ORIGINAL RESEARCH PAPER

Volume-8 | Issue-7 | July - 2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

RARE ADRENAL LESIONS- A SERIES OF FIVE CASES

Pathology

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ABSTRACT

A variety of pathological processes may arise from adrenal which include malformations, heterotopias, hyperplasias , and neoplasms. These and diagnostic categories are not as discrete as might be assumed. The integration of the histologic and macroscopic features with endocrine findings, clinical history is of utmost importance. Here we present few lesions of adrenal gland where histology played main key role in reaching the appropriate diagnosis.

KEYWORDS

adrenal gland, adrenocortical carcinoma, rare adrenal lesions

INTRODUCTION

When adrenal lesion is identified, what the clinician and patient really want to know is whether the findings are benign or malignant, as this ultimately will affect their next step in management. This study was conducted in a tertiary level hospital with an advanced surgical and medical superspeciality units .The commonest neoplastic adrenal lesions diagnosed in our setup are adrenocortical adenomas and phaeochromocytomas. Here we present few rare lesions where the appropriate diagnosis was made only after elaborate histopathological examination.

Rare Adrenal lesions:

Case 1:

An 11 month old female infant, first in birth order presented with respiratory distress. She was alright till 6 months of age when parents noticed acneiform lesions on face, hair growth all over the body and progressive weight gain. On examination, the patient had moon facies, plethora was present, acneiform lesions and hair growth as already described were noted.

Investigations revealed increased Dehydroepiandrosterone (DHEAS >1500mcg/dl) along with raised morning and evening cortisol values, loss of diurnal cortisol rhythm, overnight dexamethasone suppression test (ONDST) was done that was non suppressible. ACTH was <5pg/ml.

Ultrasound abdomen revealed hypoechoeic well defined mass measuring 36x44mm abutting right kidney.Mass showed intratumoral vascularity.

CT abdomen revealed a well defined heterogeneously enhancing mass lesion of 5.1x4.2cm arising from right adrenal gland causing inferior displacement and rotation of right kidney. No calcification or cystic change noted as shown in figure 1a.

Consulation from pediatric surgery was taken and patient underwent right adrenalectomy.This specimen was sent for histopathological examination which revealed a well encapsulated globular mass measuring 5.5x5x3.5cm.No capsular breach was identified grossly.Cut surface was fleshy with no areas of cystic change or necrosis.

Microscopy revealed an encapsulated tumor. Individual tumor cells were highly pleomorphic with abundant eosinophilic cytoplasm, round to oval bizarre vesicular nuclei and prominent nucleoli –some of them inclusion like also. Mitosis noted was <5/50hpf.The tumor was invading capsule focally but no necrosis was noted as shown in figures 1b and 1c.

Overall features were highly suggestive of an Adrenocortical carcinoma. Modified Weiss Score:3

BRIEF REVIEW

Adrenal tumors are quite rare in infancy and childhood with the exception of neuroblastoma. In fact, adrenocortical tumors (ACT) account for only 0.2% of all malignant cancers in children and adolescents [1]. The clinical manifestations and biologic behavior of these tumors can be quite distinct from their histologically similar counterparts in the adult population[2].

Several authors reported significantly better outcomes in pediatric ACC patients compared to adult patients, even when tumors display similar malignant characteristics upon histological examination [3,4]. The overall 5-year survival in the SEER study was 57% which is significantly higher than typical rates in adult populations which vary around 30–40% [5]. Moreover, survival in pediatric populations appears to be strongly correlated to age; survival rates >80% are reported in subgroups where age at presentation is <4 years [5,6]. Although most adult ACC are non-functional, in the pediatric age group, nearly 95% are functional.[7] Virilization is the most common abnormality and Cushing's syndrome and hyperaldosteronism are less frequent.[8]

Adrenocortical tumors (ACTs) in children may occur sporadically or as a component of certain hereditary tumor syndromes, ie, Li-Fraumeni syndrome, multiple endocrine neoplasia-1, Beckwith-Wiedemann syndrome, Carney complex, and congenital adrenal hyperplasia [2,8].In our case an association with Li-Fraumeni syndrome was strongly suspected considering the strong maternal family history of multiple neoplasms of breast and CNS.

Due to the rarity and heterogeneity of pediatric ACC, limited evidence exists on a definite histopathological criterion to differentiate ACC from adrenocortical adenomas. The Weiss score is widely used to assess ACC in adults [9]. The modified Weiss score [10,11] and the Wieneke index [4] have been proposed for assessing ACC in pediatric population.

A malignant pathology was defined by a Weiss score ≥3, modified Weiss score ≥3, and Wieneke index score ≥4.[12]

Case 2

A40 year old patient presented with high grade fever on and off associated with weight loss since few months. Patient was a known case of type 2 diabetes and on treatment for the same. Routine blood examination, urine examination, renal function test and chest X-ray were normal.

