Primary adrenal malignancies in Oman in the last decade (2014-2023); single tertiary hospital experience

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European Journal of Medical Case Reports
Volume XX(XX):01–07
DOI: XXXX

ABSTRACT

Background: Adrenal malignancy is a rare entity of diseases that has a low incidence, vague symptoms, and variable prognosis. Due to its rarity, case series studies from around the world can contribute to a better understanding of the disease.

Aims and Objectives: To analyze the similarities and differences in this adrenal malignancy spectrum within the Middle East.

Settings: This retrospective case series was conducted at the Royal Hospital, Muscat, Oman.

Methods: The medical records of the patients diagnosed with primary adrenal malignancies were reviewed from January 2014 to December 2023.

Results: A total of 15 patients with a mean age of 52 years were included, with a male-to-female ratio of 1:2.7. The majority of patients (80%) had a personal medical history, and the most common condition was hypertension. Four patients (26.6%) presented with abdominal pain that required computed tomography imaging to determine the cause. Left-sided malignancy was predominant (60%); however, the majority of male patients had right-sided tumors (75%) (p-value = 0.235). The largest tumor measured 169 mm, with no statistically significant difference in tumor size between males and females: 87.3 ± 10.6 mm in males versus 91.8 ± 47.4 mm in females (p-value = 0.77). Laboratory investigations revealed that 53% of the patients had elevated hormone levels, including aldosterone, cortisol, testosterone, and metanephrines.

Conclusion: With the rarity of this spectrum of diseases, more studies are needed for a better evaluation of its impact on the community. Hopefully, more advanced technology, especially at the molecular level, can allow a better understanding of its behavior.

Keywords: Primary, adrenal malignancies, tertiary hospital, experience, Oman.

Type of Article: ORIGINAL ARTICLE **Specialty:** Adrenal Cancer

Received: 09 June 2025

Revised (1): 02 August 2025

Accepted: 18 August 2025

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Introduction

Adrenal gland malignancies are rare but aggressive endocrine tumors. For instance, adrenocortical carcinoma (ACC), a primary adrenal cortical cancer, has an incidence of only about 0.7-2 cases per million population per year in Western countries [1-3]. Because of this rarity, even large centers encounter few cases, and published data are limited.

In Oman and the broader Middle East, literature on adrenal malignancies is especially scarce, often confined to single case reports or small series [4-6]. Further, no comprehensive study of adrenal gland cancers from Oman has been published to date. The national cancer registry reflects this rarity; adrenal tumors account for only a handful of cases annually (for example, approximately six cases were recorded in the year 2020 in Oman) [7]. This paucity of regional data highlights a clear knowledge gap regarding the presentation and outcomes of adrenal malignancies in Middle Eastern populations.

Given Oman's relatively small population, the number of primary adrenal malignancy cases is inherently limited; hence, this study aimed to observe the primary (non-metastatic) adrenal malignancies managed at the study center over the last decade (2013–-2023). While this would be a small cohort, it would represent all such cases treated at the country's main referral hospital during that period, making it a valuable sample of the national experience.

It was believed that examining this specific patient population is clinically relevant for several reasons. First, understanding the characteristics and outcomes of adrenal cancers in Oman can help determine whether the patients' disease patterns align with global observations or exhibit unique regional features. Factors such as genetic background, environmental exposures, and health system differences in the Middle East could conceivably

influence tumor behavior or treatment responses. Second, analyzing the management strategies and outcomes in a resource-limited setting provides insight into what challenges and successes occur when treating adrenal malignancies outside of larger, well-studied populations.

Finally, by documenting the decade-long experience, this study aimed to contribute new data to the sparse regional literature and support future comparisons. This study would therefore not only fill an information gap in Omani and Middle Eastern medical literature but also potentially inform improvements in the care of patients with adrenal malignancies in similar settings. In summary, given the limited research on adrenal cancers in the Oman and Middle Eastern region, this study offers important observations that might help in analyzing similarities and differences in this disease spectrum within the Middle East, and it underscores the value of regional data in complementing global knowledge.

Methods

This study was a retrospective case series conducted at the Royal Hospital, a tertiary referral center in Muscat, Oman. The medical records of patients diagnosed with primary adrenal malignancies over 10 years, from January 2014 to December 2023, were reviewed.

