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Incidental or Symptomatic Adrenal Masses: Series of Cases with Literature Review; An Experience at Tertiary Cancer Care Hospital

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ABSTRACT

Introduction: Adrenal gland is retroperitoneal organ located above kidney. Adrenal neoplasm ranges from asymptomatic cyst to fatal carcinoma. Primary adrenal neoplasm has varied clinical presentation being functional or non-functional, symptomatic or asymptomatic. We investigated the clinicopathological characteristics of adrenal tumors taking into account the various pathological views of these tumors and their various clinical manifestations.
Material and Method: This was a retrospective observational study including the tissue samples of adrenal gland submitted for histopathological evaluation from January 2021 to January 2023. Haematoxylin and Eosin-stained, Formalin Fixed, Paraffin Embedded tissue sections of the study sample were reviewed microscopically to study the histopathological features.
Result: The study group showed that majority of cases in >40-year age group, only 2 cases were <40 years of age. Study shows female preponderance. Out of total cases studied most commonly encountered are adreno-cortical carcinoma then pheochromocytoma. Three cases were incidental imaging findings, confirmed later as schwannoma.
Conclusion: The spectrum of studied primary adrenal neoplasms showed a varied clinical presentation. They were generally unilateral and solitary. Pheochromocytoma followed by ACC were the frequent tumors encountered. Weiss system has an invaluable role in the diagnosis of ACCs. IHC plays a key role in diagnosing metastatic tumors.

Keywords: Adrenal neoplasm, Adrenocortical carcinoma, Schwannoma, Pheochromocytoma.

INTRODUCTION

The adrenal is an endocrine gland with two distinct compartments, cortex and medulla, that differ embryologically and functionally.[1]

The adrenal cortex of mesodermal origin produces the steroid hormones aldosterone, cortisol and testosterone, and the adrenal medulla of neural crest origin produces catecholamines. [1]

Determining the functionality of a cortical neoplasm is possible based on clinical evaluation and measuring the hormone or its metabolites in the laboratory.[2]

Adrenal neoplasm ranges from a symptomatic cyst to fatal carcinoma.[2]

The primary adrenal tumours may be functional or nonfunctional presenting with nonspecific symptoms, or remain asymptomatic and are detected as incidentalomas in radio imaging studies [1]
Tumors of the adrenal cortex include adrenal cortical neoplasms such as adrenal cortical adenomas and carcinomas. Tumors of the medullary component typically present as pheochromocytomas. [5]
Adrenocortical carcinoma is a highly aggressive, rare endocrine malignancy [6]
The adrenal medulla is innervated by the phrenic nerve, the vagus nerve, and the sympathetic trunk. Adrenal schwannomas are thought to arise from Schwann cells associated with these nerves [4]
Pheochromocytomas are tumors arising from chromaffin cells of the adrenal medulla that synthesize, store, metabolize and usually but not always secrete catecholamines [3]
Adrenal gland specimens or needle biopsies are rarely received in surgical pathology.
It is a diagnostic challenge to pathologist, so must be guided by patient's clinical, radiological and biochemical profile for better evaluation.

MATERIAL AND METHODS

The tissue samples included in this retrospective observational study included specimens from adrenalectomy procedures as well as needle biopsies of adrenal masses that were submitted for histological analysis.
Exclusion criteria- Adrenal gland removed as radical nephrectomy for primary renal pathology was excluded from study. Slides received for second opinion were excluded.
This study includes total 18 cases out of which 5 were the needle biopsies. The various neoplastic conditions were analysed with reference to age, gender, clinical characteristics, functional status, radiology findings and histopathological features. Specimen were weighed, taken dimensions then kept for overnight fixation in formalin. H & E-stained sections of the study sample were studied. IHC studies were advised and carried out whenever necessary.

RESULT

Total cases studied were 18, out of which 5 were the USG guided needle biopsies. In the present study, 16 cases were from age group of 14 to 71 years and 02 were children (<7 years). 05 were males and 13 were females (M: F -1:3.8). Among the primary, adrenocortical carcinoma was the most common followed by schwannoma, pheochromocytoma, neuroblastoma and ganglio-neuroblastoma.