Contrast enhanced CT scan of the abdomen showed enlarged bilateral adrenals showing peripheral rim enhancement.

A CTguided biopsy was taken which showed numerous 2-4 microns fungal spores in an inflammatory and necrotic background. These fungal spores were positive for PAS and Methamine silver stains as shown in figures 2a and 2b.

A diagnosis of adrenal histoplasmosis was made.

BRIEF REVIEW

Histoplasmosis is an infective condition caused by a dimorphic, saprophytic fungus, *Histoplasma capsulatum* and is acquired by inhalation of its spores. Soil rich in bird and bat dropping is its natural habitat, and it exists as a mycelium in the atmosphere [13]. Adrenal involvement is seen in disseminated disease but sometimes it may be the only site of demonstrable disease[13,14].

The patients of adrenal histoplasmosis usually reveal bilateral adrenal masses of varied imaging features. The differential diagnoses of bilateral adrenomegaly are metastasis, lymphoma, adrenal haemorrhage, sarcoidosis and infections which include histoplasmosis, tuberculosis, cryptococosis, coccidioidomycosis and blastomycosis.[15,16] But, central hypodensity and peripheral rim enhancement of the adrenals narrow down the differentials only to tuberculosis and histoplasmosis.[16,17] as was seen in our case.

The characteristic histopathological examination shows numerous small spherical or oval yeast forms surrounded by a clear ring of space resembling a capsule inside the cytoplasm of histiocytes[14].

Case 3

A 44 year old male presented with a 8x8cm growth arising from right adrenal gland abutting IVC and crossing midline. Right adrenalectomy was done and specimen was sent for histopathological examination.

Grossly the specimen was received as a well encapsulated globular mass measuring 7x 7x 2.5cm.Cut surface was grey white Microscopicaslly an encapsulated tumor was noted with tumor cells arranged in nests and sheets. Individual tumor cells were round to oval with pale moderate amount of cytoplasm and showed prominent nucleoli.The tumor nests were separated by thin sepatations having dense lymphocytic infiltrate .Features were suggestive of a germ cell tumor possibly seminomatous as shown in figures 3a and 3b.

Followup postoperative ultrasound of testis didn't reveal any neoplasm. However,the possibility of metastasis from other common sites couldn't be ruled out as the patient was lost to follow up.

BRIEF REVIEW

Extragonadal germ cell tumours (GCTs) are uncommon and represent 2% to 5% of adult germ cell malignancies[18,19]. Its etiology is unknown and whether extragonadal GCTs are metastatic remains controversial. There are two theories to explain this phenomenon. The first is spontaneous regression of the primary GCT after its metastasis. Possible mechanisms are an immune response or ischemia caused by the disseminated neoplasm due to its high metabolic rate. The second is the de novo development of a primary GCT in extragonadal tissues.[20].

Case 4

A 60 year old male presented with a huge tumor mainly involving right upper quadrant adherent to IVC and lifting right renal vein.Margin of this tumor couldn't be reached.An excision biopsy of this lesion was done .

This specimen was received in histopathology laboratory as adrenal mass excision as two bosselated masses measuring 3.5x3 cm and 4x3cm.Cut surface revealed pale white vague whorled appearance.
Microscopy revealed a spindle cell tumor with features of smooth muscle cell origin.cellular atypia and increased mitotic activity,however,no evidence of necrosis was seen as shown in figures 4a and 4b.Overall features were highly suggestive of leiomyosarcoma. On IHC, the tumor was positive for SMA and was negative for S-100,CD117 and CK excluding the possibility of MPNST,GIST, metastatic carcinoma respectively which are the closest differentials in this scenario.

BRIEF REVIEW

Primary adrenal sarcomas are exceptionally uncommon and include leiomyosarcoma, malignant peripheral nerve sheath tumor (MPNST) and angiosarcoma. [21] .Primary adrenal leiomyosarcoma (PAL) is proposed to originate from the smooth muscle wall of the central adrenal vein and its branches [22].

In almost all reported cases to date, they are elderly patients with large tumors as was seen in our case . Histologically, smooth muscle tumors containing 5 or more mitoses per 50 high power fields are classified as malignant. The presence of tumor cell necrosis is also strongly suggestive of malignancy. [23] In the present case however, necrosis and lymphovascular invasion was absent. Apart from the usual spindle cell type leiomyosarcomas, pleomorphic leiomyosarcomas have been described. These tumors show numerous pleomorphic giant cells intimately admixed with a component of more uniform appearing spindle and round neoplastic cells, bizarre mitotic figures and irregular zones of necrosis. [23],[24] In our case no necrosis,LVI was noted so it was graded as conventional low grade leiomyosarcoma.There was relative paucity of bizarre neoplastic cells also. Conventional leiomyosarcomas invariably show reactivity for smooth muscle markers such as smooth muscle actin and/or muscle specific actin in 90 to 95 %, and desmin in 70-90% of the cases. [25],[26],[27] .PALs carry a poor prognosis; with the longest disease free survival being 20 months. [25]

