Section: Pathology

Case Series

A CASE SERIES OF ADRENAL GLAND TUMORS: HISTOPATHOLOGICAL SPECTRUM OF PHEOCHROMOCYTOMA AND ADRENOCORTICAL CARCINOMA

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Received *: 01/01/2026*
Received in revised form *: 10/01/2026*
Accepted *: 28/01/2026*

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DOI:10.70034/ijmedph.2026.1.246

Source of Support: Nil,
Conflict of Interest: Nonedeclared

Int J Med Pub Health
2026; 16 (1); 1412-1414

ABSTRACT

Background: Adrenal gland tumors are uncommon neoplasms with diverse clinical, biochemical, and histopathological features. Among these, pheochromocytoma and adrenocortical carcinoma represent tumors of medullary and cortical origin respectively, with significant diagnostic and prognostic implications. **Aim:** To study the clinicopathological and histomorphological features of adrenal gland tumors with emphasis on pheochromocytoma and adrenocortical carcinoma.

Materials and Methods: A cross-sectional observational analysis of six cases of adrenal gland tumors received in the Department of Pathology over a period of 2 years was performed. Clinical details, radiological findings, gross morphology, histopathology, and immunohistochemistry (where available) were reviewed.

Results: Of the six cases, four were diagnosed as pheochromocytoma and two as adrenocortical carcinoma. Pheochromocytomas showed characteristic Zellballen architecture, while adrenocortical carcinomas exhibited features of malignancy as per Weiss criteria.

Conclusion: Histopathological examination remains the gold standard for definitive diagnosis of adrenal tumors. Recognition of characteristic morphological features is essential for accurate classification and prognostication.

Keywords: Adrenal gland tumors, Pheochromocytoma, Adrenocortical carcinoma, Weiss criteria, Case series.

INTRODUCTION

Adrenal gland tumors are rare neoplasms arising from either the adrenal cortex or medulla and account for a small proportion of endocrine tumors.[1] These tumors may be hormonally functional or nonfunctional and often present with nonspecific clinical manifestations, making diagnosis challenging.[2]

Pheochromocytoma is a catecholamine-producing tumor arising from chromaffin cells of the adrenal medulla and is associated with symptoms such as hypertension, palpitations, and headache.[3] Adrenocortical carcinoma (ACC) is an aggressive malignant tumor of cortical origin, often presenting at an advanced stage with poor prognosis.[4]

Histopathological evaluation plays a pivotal role in differentiating benign from malignant adrenal tumors, especially in ACC, where Weiss scoring system is widely used.[5] This case series highlights the morphological spectrum of pheochromocytoma

and adrenocortical carcinoma encountered in routine pathology practice.

Weiss Criteria for Adrenocortical Tumors

The Weiss system is the most widely accepted histopathological scoring system used to distinguish adrenocortical carcinoma from adenoma. It is based on nine microscopic parameters, each scored as present (1) or absent (0). A Weiss score ≥3 is diagnostic of adrenocortical carcinoma.

No.	Weiss Criterion	Histological Description
1	High nuclear grade	Fuhrman grade III or IV nuclei
2	Mitotic rate	>5/50 HPF
3	Atypical mitoses	Presence of abnormal mitotic forms
4	≤25% clear cells	Predominance of eosinophilic tumor cells
5	Diffuse architecture	>33% of tumor showing diffuse growth
6	Necrosis	Presence of confluent tumor necrosis
7	Venous invasion	Tumor invasion into veins with muscular wall
8	Sinusoidal invasion	Invasion into thin-walled vascular channels
9	Capsular invasion	Tumor infiltration through capsule

MATERIALS AND METHODS

The cross- sectional observational study was conducted in the Department of Pathology at Dr. D.Y Patil Medical College, Hospital and Research Institute, Kolhapur. A total case series included six cases of adrenal gland tumors received over a period of 2 years (2023-2025).

Clinical data including age, sex, presenting symptoms, blood pressure status, and radiological findings were obtained from medical records. Surgical specimens were preserved in 10% neutral buffered formalin. A thorough visual inspection was conducted following standard procedures.

Representative sections were stained with hematoxylin and eosin, and immunohistochemistry was performed in selected cases using markers such as **chromogranin, synaptophysin, inhibin, Melan-A, and Ki-67**, wherever available. Adrenocortical carcinomas were evaluated using **Weiss criteria**.

RESULTS

Table 1: Clinicopathological profile

Parameter	Pheochromocytoma (n=4)	ACC (n=2)
Age range (years)	28–55	42–60
Sex	M:F = 3:1	M:F = 1:1
Functional status	All functional	1 functional, 1 nonfunctional

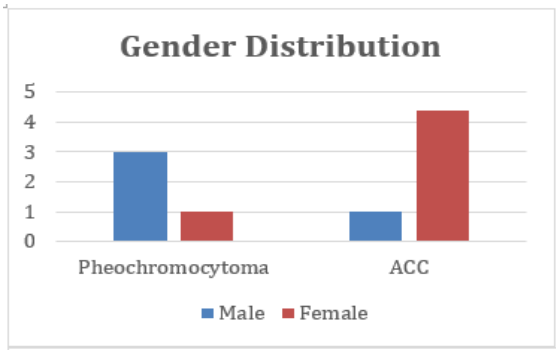


Figure 1: Gender Distribution

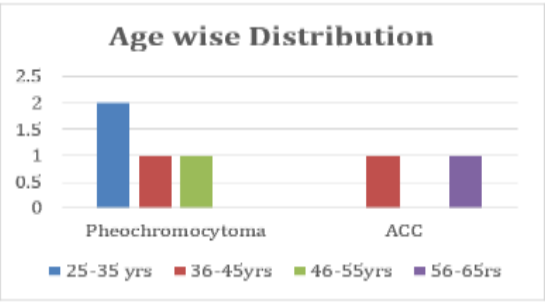


Figure 2: Age Distribution

Gross findings

Pheochromocytomas were well-circumscribed tumors ranging from 4 to 7 cm, with variegated cut surfaces showing hemorrhage.