Adrenal tumors	**Common age**	**Male**	**Female**	**Procedures (Adrenalectomy/biopsy)**
Adrenocortical carcinoma	4th-6th decade	1	5	6 Adrenalectomy
Oncocytic adrenocortical carcinoma	4th decade	0	1	Adrenalectomy
Pheochromocytoma	4th-5th decade	1	2	3 Adrenalectomy
Schwannoma	4th-5th decade	1	3	4 Adrenalectomy
Ganglioneuroblastoma	Children's <1 year	0	1	USG guided Biopsy
Neuroblastoma	< 7 years	0	1	1 Adrenalectomy
Metastatic deposits	5th-6th decade	2	0	2 USG guided Biopsy

Table/Fig 1

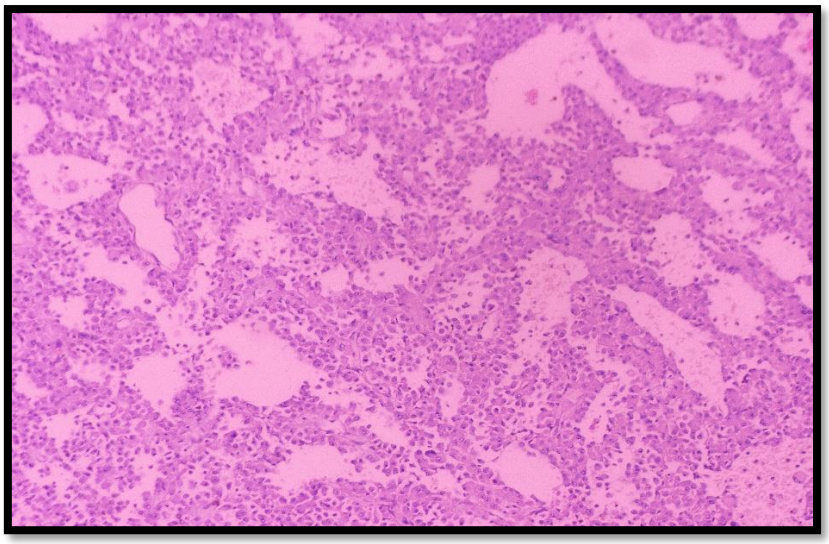
Adrenal tumor	**Clinical presentation**	**Size range & Weight**	**Gross**	**Microscopy**
Adrenocortical carcinoma	Mostly nonfunctional tumor with symptom of mass effect	4-10 cm 0.5-2kg	Capsulated, yellowish, tan variegated, necrotic, hemorrhagic cystic	Diffuse sheets, cords, trabecular pattern, large round to polygonal cells with pleomorphic vesicular nuclei with prominent nucleoli. Clear cell <25%, mitosis >5/50 hpf.

				Atypical mitosis seen. Tumor necrosis.
Oncocytic adrenocortical carcinoma	Nonfunctional tumor with mass effect	26 cm 3.2kg	Mahogany brown, Capsulated, necrotic, hemorrhagic	Large polygonal cells with moderately pleomorphic vesicular to hyperchromatic nuclei and abundant amount of intensely eosinophilic to faintly eosinophilic cytoplasm with capsular invasion. Infrequent mitosis.
Pheochromocytoma	Functional tumor with hormonal manifestations elevated 24 hr urine metanephrine level	4-7 cm 0.5-1.5kg	Globular, smooth, yellow tan with areas of necrosis	Nesting, trabecular, solid pattern. Polygonal cells with round to oval nuclei and granular eosinophilic cytoplasm with prominent vascular network
Schwannoma	Symptoms of mass effect only	5-12 cm 0.5-2.5kg	Pale yellow, capsulated, bosselated, cystic	Spindle cells with indistinct borders, arranged in bundles, interlacing fascicles and vague palisading nuclei.
Ganglio-neuroblastoma	Non-functional tumor with mass effect showing constipation	Biopsy	-	Ganglion cells with abundant cytoplasm, neural tissue intermixed with foci of small round cells.
Metastatic deposits of adenocarcinoma	Non-functional tumor with mass effect	Biopsy	-	Groups, gland like structure and papillary projection lined by large cuboidal to columnar cells having hyperchromatic nuclei with scanty cytoplasm.
Neuroblastoma	Mass effect	7cm 1.8kg	Encapsulate, bosselated, nodular. On cut surface greyish tan and necrotic	Small round blue cells with surrounding schwannian stroma and neuropil.