Case 5

An 8 day old baby who during a routine antenatal ultrasound was detected with an adrenal mass as shown in figure 5a. A repeat CECT was done on the 2nd day of her birth which revealed 3.03x5 cm soft tissue density enhancing lesion in the retroperitoneum on the right side extending into the right paravertebral space.The lesion was uplifting the diaphragm as shown in figure 5b.A preliminary diagnosis of right neuroblastoma was made and was suggested MRI for intracanalicular extension.

Right sided adrenalectomy was done on 22nd day of her birth and the specimen was sent for histopathological examination.

On microscopy no evidence of any tumor pathology was noted,however ,extensive areas of haemorrhage were seen.

The diagnosis of unilateral Adrenal Haemorrhage was made as shown in figures 5c and 5d.

BRIEF REVIEW

Fetal and neonatal adrenal glands are relatively large and very well-vascularized organs in early life, which predispose them for frequent bleeding. Risk factors associated with adrenal hemorrhage in utero include maternal hypertension, maternal diabetes, Beckwith–Wiedemann syndrome, asphyxia, shock, infections, thrombosis of inferior vena cava and left renal vein, and hemorrhagic disorders.[28],[29] Although neonatal hemorrhage is common, accounting for 1.7–2.1 per thousand births, the incidence of antenatal hemorrhage is not elicited in any study and is rarely picked up in antenatal sonography.[30] Sonographic appearance can range from simply bulky echogenic adrenals to completely cystic lesion. Sometimes, hemorrhage can complicate its appearance and may mimic neuroblastoma. Later, they can present with bilateral small adrenal glands with calcifications [28],[30].

Almost 70% NAH occurs on right side with 5–10% involvement in bilateral cases. The usual explanations for susceptibility of the right adrenal gland is that it is more likely to be compressed between the liver and spine and, the right adrenal vein usually drains directly into the inferior vena cava, so it is prone to changes in venous pressure.[31]. The closest differential diagnosis of adrenal hemorrhage is neuroblastoma particularly the cystic form. Determination of the urinary excretion of VMA is relevant, since an increase in VMA is virtually diagnostic of neuroblastoma. Over 90% of children with neuroblastoma will have elevated urinary excretion of catecholamine metabolites.[32]

CONCLUSION:

Adrenal lesions have a wide spectrum which is not limited to few diagnosis only so every diagnostic possibility needs to be kept in mind while evaluating theses lesions on imaging as well as histopathology.

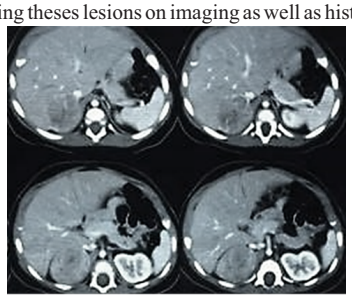

Figure 1 a:Contrast enhanced axial CT section of the upper abdomen reveals heterogeneously enhancing right adrenal lesion

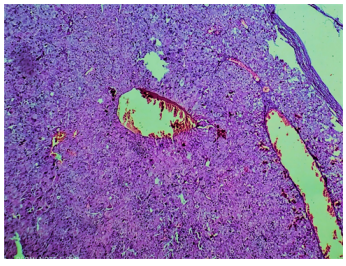

Figure 1b :Low power photomicrograph revealing an encapsulated tumor with increased vascularity

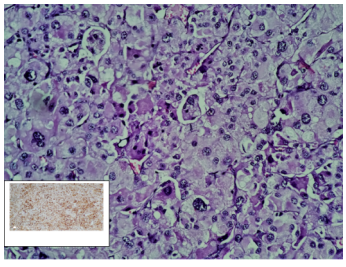

Figure 1c: High power photomicrograph of the same revealing cells with high nuclear atypia and abundant eosinophilic cytoplasm Inset: IHC for vimentin revealing diffuse positivity

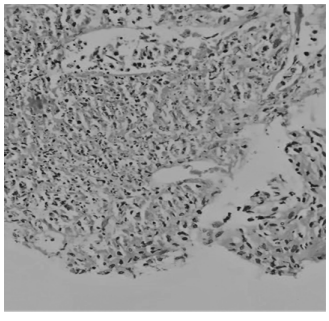

Figure 2a : Photomicrograph revealing fungal spores in a necroinflammatory background