The study included all patients diagnosed with histologically confirmed primary adrenal malignancies who were managed at the Royal Hospital during the specified 10-year period. As the primary national referral center for complex endocrine and oncologic surgeries, the Royal Hospital serves a central role in managing such cases. A total of 15 patients were included in this cohort.

Patients aged ≥13 years (younger patients are treated in the pediatric surgery department in the study hospital), those with histopathological diagnosis of a primary adrenal malignancy (e.g., ACC, pheochromocytoma with malignant features), patients with adrenocortical neoplasm of undetermined malignancy were included in the study when the Weiss score was high (higher than 4/7). Further, only those patients who were managed surgically at the Royal Hospital between 2013 and 2023 were included.

Cases of adrenal metastases from other primary cancers, those with incomplete or missing patient records, and patients whose initial diagnosis or treatment occurred outside of the Royal Hospital were all excluded.

Data were extracted from the hospital's electronic medical record system. A structured data collection sheet was used to record demographic data, clinical presentation, imaging findings, hormonal evaluation, histopathology, surgical interventions, complications, follow-up outcomes, and survival status. All data were anonymized before analysis.

Given the small number of cases and the descriptive nature of this study, no formal statistical software was used. Basic calculations such as means, medians, ranges, and percentages were performed manually using Microsoft Excel. No inferential statistical tests were conducted, as the objective was to provide a descriptive overview of the cases.

Results

Most patients diagnosed with adrenal cancer were female, accounting for 73% (11/15). The male-to-female ratio was 1:2.7. The mean age was 52 years (range: 22-80). None of the patients had a positive family history of adrenal cancer. However, the majority of patients (80%, 12/15) had a personal medical history. The most common conditions were hypertension, followed by diabetes mellitus and dyslipidemia. The highest number of patients was diagnosed in the year 2023 ($n = 5$) (Table 1).

In the current study cohort, 8 out of 15 patients (53%) were diagnosed incidentally. Four patients (26.6%) presented with abdominal pain that required computed tomography (CT) imaging to determine the cause, two of whom (13%) had both abdominal pain and a palpable mass. One patient (6.6%) was diagnosed during a hypertension workup (Figure 1).

All patients in this series underwent a CT scan, with or without an adrenal protocol (100%). Two-thirds of them (66.6%) subsequently underwent magnetic resonance imaging (MRI). One patient had a metaiodobenzylguanidine scan (MIBG scan), and one patient underwent Positron Emission Tomography - CT (PET/CT) with gallium-68 DOTA-peptides. Left-sided malignancy was predominant, accounting for 60% of all cases; interestingly, however, the majority of male patients had right-sided tumors (75%), although this difference was not statistically significant (p-value = 0.235). The largest tumor measured 169 mm, and the smallest was 41 mm, with a mean maximum dimension of 90.6 ± 40.4 mm. There was no statistically significant difference in tumor size between males and females: 87.3 ± 10.6 mm in males versus 91.8 ± 47.4 mm in females (p-value = 0.77).

The tumor marker, chromogranin A, was also found to be elevated in two patients only (13 %). Further, laboratory investigations revealed that 53% (8/15) of the patients had elevated hormone levels. Among these, aldosterone was the most commonly elevated hormone. Interestingly, hormone elevation was observed in 4 out of 7 asymptomatic patients (Figure 2).

Approximately 53% of patients (8/15) underwent open surgery, while 26.7% (4/15) had laparoscopic surgery. Moreover, 33.3% of patients (5/15) underwent adrenalectomy combined with resection of another organ. The organs resected alongside the adrenal gland included the kidney, liver, and spleen (Table 2).

Histopathological analysis revealed that the most common diagnosis was ACC (66.7%, 10/15). These cases were included in the study due to a high Weiss score (≥4/7). Based on histopathology reports, one patient

Table 1. *Demographic and comorbidity characteristics of the study population (n = 15).*

VARIABLE	CATEGORY	FREQUENCY (*N*)	PERCENTAGE (%)
Sex	Male	4	27
	Female	11	73
Co-morbidities	Yes	12	80
	No	3	20
Hypertension	Yes	11	73
	No	4	27
Dyslipidemia	Yes	7	47
	No	8	53
Diabetes mellitus	Yes	8	53
	No	7	47
Year of diagnosis	2014	1	7
	2016	1	7
	2017	1	7
	2018	2	13
	2019	3	20
	2020	1	7
	2022	1	7
	2023	5	33