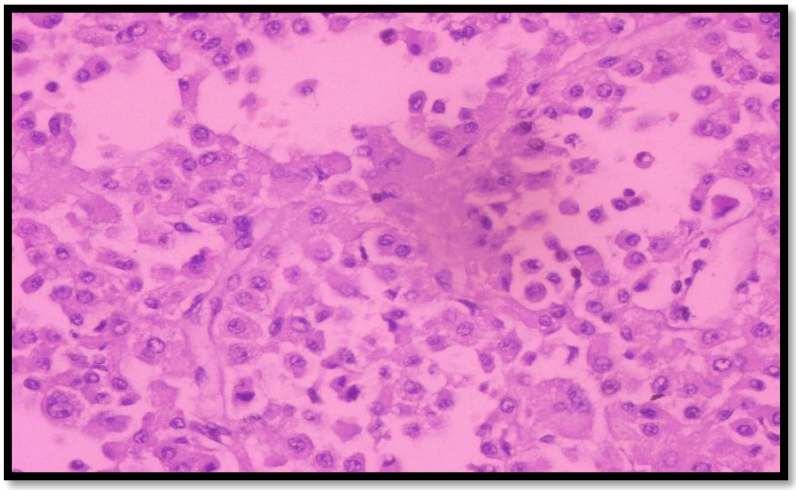
Table/Fig 2

Adrenocortical carcinoma

Table/Fig 3: ACC: Capsulated, yellowish, tan variegated with necrotic, hemorrhagic, cystic areas.

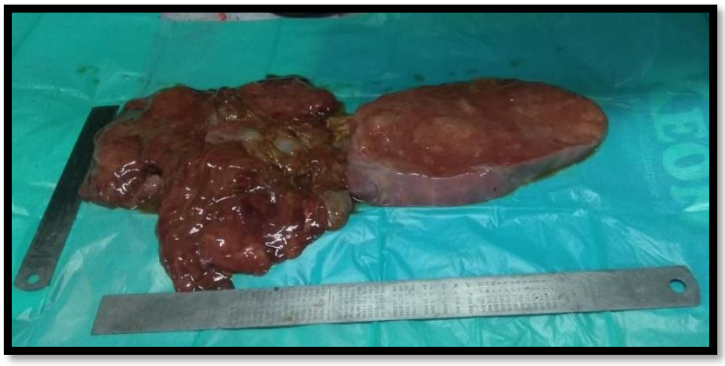


Table/Fig 4: ACC: Tumour arranged in diffuse sheets, cords, trabecular pattern

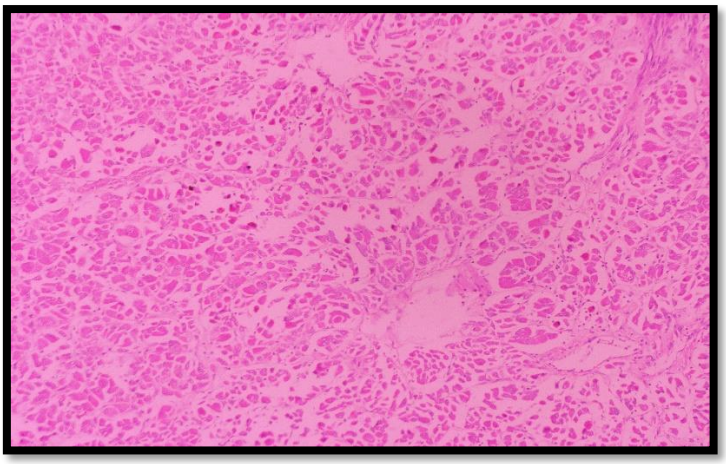


Table/Fig 5: ACC: large round to polygonal cells with pleomorphic vesicular nuclei with prominent nucleoli.

