proposed a threshold of larger than 6.5 cm for distinguishing malignancy with 100% sensitivity and 91.7% specificity [6].

Applying these criteria Wang C et al. in their retrospective study of 50 adrenocortical tumours showed 100% sensitivity and 100% specificity in relation to weight, 68% sensitivity and 100% specificity in relation to the size of the tumour [7].

In present study case-1 and case-2 which were diagnosed as malignant weighed >50g and larger than 6.5cm in dimension. Case-3 which was diagnosed as adrenocortical adenoma was also more than 50g and measuring 5cm in the largest dimension.

Three histopathological scoring systems for distinguishing benign from malignant ACCs have been proposed. The Hough system employs 12 criteria, 7 histologic and 5 non-histologic [5]. Scoring system proposed by Slooten et al includes seven histological criteria and no non-histological criteria [8]. The Weiss criteria introduced in 1984 with nine histologic criteria and later revised and modified in 2002 by Aubert at al. with five histologic criteria are the current standard of practice to establish the diagnosis of ACC.

Weiss criteria based on nine histopathological criteria listed below [9]:

1. Grade 3 or 4 nuclear grade (enlarged, oval to lobulated nuclei with coarsely granular to hyperchromatic chromatin and easily discernible, prominent nucleoli)
2. Mitotic grade >5/50 hpfs
3. Atypical mitoses
4. Clear cells comprising 25% or less of the tumour
5. Diffuse architecture greater than one-third of the tumour
6. Necrosis
7. Invasion of venous structures
8. Invasion of sinusoidal structures
9. Invasion of the tumour capsule.

The original threshold for malignancy, established in 1984, was the presence of at least four criteria which was reduced to three or more criteria in 1989 [7].

In 2002 a revised system was proposed by Aubert et al. which comprises of only five Weiss criteria i) mitotic grade, ii) percentage of clear cells comprising the tumour, iii) abnormal mitoses, iv) necrosis and v) capsular invasion [6].

Applying the Weiss and modified Weiss criteria first two cases fulfilled three criteria so labelled as carcinoma whereas case-3 fulfilled only one criterion and was reported as adenoma.

Case-2 patient died with liver metastasis which is the most common site of metastasis as per Wanis KN [5] et al and Abiven G et al [10].

As per Sandrini R et al [11] during perioperative period special attention has to be given electrolyte balances, hypertension, surgical wound care and infectious complications. Case-3 in our series presented with electrolyte imbalance during the immediate postoperative period which had led to ventricular fibrillation and death.

Conclusion

Therefore, the differential diagnosis of adrenal cortical carcinoma from adenoma requires

comprehensive clinical characteristics, pathological morphological evaluation and a variety of ancillary investigations.

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