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HISTOPATHOLOGICAL SPECTRUM OF ADRENAL LESIONS

Pathology

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ABSTRACT

Background- The bipartite adrenal gland has tumours arising from cortex, medulla or as metastasis from extra-adrenal sites. Distinguishing benign from malignant types is a challenging task for pathologists, this study gives an insight into adrenal lesions with their histopathological findings and its role in categorizing these tumours to aid in their diagnosis and proper management. **Aims And Objectives-** This study was to analyse the clinical presentation and histopathological spectrum of adrenal lesions in our centre. **Materials And Methods-** This is a retrospective observational study conducted over a course of 2 years. A total of 15 adrenelectomy specimens were received and submitted for histopathological assessment. Based on the criteria they are classified as benign and malignant neoplasms. **Results-** Most of the adrenal lesions were identified in the right adrenal gland and most of them showed female prelidection. Out of 15 neoplasms identified, 20% of the lesion belongs to malignant category, 80% of the lesions were under benign category. Among all the neoplasms, Pheochromocytoma (46%) was the most common neoplasm in our study. **Conclusion-** Pathological evaluation and immunohistochemical profiling has got important role in categorizing adrenal tumours along with clinical, radio logical and biochemical inputs and their subsequent management.

KEYWORDS

Weiss criteria, Myelolipoma, Adrenal cortical adenoma, Pheochromcytoma, Myolipoma

INTRODUCTION

The adrenal gland is a bipartite endocrine gland has two separate compartments, the cortex and the medulla, that are embryologically and functionally different [1]. The steroid hormones aldosterone, cortisol, and testosterone are produced by the adrenal cortex of mesodermal origin, while catecholamines are produced by the adrenal medulla of neural crest origin [1]. Tumours arising from cortex are mainly adenomas and carcinomas whereas from medulla are pheochromocytomas and neuroblastomas[3]. Adrenal glands are removed for histological analysis as part of a radical nephrectomy or for surgical excision of an adrenal tumor[2].

The main use of an adrenal needle biopsy is to establish malignancy when there is a suspicion of metastatic involvement or to confirm the diagnosis of ACC when surgical resection is not possible [2].

Adrenal lesions are rarely encountered in surgical pathology, therefore we need to understand the spectrum of histopathological adrenal lesions, their clinical presentation and correlation with clinicopathological variables.

Aims And Objectives

This study was to analyse the clinical presentation and histopathological spectrum of adrenal lesions in our centre over a course of two years.

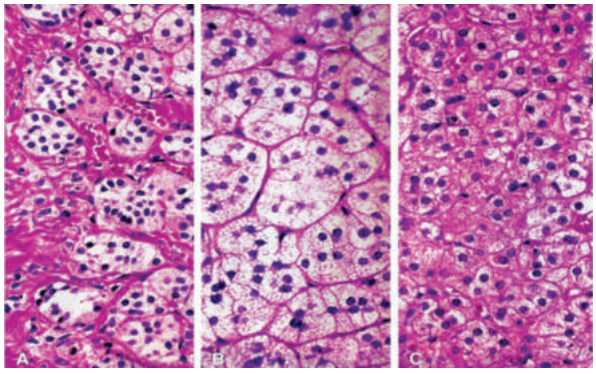
MATERIALS AND METHODS

Over the course of 2 years, a retrospective observational study was conducted on all adrenal gland specimens submitted for histological assessment. The needle biopsies from the adrenal gland and adrenalectomies performed for a pathologic process of the adrenal gland were included in the research sample. The research does not include adrenal glands removed as part of a radical nephrectomy for primary renal pathology. There were a total of fifteen cases evaluated, all of them were adrenalectomy specimens. Based on data retrieved from the institute's histopathology registers, the neoplastic and non-neoplastic conditions observed were analysed with reference to age, gender, clinical features (including functional status, radiological findings, and relevant biochemical investigations done), gross and histopathological features (including immunohistochemical findings). Microscopically, tissue sections stained with haematoxylin and eosin were examined and histopathological characteristics documented. The IHC had been performed whenever it was required.

Rievew Of Literature

Adrenal gland is composite of two organs- cortex and medulla. Adrenal cortex is divided into three zones, all of which are under the influence of ACTH- zona glomerulosa, zona fasiculata and zona reticularis.