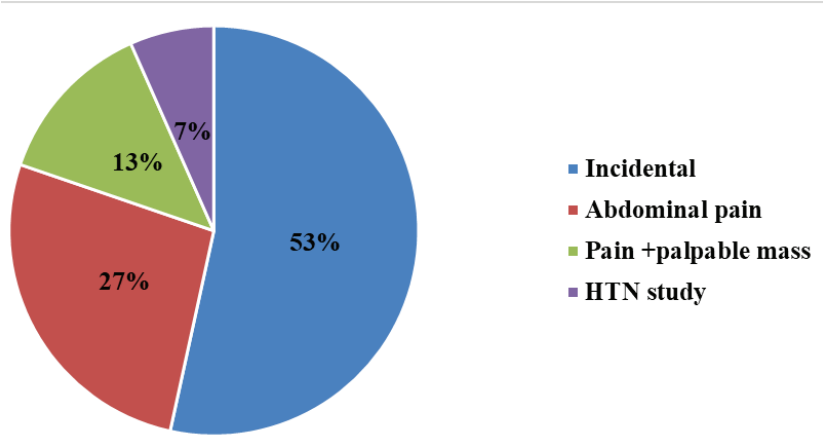

Figure 1. *Clinical presentation of the included participants.*

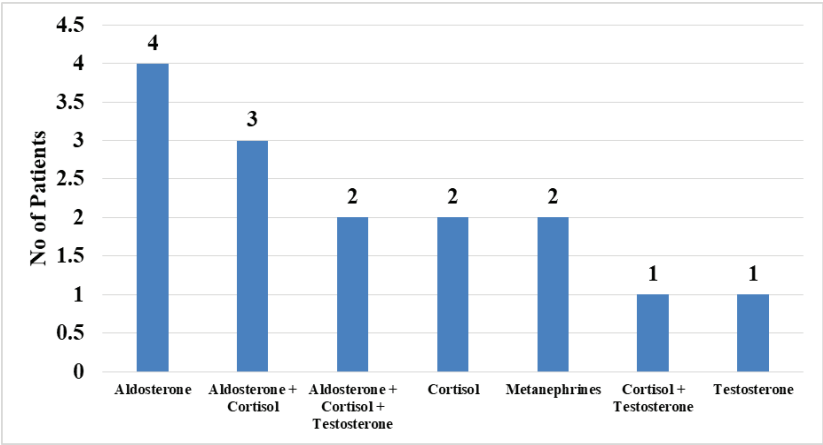

Figure 2. *Distribution of elevated hormones in patients.*

Table 2. *Surgical anatomy statistics.*

		FREQUENCY (*N*)	PERCENTAGE (%)
Location of tumor	Right	6	40.0
	Left	9	60.0
Type of surgery	Open	8	53.3
	Laparoscopic	4	26.7
	Laparoscopic converted to open	3	20.0
Another organ resected with adrenal	No	10	66.7
	Yes	5	33.3
Additional organ resected	None	10	66.7
	Kidney + Liver	1	6.7
	Spleen + kidney	2	13.3
	Kidney	2	13.3

Table 3. *Histopathology staging of the patients.*

		FREQUENCY (*N*)	PERCENTAGE (%)
HISTOPATHOLOGICAL DIAGNOSIS	ACC	10	66.6
	Adrenocortical neoplasm (undetermined malignancy)	3	20.0
	Paraganglioma	1	6.7
	Phaeochromocytoma	1	6.7
T STAGE	T1	1	6.7
	T2	7	46.7
	T3	5	33.3
	T4	2	13.3
N STAGE	N0	6	40
	N1	2	13.3
	Nx	7	46.7
M STAGE	M0	13	86.7
	M1	2	13.3

(6.7%) was classified as having a T1 tumor, seven patients (46.7%) had T2 tumors, five patients (33.3%) had T3 tumors, and two patients (13.3%) had T4 tumors. Among the three patients diagnosed with adrenocortical neoplasm of uncertain malignant potential, two were staged as T2 and one as T3, with all meeting the criteria for malignancy based on a Weiss score ≥4/7. Lymph node assessment showed no involvement (N0) in 40% of patients (6/15), while 13.3% (2/15) were classified as N1. Distant metastasis (M1) was identified preoperatively in two patients (13.3%) (Table 3).