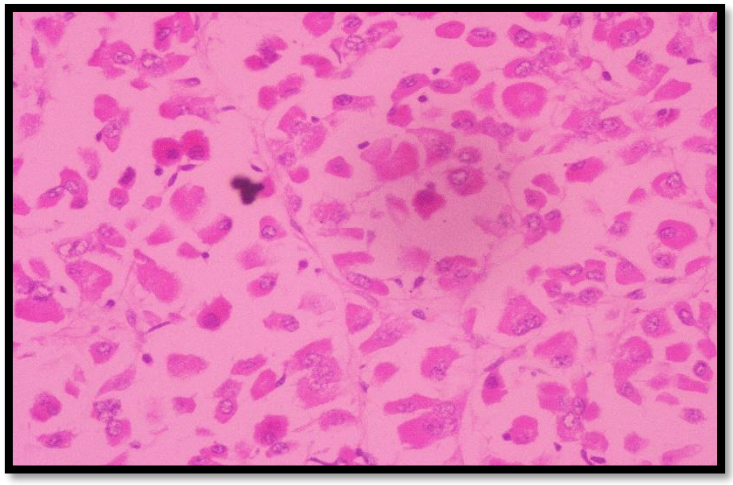
Oncocytic variant of ACC



Table/Fig 6: Oncocytic variant of ACC: On cut section mahogany brown, necrotic, hemorrhagic.

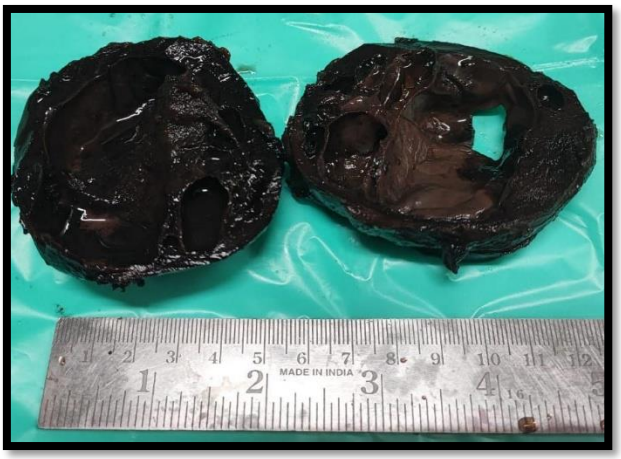


Table/Fig 7: Oncocytic variant of ACC: Large polygonal cells with moderately pleomorphic vesicular to hyperchromatic nuclei and abundant amount of intensely eosinophilic to faintly eosinophilic cytoplasm with capsular invasion. Infrequent mitosis.

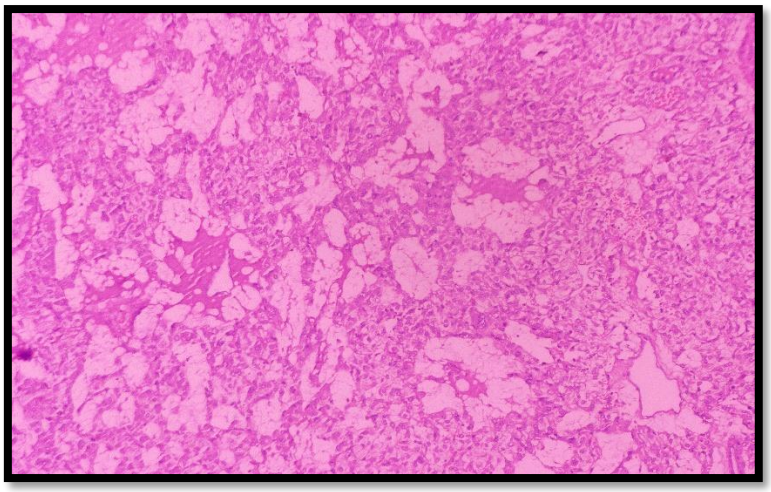


Table/Fig 8: Oncocytic variant of ACC: Large polygonal cells with moderately pleomorphic vesicular to hyperchromatic nuclei and abundant amount of intensely eosinophilic to faintly eosinophilic cytoplasm.

