

## A histopathological significance in the detection of adrenocortical carcinoma, an unprecedented condition

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### ABSTRACT

Adrenocortical carcinoma (ACC) often remains undiagnosed due to its subtle and variable symptoms. This highlights the need for radiological, immunohistochemistry, and histopathological studies to identify the disease and grade the condition. This case report emphasizes the role of immunohistochemistry and histopathological findings in establishing an accurate diagnosis and guiding management. A 64-year-old woman with high blood pressure on medications (160/100 mmHg), on-and-off abdominal pain radiating to the back, gurgling and rumbling abdominal sounds, and an irreducible umbilical hernia underwent radiological studies, which revealed hypodense lesions noted in the adrenal gland and right suprarenal region. Subsequently, computed tomography contrast studies confirmed a right renal complex cyst classified as Bosniak IV. The patient underwent total nephrectomy, resulting in a significant reduction in blood pressure on medication (110/70 mmHg). A follow-up over 3 months showed sustained improvements. Histopathological examination and immunohistochemistry grading confirmed that the primary ACC metastasized into the upper pole of the right kidney, offering a novel and comprehensive therapeutic strategy.

**Key words:** Adrenocortical carcinoma, Bosniak classification, Histopathological findings, Nephrectomy

Adrenocortical carcinoma (ACC) is a rare and highly aggressive cancer that affects the outer layer of the adrenal glands [1]. It affects 1–2 new patients per million people a year worldwide. It exhibits a bimodal age distribution with a female predominance that occurs in childhood and during the fourth to fifth decades of life [2]. The adrenal gland produces various hormones that help to manage the body's metabolism and stress. A genetic mutation typically causes this condition. Based on the research studies, mutations in tumor suppressor genes (TP5<sub>3</sub> and insulin-like growth factor) are the reason for developing ACC [3,4]. Adrenal tumors significantly affect blood pressure due to overproduction of hormones such as aldosterone, cortisol, adrenaline, and noradrenaline, which results in inadequate regulation of fluid balance, stress response, and vascular constriction. The irregular hormones cause high blood pressure, high blood sugar, weight gain, and hirsutism [5,6]. For diagnosis, initial screening involves measuring high blood pressure in both extremities, followed by imaging studies such as computed tomography (CT) contrast, magnetic resonance imaging, and positron emission

tomography (PET) to confirm the tumor [7,8]. Although many patients do not recognize the symptoms, they can be managed conservatively with antihypertensive, glycemic, and lipid control. Symptomatic patients may experience abdominal pain, back pain, and hirsutism. Despite advances in understanding and management of ACC, the role of complete removal of the tumor (adrenal gland) is a significant one to prevent complications. This report highlights a unique explanation of the diagnosis and treatment of ACC, a condition that is managed both medically and surgically [9,10]. This case report is to provide high-level clinical evidence of a disease exceptionally rare and lacks extensive prospective randomized clinical trials. Initially, the patient was diagnosed with complex renal cyst, Bosniak classification IV and suspected as the tumour originating from the renal region. However, the tumour originating from the adrenal gland would be illuminated by the histopathological and immunohistochemical studies. This case report helps to differentiate the tumor origin from ACC to renal cell carcinoma, which emphasises the importance of adrenal incidentalomas (asymptomatic masses found during unrelated scans), which are key indicators for malignancy.

#### Access this article online

Received - 02 January 2026  
Initial Review - 19 January 2026  
Accepted - 24 January 2026

#### Quick Response code



DOI: 10.32677/ijcr.v12i2.8027

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## CASE REPORT

### Presenting Complaints and Medical History

A 64-year-old female patient with a complaint of on-and-off abdominal pain, gurgling and rumbling abdominal sounds, back pain, and high blood pressure with medications (160/100 mmHg) for 2 years. She consulted a general surgeon for evaluation of her symptoms. Physical examination findings revealed that her abdominal muscles protruded through the umbilicus and looked like a pouch, along with a rumbling sound heard while auscultating the abdomen. A plain CT scan of the abdomen and pelvis was performed for the confirmation of an irreducible umbilical hernia and planning for hernia repair surgery. The plain CT study findings show a right renal complex mass and suggested for the nephrologist consultation. She had a medical history of hypertension, diabetes mellitus, and hyperlipidaemia for 10 years and was under regular medical management. Despite regular treatment of hypertension and diabetes, she has high blood sugar and blood pressure for the past few years.

