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Pathology

ADRENAL GLAND TUMOURS: A 2-YEAR TERTIARY CARE HOSPITAL BASED CASE SERIES

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ABSTRACT **Introduction:** Adrenal gland tumors are rare. Asymptomatic adrenal tumours are found in 2-10% of the population worldwide, out of which, adrenocortical carcinomas(ACC) have an incidence of 0.5-2 cases/million population/year. ACC accounts for 0.05% -0.2% of all malignancies with a bimodal age distribution, in the first two decades and then in the fifth decade. They can be asymptomatic and diagnosed as Incidentalomas or present with signs and symptoms of hormone imbalance.

Materials and methods: In this 2 year hospital-based retrospective case series from June,2018 to May,2020 , 5 cases of adrenal gland tumors diagnosed in the Department of Pathology , GMCH, were retrieved from the archives and reviewed. Each case was analyzed with respect to age , sex, site and tumor characteristics.

Results: In this 2-year period, 5 cases of adrenal tumors were found. The age range of the patients was 8-54 years. Out of 5 cases,2 cases were male and 3 cases were female. Out of 5 cases of , 4 were on the left side and 1 was on the right side.2 out of the 5 cases were diagnosed as Adrenocortical carcinoma(low grade), 1 as Phaeochromocytoma and 2 as Adrenocortical Adenoma.

Conclusion: Adrenal gland tumors are rare, so the pathologic classification and determination of prognosis are very challenging.

KEYWORDS : Adrenal gland, Adrenocortical carcinoma

INTRODUCTION

Adrenal gland tumors are not very common. About 2-10% of the population worldwide have clinically unapparent adrenal glands tumours.[1] Adrenocortical carcinoma(ACC) has an incidence of 0.7-2 cases/million population/year[2] and presents 0.05% - 0.2% of all malignancies with a bimodal age distribution, first in the first two decades and second, in the fifth decade.[3] Adenomas and carcinomas are almost equally found in adults, but in children, carcinomas are more common.[4] The female-to male ratio is as high as 2.5:1.[5] These can be asymptomatic and discovered as Incidentalomas, or present with hormonal symptoms of adrenal origin, or present with non-specific symptoms like pain abdomen, abdominal fullness, or found as metastases during malignancy work-up like in lung cancer.[6] Chances of malignancy increases with increase in the size of the tumor.[7] Adrenal tumors are increasingly recognized due to widespread use of imaging techniques and are a pathological challenge.[8] Although majority of adrenal incidentalomas are benign, upto 12% cases can be incidental ACC.[9] Imaging should be followed by pathological confirmation, as histopathological findings are still the "gold standard" in the diagnosis of ACC .[10,11]

MATERIALS AND METHODS

The case series is a hospital-based and retrospective study conducted in the Department of Pathology, Gauhati Medical College and Hospital, Guwahati, Assam from June,2018 to May,2020. All adrenal gland tumors with available formalin fixed, paraffin embedded tissue were selected from the departmental pathology records .Nature of the specimen was excisional biopsy for 4 cases and outside slides and blocks for review in 1 case. Tissues for excision biopsy were received in 10% buffered formalin, processed routinely with haematoxylin and eosin staining and diagnosed based on the histopathological examination. The patient characteristics(age and sex) and tumor characteristics(site, architecture, cytoplasm and nuclear characteristics , necrosis and mitotic activity)were analyzed in these cases.

RESULTS

A total of 5 cases of adrenal gland tumors were reported during the 2 year study period. The age range of the patients was 8-54 years, with a median age of 31 years. Out of 5 cases,2 cases were male and 3 cases were female. Out of 5 cases, 4 were on the left side and 1 was on the right side.Out of the 5 cases, 2 cases were diagnosed as Adrenocortical carcinoma(ACC).Other cases were that of Adenoma(2 cases) and Phaeochromocytoma (1 case)

Table 1: Complete data of the five cases

Number	Age	Sex	Specimen	Side	Diagnosis
1	54	Male	Excision biopsy	left	Phaeochromocytoma
2	32	Female	Excision biopsy	left	Adrenocortical adenoma
3	8	Female	Excision biopsy	right	Adrenocortical adenoma
4	43	Female	Excision biopsy	left	Adrenocortical Carcinoma (low grade)
5	49	Male	Slide and block for eview	left	Adrenocortical Carcinoma (low grade)