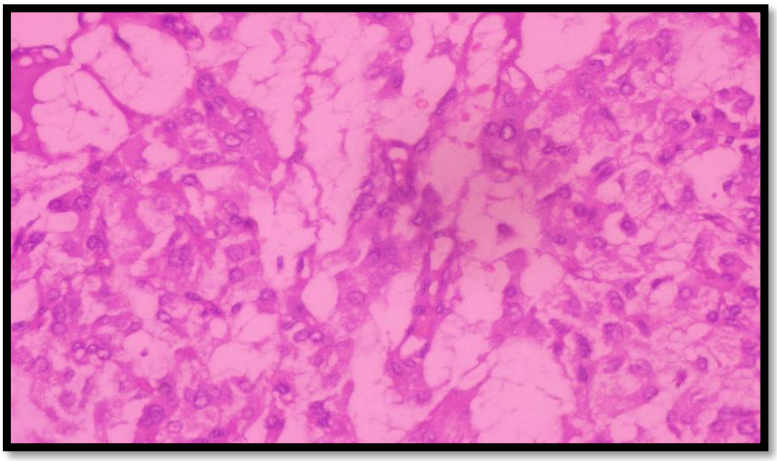
Pheochromocytoma



Table/Fig 9: Pheochromocytoma: Nodular mass with solid gray-tan areas, cystic areas.

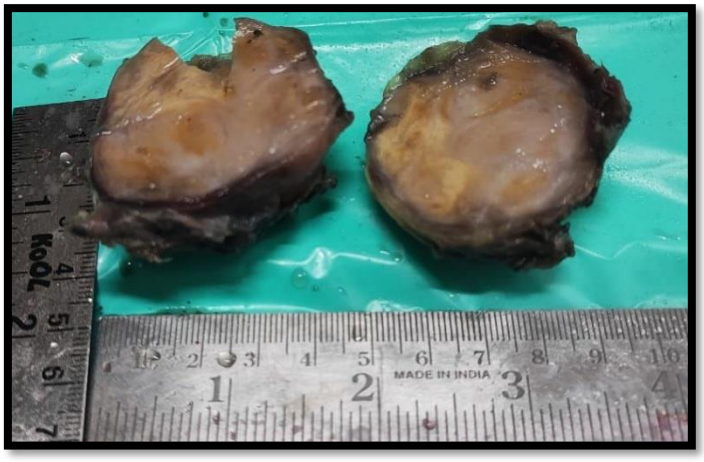


Table/Fig 10: Pheochromocytoma: Nesting, trabecular, solid pattern. Polygonal cells with round to oval nuclei and granular eosinophilic cytoplasm with prominent vascular network.

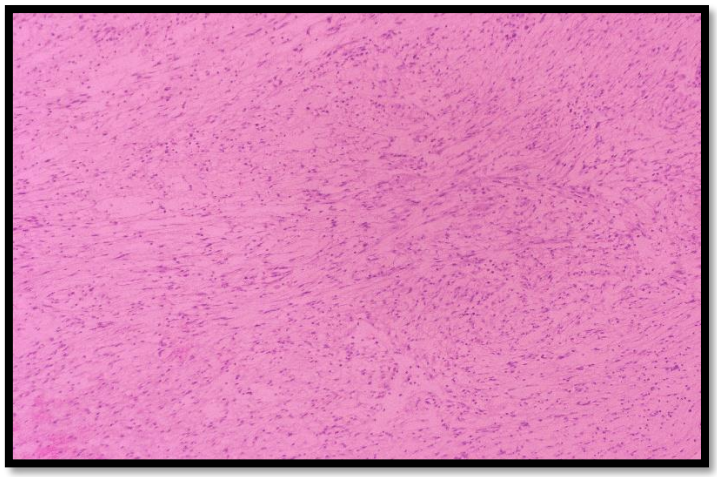


Table/Fig 11: Pheochromocytoma: Polygonal cells with round to oval nuclei and granular eosinophilic cytoplasm with prominent vascular network.