### Nephrologist Consultation

After the nephrology consultation, she underwent the CT abdomen and pelvis contrast study, a partial exophytic complex cyst of size 3.6×2.6 cm was seen in the upper pole with coarse calcifications and thin internal separation (Figs. 1 and 2). It is significantly concluded that the right renal complex cyst is a Bosniak IV classification. They recommended a treatment plan to remove the cyst by partial nephrectomy. Considering her advanced age and complications of internal bleeding, the total nephrectomy was performed.

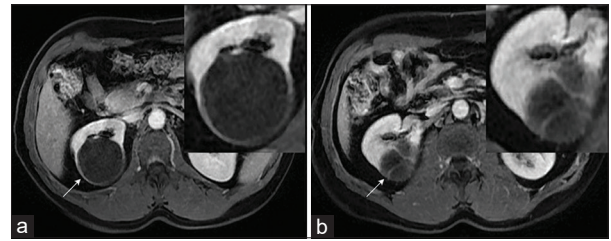
### Differential Diagnosis

The initially diagnosis was a complex renal cyst Bosniak classification IV. After the surgery, the resected tissue was sent for the histopathological studies and found to be low-grade ACC infiltrating the upper pole of the kidney (pT4 stage) [10].

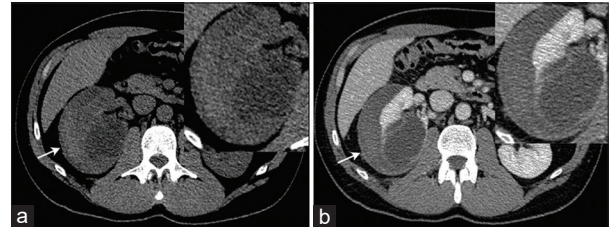
### Therapeutic Intervention

The patient attended a total of 12 visits and 5 days of admission for surgery from October 2025 to December 2025. Blood pressure measurements were documented throughout the treatment period. During the initial visits, she reported persistent symptoms, including abdominal pain, back pain, and high blood pressure (160/100 mmHg). However, after the surgery, the patient experienced minimal improvement in symptoms and a substantial change in blood pressure (110/70 mmHg), leading to further management.

The tumor was sent for histopathological and immunohistochemistry studies, which resulted in tumors



**Figure 1:** Both A and B represent a hypodense lesion measuring 20 mm with mild hyperdensity and a noted right renal cyst in the right suprarenal region.



**Figure 2:** Both A and B represent a partial exophytic complex cyst of size 3.6×2.6 cm seen in the upper pole with coarse wall calcifications and thin internal septation.

showing ACC (pT4 stage) and a histological grade of <20 mitoses/50 high-power fields.

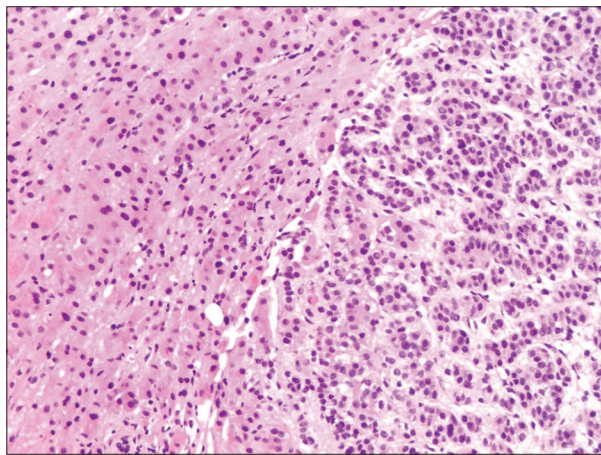
### Follow-up and Outcome

There was a significant reduction in the systolic blood pressure and other symptoms after the surgery. The histopathological studies demonstrate that further evaluation is required for conservative management. These findings suggest that PET can be used to make significant decisions for further conservative management. Her current medications include amlodipine 5 mg, enalapril 5 mg, metformin 500 mg, glipizide 5 mg twice daily, and atorvastatin 10 mg once daily.