Surgery-related complications occurred in 26.7% of patients (4/15). One patient experienced intraoperative bleeding, which was successfully controlled following conversion from laparoscopic to open surgery (Table 4).

Approximately half of the patients received chemotherapy. Among them, most were treated with mitotane, either as monotherapy or in combination with other chemotherapeutic agents. (Table 5).

In this study, seven patients died, with a mean overall survival of 43.4 ± 30.4 months (range: 10-93 months). Among the surviving patients (8 out of 15), the mean follow-up duration was 45.9 ± 32.0 months (range: 15-108 months). The 2-year survival rate in the cohort was 84.6%, while the 5-year survival rate was 33.3%. Survival rates were calculated based on patients with adequate follow-up to assess each time point (Table 6).

Discussion

Adrenal malignancies, though rare, present significant clinical challenges due to their diverse presentations and potential for aggressive behavior. This study exclusively focused on primary adrenal malignancies. While population-based epidemiological data suggested a higher incidence of malignant pheochromocytoma (2-8 per million) compared to ACC (1-2 per million) [1-3], while this case series demonstrated a notable divergence, with ACC constituting the majority of diagnosed adrenal malignancies

within the current study patient cohort. This observation, though based on a small sample, warrants further consideration regarding regional variations or referral patterns. Consistent with existing literature [3,8,9], our cohort demonstrated a female predominance, with a mean age at diagnosis of 52 years, aligning with the typical age of presentation reported for these malignancies [10].

Functional status of ACC varies, with approximately 50% traditionally reported as non-functioning, and hormone secretion distributed among cortisol (30%), androgens (20%), aldosterone (10%), or multiple hormones (35%) [11]. In striking contrast to these established proportions, this series revealed a remarkably high prevalence of aldosterone hypersecretion. Among the 7 functioning tumors identified, 5 (71%) demonstrated elevated aldosterone levels, representing 33% of the total malignancy cohort. This unusual predominance of hyperaldosteronism in the current study functioning ACC cases is a distinctive finding that merits further investigation and might suggest unique biochemical profiles in certain patient populations or might simply be an artifact of the small and non-randomized nature of the current study cohort.

The clinical presentation of adrenal malignancies is highly variable, ranging from asymptomatic incidentalomas to severe symptoms related to hormone hypersecretion or mass effect [10]. ACC often presents with symptoms of excess hormone production (e.g., Cushing's syndrome, virilization) or, when non-functional, through mass effect (e.g., abdominal pain, palpable mass). Pheochromocytomas typically manifest with catecholamine-related symptoms such as hypertension, palpitations, and headache; they might also be part of inherited syndromes. The diverse clinical presentations of adrenal malignancies offer critical clues to their underlying pathophysiology and biological behavior [10,11].

The current case series illustrated this clinical heterogeneity. A significant proportion of the included patients, 8 out of 15 (53%), were diagnosed incidentally through radiological imaging performed for unrelated indications. This highlights the increasing detection of asymptomatic adrenal lesions in the era of widespread cross-sectional imaging, a trend also noted in autopsy studies, which estimate adrenal tumor prevalence as high as 8%-10% [1]. The remaining 7 patients (47%) presented with symptoms directly attributable to the tumor. Specifically, abdominal pain was the primary complaint for seven patients, with two of them (13% of the total cohort) also presenting with a palpable abdominal mass, indicating a larger tumor burden. One patient was diagnosed during an investigation for hypertension, suggesting a functional tumor, though not presenting with classic symptoms. The presence of hypersecretion of more than one hormone, considered pathognomonic for ACC, underscores the importance of a thorough biochemical evaluation in symptomatic patients.

Table 4. *Complications after surgery among the included patients.*

COMPLICATION	FREQUENCY (*N*)	PERCENTAGE (%)
No	11	73.3
Yes	4	26.7
Type of complication (*n* = 4)		
Bleeding	1	25
Pancreatic leak	1	25
Pleural effusion	1	25
Surgical site infection	1	25

Table 5. *Type of chemotherapy given to patients.*

TYPE OF CHEMOTHERAPY	FREQUENCY (*N*)	PERCENTAGE (%)
Mitotane only	3	20.0
Mitotane + other	3	20.0
Other	1	6.7
N/A	8	53.3

Table 6. Summary of the statistical analysis of age at diagnosis, radiological maximum size, admission days, and histopathological size.