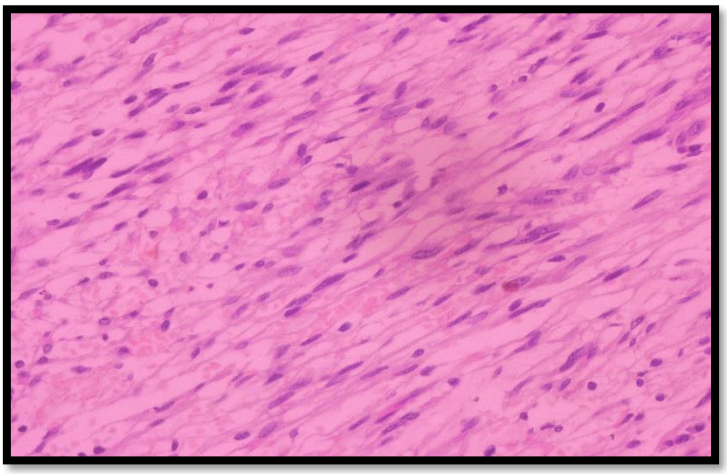
Schwannoma



Table/Fig 12: Schwannoma: Encapsulated, globular mass, on cut section fleshy, mucinous.

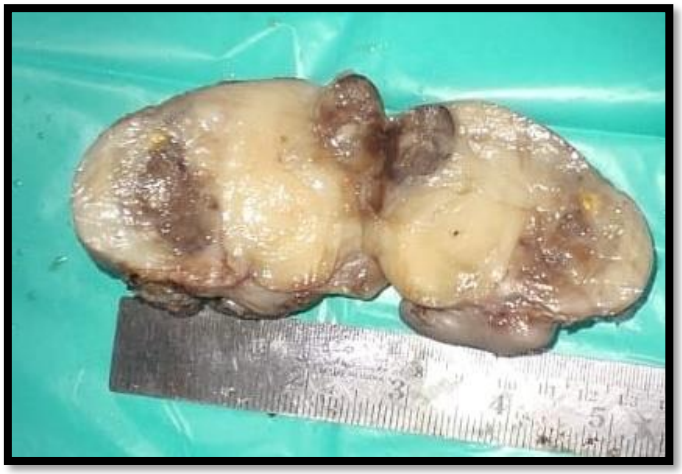


Table/Fig 13: Schwannoma: Spindle cells with indistinct borders, arranged in bundles, interlacing fascicles and vague palisading nuclei elongated buckled and wavy.

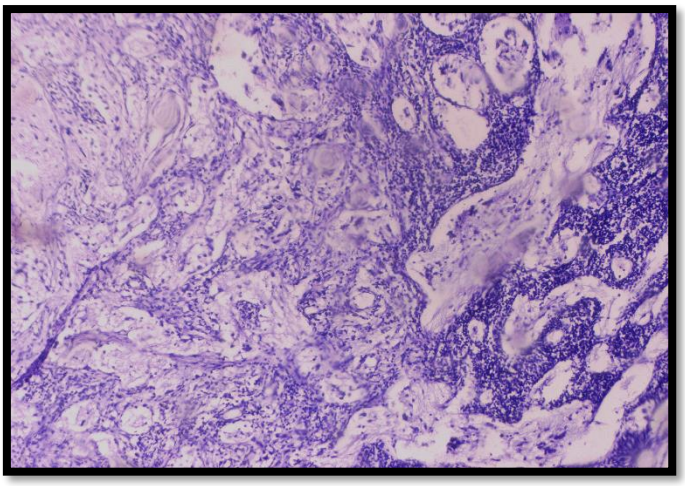


Table/Fig 14: Schwannoma: Spindle cells with indistinct borders, arranged in bundles, interlacing fascicles and vague palisading nuclei elongated buckled and wavy.