DISCUSSION

Tumors of the adrenal gland are rare. They can be functional or non-functional, benign or malignant or arise in adrenal cortex or medulla.[11]

The recent WHO classification of Adrenal Gland has described the following categories: (1) tumors of adrenal cortex (2) tumors of adrenal medulla. Tumors of adrenal cortex are sub-classified as: (a)Adrenal cortical carcinoma (b) Adrenal cortical adenoma (c) Sex cord - stromal tumors(d) Mesenchymal tumors- myelolipoma, schwannoma (e) Haematolymphoid tumors (f) Secondary tumors

Tumors of adrenal medulla are further sub-divided as:
(a)Pheochromocytoma (b) Extra-adrenal paraganglioma (c) Neuroblastic tumors of the adrenal gland(d) Composite pheochromocytoma (e) Composite paraganglioma. [5]

Adrenal carcinoma develops at all ages. However, there appears to be bimodal age distribution with the first peak occurring in the first decade and the second peak in the fourth to fifth decade of life.[3] In this case series , the 2 cases of ACC presented in the fourth decade of life.

There is a slight female preponderance in adrenal tumors.[5] In this case series, female to male ratio was 1.5:1.

According to the study by Wajchenberg et.al , presentation on the left side was more common, with few tumors presenting bilaterally.[12]In this case series, out of 5 cases , 4 were on the left side.

Pheochromocytoma is a rare neuroendocrine tumor with prevalence between 0.1% to 0.6% in individuals suffering from hypertension.[13] It originates from the adrenal medulla or from the chromaffin cells in sympathetic ganglia and is most common in women in the fourth and fifth decade.[14,15,16] These are non-familial or familial. Non familial tumors are typically unilateral, sharply circumscribed, solid masses with fibrous psedocapsules. Familial tumors are generally bilateral and multicentric with hyperplastic medulla grossly.[3]Most tumors measure about 7 cms in diameter.[17] Microscopically, these typically exhibit an alveolar(Zellballen) pattern, consisting of nests of polygonal cells separated by peripheral capillaries. Trabecular and diffuse growth patterns can also be seen.[18] In this case series, 54 year old, male had a left sided adrenal tumor measuring (4.5x4x4)cu.cm. with variegated cut surface.. Microscopy showed solid, alveolar and trabecular patterns composed of intermediate to large polygonal cells with round to oval nuclei with prominent nucleoli and granular eosinophilic cytoplasm.

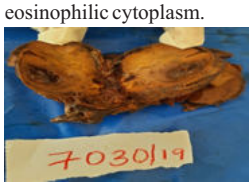

Fig.1: Gross picture of Pheochromocytoma

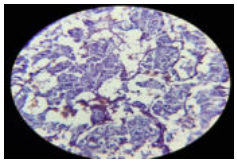

Fig.2:Low power view of pheochromocytoma showing the typical zellballen appearance

Adrenal adenomas are benign neoplasm of the adrenal cortex and the most common cause of "Adrenal Incidentaloma".[19] : Adrenal adenoma affects 10% of the population, with incidence increasing with age. They occur in all age groups and in both sexes.[5] Grossly, these are well circumscribed, nodular that expand the adrenal gland.[4] Microscopically, adenomas have pushing borders with a pseudocapsule[3] and are composed of cells with small nuclei and eosinophilic to vacuolated cytoplasm depending on the lipid content. Mitotic activity is generally absent.[4] Large adenomas may show atypical features like calcification, cystic change and necrosis.[20] In this case series, the first case was a left sided adrenal tumor in a 32 year old female measuring (12.8x9.8x6.9)cu.cm. , encapsulated with solid, greyish white cut surface showing areas of cystic degeneration. Microscopy showed tumor cells with solid and trabecular growth patterns, composed of pleomorphic cells with large hyperchromatic nuclei ,coarse chromatin and prominent nucleoli and vacuolated cytoplasm. There were areas of calcification.