Zona glomerulosa- site of mineralocorticoid (aldosterone) production.
Zona fasiculata- site of glucocorticoid and sex hormone production.
Zona reticularis- also involved in the secretion of glucocorticoid and sex hormones.



A. Glomerulosa B. Fasiculata C. Reticularis

Medulla- predominant cell type is pheochromocyte (medullary cell or chromaffin cell) admixed with scattered cortical cells and ganglion cells.

WHO classification of adrenal tumours [7]

Adrenal Cortex

- Adrenal cortical carcinoma
- Adrenal cortical adenoma
- Sex-cord stromal tumors
- Adenomatoid tumor
- Mesenchymal and stromal tumours
- Hematolymphoid tumours
- Secondary tumors

Adrenal Medulla

- Pheochromocytoma
- Extra- adrenal paragangliomas
- Neuroblastic tumors of adrenal gland
- Composite pheochromocytoma
- Composite paraganglioma

Non neoplastic lesions associated with adrenals include hypoplasia, hyperplasia, cytomegaly, cysts, nodules and accessory tissue. Most of these are nonfunctional even though some functional tumors may show clinical features like virilisation, cushingoid features, feminisation and hyperaldosteronism.[4]

Adenomas and carcinomas are about equally common in adults; in children, carcinomas predominate. While most cortical neoplasms are sporadic, two familial cancer syndromes are associated with a predisposition for developing adrenocortical carcinomas: Li-Fraumeni syndrome, caused by germline TP53 mutations and Beckwith-Wiedemann syndrome, a disorder of epigenetic imprinting

involving the gene for insulin-like growth factor 2.

Adrenal cortical adenomas represent the most common primary adrenal lesion. They may be functioning (producing aldosterone, cortisol or sex hormones) or non-functioning.

Adreno cortical carcinomas are very rare tumors with a frequency of 2 in a million per year. The relative incidence among malignant tumors is 2% and shows a bimodal presentation with peak occurence at < 5years and 50-70 years. [3]

Weiss System which is considered gold standard was used to distinguish between benign and malignant lesions in adrenal cortical tumors. The presence of 3 or more of the following features is correlated with malignant behaviour - Weiss criteria.[5]

1. High nuclear grade (Fuhrman grade system)
2. >5 mitotic figures/50 HPF
3. Atypical mitotic figures
4. Eosinophilic cytoplasm in >75% of tumour cells
5. Diffuse architecture in >1/3rd of the tumour
6. Necrosis
7. Venous invasion
8. Sinusoidal invasion
9. Capsular invasion

In most cases, correlation of histopathological features with clinical and laboratory findings helped in arriving at the diagnosis.

The study by Stewart et al (2004) which included 9 cases of adrenocortical tumors showed: The mean age of presentation as 2 Year and 5 months, male to female ratio as 1.3:1 and the common presentation as abdominal distention. Particularly virilisation was mostly associated with adrenocortical carcinoma and cushingoid features with adrenal adenoma.

RESULTS AND OBSERVATION

In the present study a total of 15 adrenal neoplasms were diagnosed within two year period. The patients in this study were between 20-60 years of age. Among them male to female ratio was found to be 2:1. Most common distribution of the neoplasms were on the right adrenal gland.

The data was collected on Microsoft Excel and descriptive statistics was analysed.

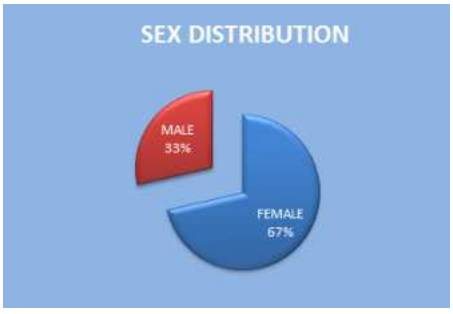
Table 1 Denotes The Histopathological Spectrum Of Adrenal Lesions