## DISCUSSION

This case study underscores the significance of histopathological study findings and their grading system in understanding tumor morphology and cellular changes, useful for making clinical decisions. Due to limited early symptom identification and delayed diagnosis results the development of secondary hypertension and related complications occurs [11].

Histopathological studies involve microscopic examinations of diseased tissue to diagnose conditions and understand disease progression. Primarily, analysing tissue structure, cellular abnormalities, and solid tumor diagnosis. In this case, the tumor was unencapsulated infiltrating, arranged predominantly in sheets and nests separated by thin fibrovascular stroma with areas of cystic change. The cysts are lined by hobnail to cuboidal cells. The tumor is seen infiltrating the capsule into the perirenal fat and into the renal parenchyma surrounding normal tubules and glomeruli. Focus on sinusoidal invasion and capsular invasion seen (Fig. 3).



**Figure 3: Histopathological findings of adrenocortical carcinoma 20 mitoses/50 high power fields**

According to the European Society of Endocrinology, comprehensive diagnostic investigation is essential for the best patient outcomes. They suggested that adequate visualization of the tumor and potential metastases is also crucial before any management [12]. The guidelines on adrenal incidentalomas state that a low tumor density (Hounsfield units  $\leq 10$ ) on unenhanced CT scans is still the best method for ruling out a malignant tumor. However, no imaging method can establish whether an adrenal mass is really ACC. In all patients with suspected ACC, abdominal, pelvic, and thoracic imaging is necessary, as overlooked metastases can lead to inappropriate treatment [13].

Securing a pathological diagnosis of ACC is not easy; the rate of misdiagnosis was found to be between 9% and 13% of cases. It is often difficult to differentiate ACC from non-cortical tumors [14]. Immunohistochemistry for steroidogenic factor-1, a specific marker of adrenocortical tumor origin, is helpful in making this differentiation. Pathological assessment should include the Weiss score, which considers nine specific histological features of the tumor (high nuclear grade,  $>5$  mitoses per 50 high-power fields, atypical mitoses, clear cells being  $<25\%$  of the total cells, diffuse architecture in more than 33% of the tumor, necrosis, venous invasion, sinusoidal invasion, and capsular invasion). If this score is 3 or more points, the diagnosis of ACC can be assumed to be confirmed [15,16].

The present case study revealed the pathological changes in the adrenal gland and showed the high nuclear grade ( $<20$  mitoses/50 high power fields diffuse, infiltrated tumor tissues in the adrenal and upper pole of the right kidney. Addressing the histopathological findings not only helped to confirm the diagnosis but also contributed to long-term management [17]. Our therapeutic aim was to eradicate the cancer cells. Over time, the patient reported improvements in blood pressure, glycemic level, and renal profile, suggesting continuous follow-up in managing ACC. Despite the promising results, this study has limitations: The conservative management after the surgery is based on

the PET scan findings. These are limited to knowing the patient's progress and the long-term management process. These limitations highlight the need for a larger, controlled case study to validate the detailed findings.

## CONCLUSION

ACC is an extremely rare condition and poses a diagnostic challenge on imaging due to its anatomic proximity and direct extension, where it is sufficiently large to involve the kidneys. This case demonstrates how histopathological studies and their grading system help to diagnose the disease and potentially plan for additional management. However, multiple case-control studies related to ACC are necessary to confirm these findings and explore broader applications of histopathological study and grading systems for identifying the condition earlier.

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*Funding: Nil; Conflicts of interest: Nil.*

**How to cite this article:** Vidhya G. A histopathological significance in the detection of adrenocortical carcinoma, an unprecedented condition. *Indian J Case Reports*. 2026; 12(2):126-129.