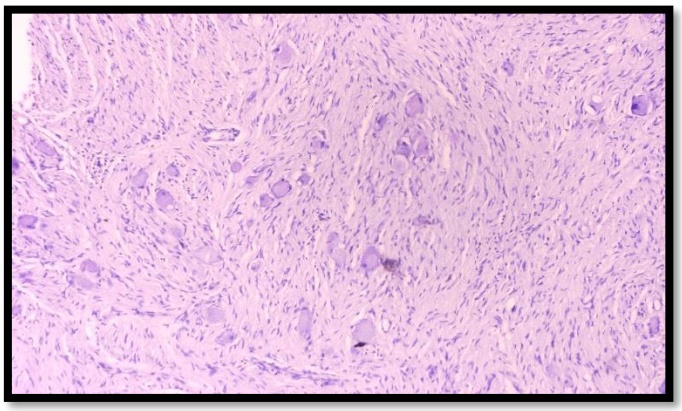
Neuroblastoma



Table/Fig 15: Neuroblastoma: Encapsulated, bosselated lobular tissue mass. Cut surface is grayish and at places necrotic.

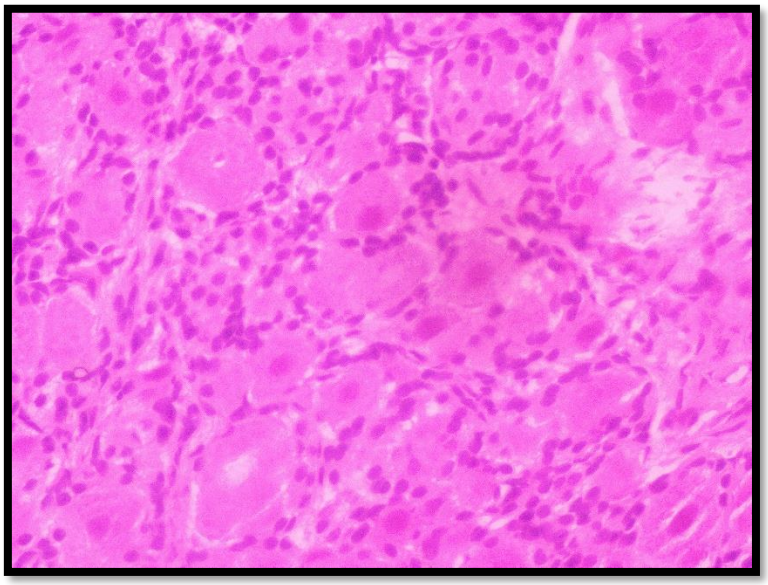


Table/Fig 16: Neuroblastoma: Small round blue cells with surrounding Schwannian stroma and neuropil.



Table/Fig 17: Neuroblastoma: Ganglion cells surrounded by Schwannian stroma.

Ganglio-neuroblastoma



Table/Fig 18: Ganglio-neuroblastoma: Ganglion cells with abundant cytoplasm, neural tissue intermixed with foci of small round cells.

Weiss scoring was done and all the tumors revealed score >3, which confirms the adrenocortical carcinoma. IHC was done to confirm the case of oncocytic variant of ACC which revealed positive staining for vimentin, calretinin, CK and CD 56. All other ACC cases had positive staining for calretinin and CD10. Pheochromocytoma had diffuse positivity for chromogranin, synaptophysin and S100 in sustentacular cells. Two cases of schwannoma were confirmed on IHC had strong positivity for S100 and SOX10.

DISCUSSION

Primary adrenal neoplasms were most frequent in 3rd to 5th decade of life and females were more commonly affected [1]. Majority of the cases are unilateral. Majority of the adrenocortical tumors are nonfunctional with some are showing mass effect. Mondal SK et al, stated that the threshold for malignancy was revised in 1989: the presence of three or more of the nine histopathologic criteria, as defined by the Weiss system, was considered significant for a malignant clinical behavior and it was reported as the modified Weiss system [7]. According to CAP protocol 2022 Modified Weiss scoring system, a score of ≥ 3 indicates a diagnosis of adrenal cortical carcinoma [8]. In present study all the cases of ACC had score > 3, which confirms malignancy. Deepa Krishnan et al, in their retrospective observational study, all the 15 cases of ACC had a score of >3 [1]. Jain M et al., in their retrospective study on 42 adrenal cortical tumours observed all the 23 cases of ACC had a score of >3 [10]; Mondal SK et al., also observed a score of >3 in all the 10 cases of ACC studied [11]. Weiss system is most widely used, which is modified in 2002 and is excellent to diagnose malignancy in adrenal Tumors.