AGE	SEX	SIDE	SPECIMEN	DIAGNOSIS
48	F	LEFT	ADRENALECTOMY	PHEOCHROMOCYTOMA
36	F	RIGHT	ADRENALECTOMY	PHEOCHROMOCYTOMA
60	M	RIGHT	ADRENALECTOMY	ADRENAL ANGIOYOLIOPMA
44	F	RIGHT	ADRENALECTOMY	PHEOCHROMOCYTOMA
33	F	LEFT	ADRENALECTOMY	PHEOCHROMOCYTOMA
53	F	RIGHT	ADRENALECTOMY	ADRENOCORTICAL CARCINOMA
42	M	RIGHT	ADRENALECTOMY	MYELOLIPOMA
65	F	RIGHT	ADRENALECTOMY	PHEOCHROMOCYTOMA
58	F	LEFT	ADRENALECTOMY	PHEOCHROMOCYTOMA
65	M	LEFT	ADRENALECTOMY	MALIGNANT PHEOCHROMOCYTOMA
37	F	RIGHT	ADRENALECTOMY	PHEOCHROMOCYTOMA
47	F	LEFT	ADRENALECTOMY	ADRENOCORTICAL CARCINOMA-ONCOCYTIC VARIANT
36	M	RIGHT	ADRENALECTOMY	MYELOLIPOMA
27	M	RIGHT	ADRENALECTOMY	ADRENOCORTICAL ADENOMA
50	F	RIGHT	ADRENALECTOMY	ADRENOCORTICAL ADENOMA

Table 2 Age Wise Distribution Of Adrenal Neoplasms

20- 30	1 case- adrenocortical adenoma
30- 40	3 cases- pheochromocytoma 1 case- myelolipoma
40- 50	1 case- adrenocortical adenoma 1 case- myelolipoma 1 case- adrenocortical carcinoma- oncocytic variant 2 cases- pheochromcytoma
50-60	1 case- adrenocortical carcinoma 1 case- angiomyolipoma 1 case- Pheochromocytoma
60-70	1 case- Pheochromocytoma 1 case- Malignant pheochromocytoma

Sex Wise Distribution Of Cases

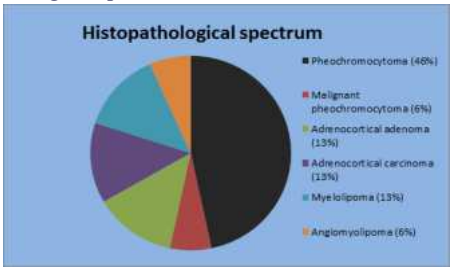


Out of 15 cases, 10 cases occurred in females and 5 cases were males and thus most of the adrenal neoplasms had female prelidection.

Distribution Based On The Side Of The Adrenal Gland Involved

Out of 15 cases, most of the neoplasms were on right adrenal gland.

Histopathological Spectrum Of Adrenal Lesions



DISCUSSION

Pheochromocytoma was the most common tumour observed, accounting for 46 percent (7/15). The tumour was more prevalent in the third and fourth decades and all the cases were females. All individuals had functional tumours with higher serum catecholamines and their metabolites (adrenaline, noradrenaline, dopamine,

metanephrine), and/or elevated urine vanillyl mandelic acid and metanephrine levels, as well as adrenal mass on imaging (CT/MRI). The tumours had the classic zellballen pattern separated by delicate fibrovascular septa. The cells are round to ovoid nuclei with prominent nucleoli, finely granular basophilic or amphophilic cytoplasm, with focal areas of nuclear pleomorphism, odd large cells in some cases, and enhanced mitotic activity, with abnormal mitotic patterns detected in a few cases. There was no evidence of capsular or vascular invasion in any of the tumours.

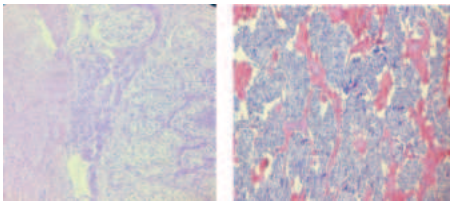


Fig 1: Pheochromocytoma with Zellballen pattern

65 year old male with complaints of headache and palpitations. Histopathology shows poorly encapsulated neoplasm with capsular invasion. Atypical mitotic figures made out. As PASS (Pheochromocytoma of the Adrenal gland Scaled Score) was more than 11, reported as Malignant Pheochromocytoma.