The second case was a right sided adrenal tumor measuring (7x4x4)cu.cm. with solid, greyish white cut surface alongwith areas of haemorrhagic and cystic degeneration in an 8 year old female. Microscopy showed diffuse solid pattern with focal cystic and myxoid areas. Cells were an admixture of compact and clear cells having round nuclei and indistinct nucleoli. Focally marked nuclear pleomorphism was noted. Mitosis was not seen. Significant areas of necrosis were seen. Capsular and vascular invasion were not seen. Foci of myelolipomatous change was noted.

Adrenal cortical carcinoma is a malignant tumor with poor prognosis, most series showing the 5-years overall survival being below 40%.[21-28] These are often, large and invasive lesions effacing the native adrenal gland.[4] ACC present as a bulky mass with coarse nodularity and areas of necrosis, hemorrhage and cystic generation.[18] Microscopically, varied architectural patterns such as trabecular, alveolar, or diffuse(solid) and admixtures may be noted.[29,30] Most cells have compact eosinophilic cytoplasm with occasional condensation of cell cytoplasm. Sometimes intracytoplasmic hyaline globules are seen. Nuclear pleomorphism, tumor necrosis and vascular invasion are features alongwith mitotic figures ,including atypical forms.[31,32,33] Mitotic counts have been used to distinguish low grade(</=20mitotic figures/50 hpf) from high grade(>20 mitotic figures/50 hpf) tumors.[33]

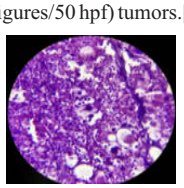

Fig.3:Myelolipomatous foci in Adrenal Adenoma

Fig.4:Gross picture of Adrenal Adenoma

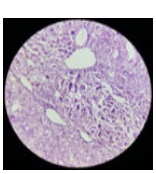

Fig.5:Low power view of Adrenal Adenoma

Reliable identification of Adrenocortical tumors are difficult. The most widelyaccepted criteria are given by Hough and colleagues[32] and Weiss.[33] Original Weiss criteria[34] had some observer variability, so Modified Weiss system was proposed, and recent studies have confirmed its diagnostic value and correlation with time of survival in patients.[35] At present, immunohistochemistry is often used, but thorough gross and microscopic examination remains the gold standard to differentiate benign from malignant adrenocortical tumors.[18] In this case series, one case of ACC of left adrenal in a 43 years old female presented grossly as a tumor measuring (9.5x7x4.5) cu.cm. with solid, yellowish cut surface with areas of haemorrhage and infiltrating the adjacent soft tissue. Microscopy showed solid, alveolar and trabecular pattern formed by cells with marked pleomorphism having binucleation at places and granular to clear cytoplasm. Capsular invasion was seen. Mitosis- 6/50 HPF.

Another case of ACC was an outside slide received for second opinion of a 49 year old, male with suprarenal mass. Microscopic examination revealed solid, trabecular and pseudoglandular pattern formed by cells with marked nuclear pleomorphism and clear to eosinophilic cytoplasm. Mitotic activity 8/50 HPF. Areas of necrosis and vascular invasion seen.

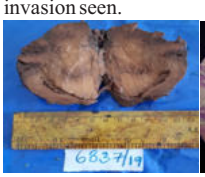

Fig.6: Gross specimen of ACC

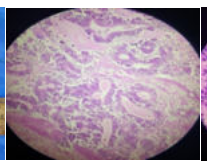

Fig. 7: Scanner view of ACC showing areas of necrosis and vascular invasion

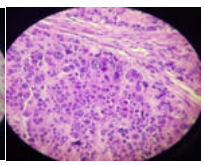

Fig.8:Low power view of ACC showing nuclear pleomorphism and diffuse architecture

CONCLUSION

Adrenal gland tumours are rarely encountered, so its diagnosis is challenging at times. With the advent of improved diagnostic methods, prognostic and predictive biomarkers and improved therapeutic strategies, outcomes of adrenal gland tumors have improved but their pathological and prognostic classification are still difficult due their heterogenous nature and rarity.

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