Parameters	Score
Mitotic count > 5 per 50 high-power fields (10 mm2)	2
Clear cells in ≤ 25%	2
Atypical mitosis	1
Necrosis	1
Capsular invasion	1
Total score	7

Table/Fig 19

Only one case of oncocytic variant of ACC confirmed by Lin-Weiss -Bisceglia system 2022 which is specific for it, the parameters included in it are:

Major-

1. Mitosis >5/50 high power field.
2. Atypical mitotic figure
3. Venous invasion

Minor-

1. Size >10cm &/or weight >200 gram.
2. Necrosis
3. Sinusoidal invasion
4. Capsular invasion

One major confirms the malignancy and if one to four minor criteria present shows uncertain malignant potential. In our case 3 minor criteria were present which confirm uncertain malignant potential.

According to Deepa et al, ACCs are graded based on their mitotic rate into low grade and high grade, <20 mitosis/ 50 hpf is low grade and >20 mitosis/50 hpf is high grade [1]. In our study only one case of ACC was high grade(>20mitoses/50hpf), all others were low grade (<20 mitoses/50hpf). IHC play's major role to confirm the primary site, the majority of the adrenal tumors are primary only 2 were the metastatic deposits of adenocarcinoma.

Majority of schwannoma are nonfunctional showing only mass effect. According to Yassen et al, adrenal schwannomas ranging in size from 0.6 to 14.5 cm, with a median of 5.5 cm [9]. Majority of the tumors are >4cm in size. Size of the mass is major determinant

of malignancy in adrenal tumors. Two out of four are incidental findings. A careful correlation between radiological, surgical evaluation and microscopic analysis is necessary. Prompt diagnosis and treatment are emphasized in this tumor, that is readily amenable to surgery.

In accordance with literature [1] pheochromocytoma are mostly functional with hormonal manifestations including hypertension, headache, sweating, palpitations, chest pain and elevated level of serum catecholamines. The study found a slight female predilection. Female preponderance was also noted by Kumari NS et al., in their study [12]. Pheochromocytoma of the adrenal gland scaled score used to know malignant potential of the tumour. Score >4 considered as malignancy. Out of 03 cases, 01 case had score 6+ which confirms the malignant potential of pheochromocytoma.

Pheochromocytoma of the adrenal gland scaled score (PASS)

Histologic feature	Score (score >4 is considered for malignancy)
Periadrenal adipose invasion	+2
>3 mitoses/10 high power field	+2
Atypical mitoses	+2
Necrosis	+2
Cellular spindling	+2
Marked nuclear pleomorphism	+1
Cellular monotony	+2
Large nests or diffuse growth	+2
High cellularity	+2
Capsular invasion	+1
Vascular invasion	+1
Hyperchromasia	+1

Table/Fig 20

Neuroblastoma is the most common extracranial solid tumor of childhood. According to Missaoui et al., 2011; Mehdiabadi et al., 2013 it commonly presents in children younger than 2 years of age, with 90% being younger than 5 years of age [13,14]. In current study the child was less than 7 years of age. Neuroblastoma arises in tissue of sympathetic nervous system, mostly on adrenal medulla. It is a most common malignant neoplasm of infancy.

Post NACT neuroblastoma following parameters needs to be reported as per CAP protocol:

- Neuroblastic tumor size.
- Appearance on gross
- Degree of differentiation.
- Mitotic karyorrhectic index (MKI).
- Treatment effect in the form of tumor necrosis.
- Lymph node status.

CONCLUSION

Adrenal tumours may present with varied clinical presentation and may or may not be functional in nature. Routine histopathology with basic parameters like weight and dimensions of the specimen and extensive sampling are prerequisite for approaching adrenalectomy specimen. IHC may be required for confirmation of findings along with clinical symptoms, radiological and biochemical investigations.

Limitations

Although present study included spectrum of adrenal lesions small sample size and lack of follow-up data in most cases was limitation in present study.

Declaration by Authors

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Conflict of Interest: The authors declare no conflict of interest.

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