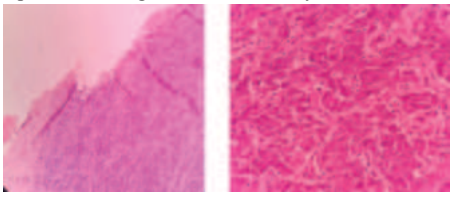


Fig: 2 Malignant Pheochromocytoma with Capsular invasion

Cortical carcinomas are relatively uncommon. They have bimodal age distribution with peaks in first and fifth decades of life. [6] 2 cases of adrenal cortical carcinoma were reported both cases were around fifth decade. Grossly the tumor had variegated appearance with areas of necrosis and haemorrhage. Lymphovascular invasion and capsular invasion was present. Weiss scoring was done and had a score of more than three.

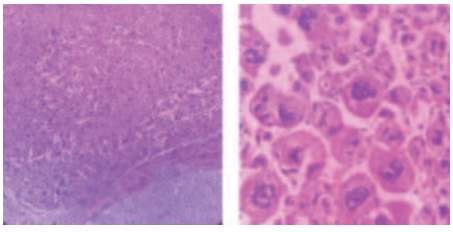


Fig 3: Adreno cortical carcinoma

Adrenal cortical adenomas are common lesions when compared with carcinomas. They may present as functioning adenomas or nonfunctioning adenomas. 2 cases of cortical adenomas were reported. Grossly adenomas appeared as solitary lesion. They are well circumscribed and encapsulated with homogenous yellow appearance. Microscopy- both cases showed polyhedral cells with abundant clear to granular cytoplasm, few cells with eosinophilic cytoplasm. No areas of necrosis seen. Most cases are diagnosed based on morphology alone, but few cases require immunophenotypic analysis. IHC markers used are Inhibin, Melan A, synaptophysin.

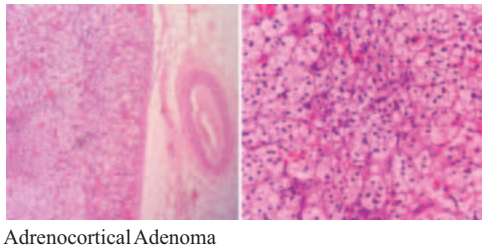


Fig: 4 Adrenocortical Adenoma

Adrenal myelolipoma, a rare benign tumour was also reported. The patients presented with abdominal pain and distension. Grossly the tumour was well encapsulated and showed yellowish areas. The tumours showed the characteristic morphological features with varying proportions of mature adipose tissue and hematopoietic cells.

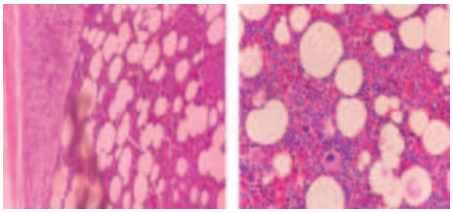
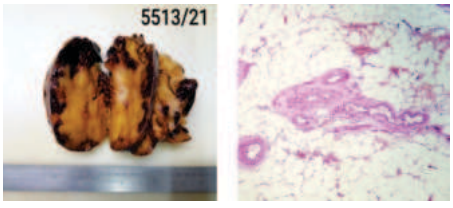


Fig: 5 Adrenal Myelolipoma (10x) (40x)

Adrenal angiomyolipoma is a very rare tumor in the adrenal. It is a benign mesenchymal tumour composed of variable proportion of adipose tissue, spindle cells or epithelioid smooth muscle cells and abnormal thick walled blood vessels. In our case a 60 year old male presented with complaints of dull aching diffuse abdominal pain and vomiting or 7 days. Initially the provisional diagnosis was cholecystitis. CECT abdomen showed a non enhancing well defined fat density lesion o size 1.8x10.8x9.8 cm noted in the suprarenal region. The lesion shows distinct plane with right kidney.

Histopathology showed normal adrenal gland parenchyma and a adjacent lesion composed of lobules of adipocytes, dysmorphic variable sized vessels and radial array of smooth muscle fibres around the blood vessels



Gross Microscopy

Fig : 6 Angiomyolipoma

SUMMARY AND CONCLUSION

In the current analysis, primary adrenal neoplasms were the most common adrenal pathology. The initial tumours were usually unilateral and solitary, and they were more prevalent in women in their third to fifth decades of life. The most frequent tumour found was pheochromocytoma, with many of them being functioning. The Weiss criteria were helpful in distinguishing between ACC and adenoma. IHC is useful for identifying primary adrenal tumours as well as distinguishing metastatic tumours from original malignancies.

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