Adrenocortical carcinomas were larger, measuring 8–12 cm, with irregular margins, areas of necrosis, and hemorrhage.

Histopathological findings

Pheochromocytoma:

All four cases showed classical Zellballen pattern, composed of clusters of polygonal tumor cells interspersed with fine fibrovascular stroma. The tumor cells exhibited plentiful granular eosinophilic cytoplasm with round to oval nuclei. Sustentacular cells were identified at the periphery of nests. No capsular or vascular invasion was noted.

Adrenocortical carcinoma

Both cases showed diffuse sheets of pleomorphic tumor cells with high nuclear grade, increased mitotic activity, atypical mitoses, necrosis, and capsular invasion. Weiss score ≥4 was observed in both cases, confirming malignancy.

Table 2: Gross and Histopathological Characteristics of Tumor Cases

Case No.	Tumor Size (cm)	Gross Appearance	Key Histopathological Features
1	5.0	Well-circumscribed, variegated	Zellballen pattern, uniform polygonal cells, rich vascular stroma
2	6.5	Encapsulated, hemorrhagic	Nested architecture, mild pleomorphism, sustentacular cells present
3	4.0	Well-defined, brownish	Classical Zellballen pattern, no necrosis or mitoses
4	7.0	Hemorrhagic areas	Zellballen and trabecular pattern, focal hemorrhage
5	9.0	Irregular, necrotic	Diffuse sheets, high mitotic activity, necrosis, capsular invasion
6	12.0	Large, infiltrative	Marked pleomorphism, atypical mitoses, vascular invasion, necrosis

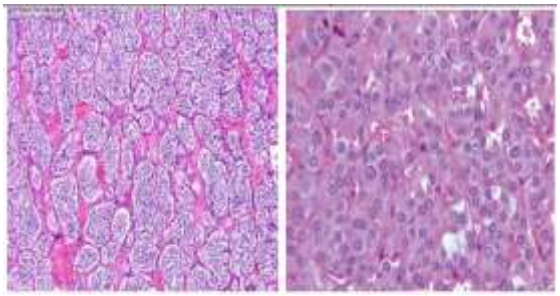


Figure A: Pheochromocytoma showing classical Zellballen architecture, with nests of tumor cells isolated by fine fibrovascular tissue (H&E, ×100).

Figure B: High-power view showing polygonal neoplastic cells containing abundant granular eosinophilic cytoplasm and nuclei that are round to oval in shape (H&E, ×400)

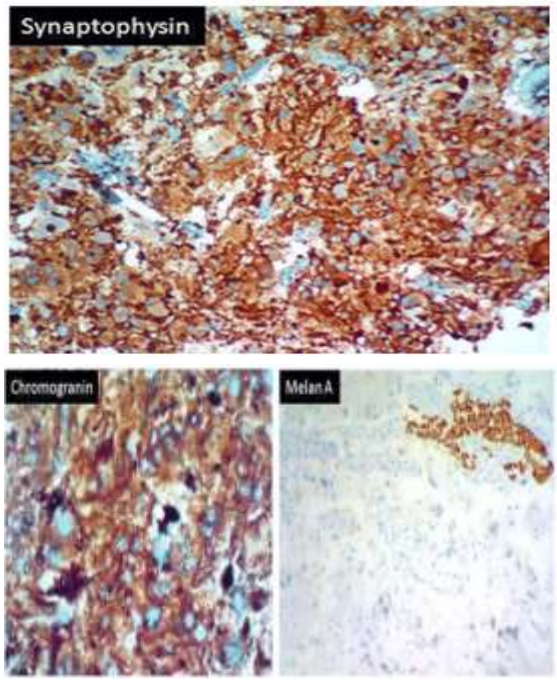
Immunohistochemistry

Pheochromocytomas were positive for chromogranin and synaptophysin, with sustentacular cells highlighting S-100 positivity.

Adrenocortical carcinomas showed positivity for inhibin and Melan-A, and were negative for chromogranin. Ki-67 labeling index was elevated (>10%).

Table 3: Immunohistochemical Profile of Adrenal Gland Tumors (n = 6)

Tumor Type	Chromogranin	Synaptophysin	Inhibin	Melan-A	Ki67
Pheochromocytoma (n=4)	Positive	Positive	Negative	Negative	<5%
ACC (n=2)	Negative	Negative	Positive	Positive	>10%



Figure

DISCUSSION

Adrenal tumors comprise a diverse collection of neoplasms with distinct histogenetic origins.[1] Pheochromocytoma is the most common adrenal medullary tumor and shows characteristic histological features, although assessment of malignancy remains challenging and relies on clinical behavior rather than histology alone.[3,6]

Adrenocortical carcinoma is a rare but highly aggressive malignancy, with Weiss criteria serving as the most widely accepted histopathological tool for diagnosis.[5] Large tumor size, necrosis, high mitotic rate, and capsular invasion observed in our cases correlate with previously published studies.[4,7] Early recognition and accurate histopathological diagnosis are crucial, as management strategies and prognosis differ significantly between pheochromocytoma and ACC.

CONCLUSION

This case series highlights the histopathological diversity of adrenal gland tumors, highlighting the significance of gross examination, microscopic evaluation, and immunohistochemistry. Accurate differentiation between pheochromocytoma and adrenocortical carcinoma is essential for appropriate clinical management and prognostication.

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