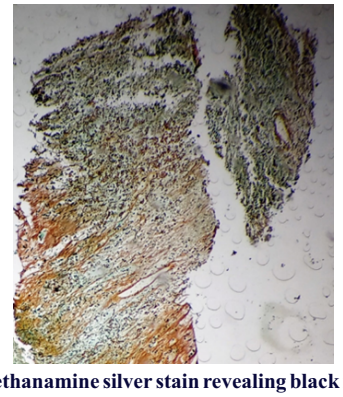

Figure 2b: Methanamine silver stain revealing black fungal spores

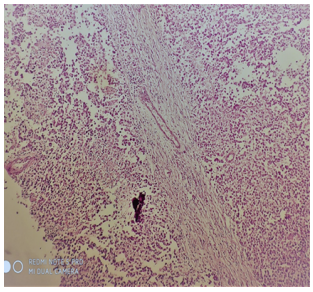

Figure 3a: low power photomicrograph revealing uniform round tumor cells separated by delicate fibrous septae

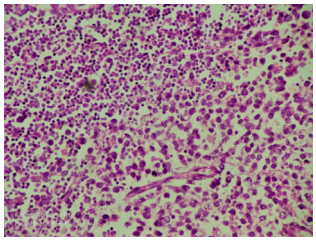

Figure 3b: High power photomicrograph of the same tumor revealing round tumor cells and a band of lymphocytes within septae

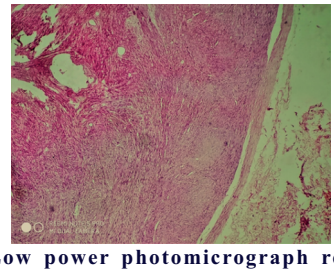

Figure 4a:Low power photomicrograph revealing an encapsulated spindle cell tumor

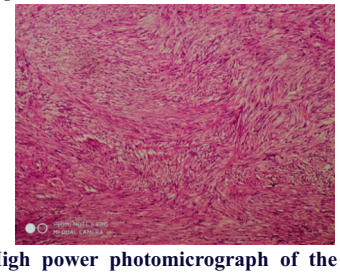

Figure 4b :High power photomicrograph of the same tumor revealing spindled tumor cells arranged in interlacing fascicles.

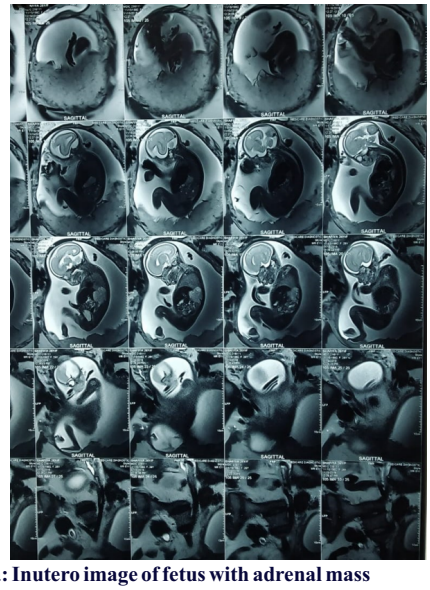

Figure 5a: Inutero image of fetus with adrenal mass

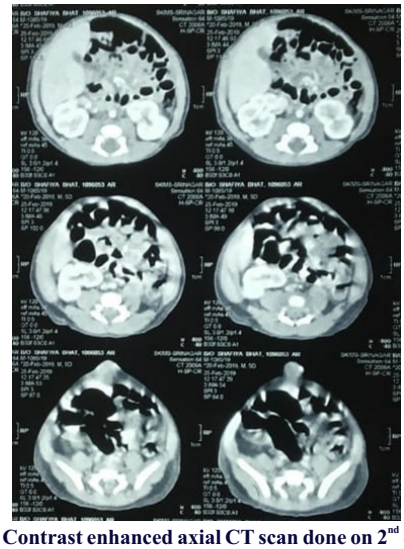

Figure 5b: Contrast enhanced axial CT scan done on 2nd day of her birth

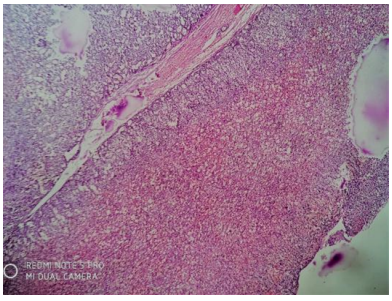

Figure 5c: low power photomicrograph revealing haemorrhage inside adrenal parenchyma

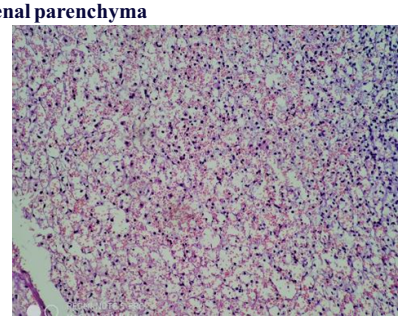

Figure 5d:high power photomicrograph of the same

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