		AGE AT DIAGNOSIS	RADIOLOGICAL MAXIMUM SIZE (MM)	ADMISSION DAYS
N	Valid	15	15	15
	Missing	0	0	0
Mean		52.47	90.60	7.47
Median		54.00	79.00	8.00
SD		16.401	40.444	2.295
Minimum		22	41	4
Maximum		80	169	12
Percentiles	25	41.00	60.00	6.00
	50	54.00	79.00	8.00
	75	65.00	117.00	9.00

Rapid onset, severe symptoms, or significant electrolyte imbalances warrant high suspicion for malignancy.

The diagnosis of adrenal malignancies involves a combination of biochemical testing, imaging studies, and histopathological examination. A comprehensive biochemical evaluation is paramount for detecting hormone-producing tumors [10,11]. In the presented series, all patients with suspected adrenal malignancy underwent a complete panel of adrenal hormone tests, including aldosterone, renin, aldosterone/renin ratio, metanephrines, cortisol, chromogranin A, and Dehydroepiandrosterone, reflecting adherence to contemporary diagnostic guidelines.

Imaging studies, primarily CT and MRI, are crucial for characterizing adrenal masses, assessing their local extent, and detecting metastatic disease. While both modalities are valuable, CT is often preferred for initial evaluation due to its accessibility and superior spatial resolution [12]. Functional imaging, such as PET or MIBG scans, offers additional diagnostic utility, particularly in the workup of pheochromocytoma or metastatic disease [13].

Histopathological examination remains the definitive diagnostic gold standard. While fine-needle aspiration or core needle biopsy can be considered in select cases with indeterminate imaging findings, their utility in adrenal masses is debated due to the risk of hemorrhage, tumor seeding, and, critically, the potential for precipitating a hypertensive crisis in undiagnosed pheochromocytomas [10]. Reflecting these considerations, no percutaneous biopsies were performed in any patient within the presented series, with definitive diagnosis achieved through surgical resection. Histopathological analysis confirmed the predominance of ACC in the presented series, accounting for 10 out of 15 cases.

Surgical resection is the primary treatment for adrenal malignancies. For ACC, complete surgical excision with negative margins offers the best chance for long-term survival. Due to the aggressive nature of ACC, recurrence rates are high. As such, adjuvant therapies such as mitotane, radiotherapy, or chemotherapy may be considered in advanced cases [10]. For malignant pheochromocytomas, surgical resection remains the cornerstone of treatment, but the prognosis is less favorable than that of benign pheochromocytomas, often necessitating additional systemic therapies, including chemotherapy and targeted agents [11].

The choice of surgical approach, whether laparoscopic or open adrenalectomy, is largely guided by tumor size, suspicion of malignancy, and the surgeon's expertise. Current guidelines generally recommend open adrenalectomy for tumors exceeding 5-6 cm due to increased complexity and oncologic risk [14]. The surgical experience aligns largely with these recommendations: four cases underwent successful laparoscopic resection (all less than 60 mm, with one notable exception being a 78 mm tumor successfully removed laparoscopically, indicating highly selected cases or surgeon preference). Three cases, initially attempted laparoscopically, required conversion to open surgery due to factors including tumor size (ranging 60-117 mm, mean 79.3 mm) or intraoperative findings, underscoring the challenges of minimally invasive approaches for larger lesions. The remaining eight cases, characterized by larger tumor sizes (79-169 mm), were managed primarily with open adrenalectomy.

The 5-year survival rate for ACC and pheochromocytomas varies across studies and as expected, is influenced by stage, surgical margins, and other prognostic factors. Generally, it ranges from 15% to 73% [4,15-17] for ACC and 40%-70% for Pheochromocytomas [18].

Future research should aim to validate current epidemiological and hormonal secretion findings in larger, more diverse cohorts, while also exploring novel diagnostic biomarkers and targeted therapeutic options to improve the currently guarded prognosis associated with these malignancies.

Conclusion

Adrenal malignancies, though rare, pose significant diagnostic and therapeutic challenges due to their heterogeneity and aggressive potential. This case series, despite limitations inherent to its retrospective design, small sample size, and the absence of molecular profiling, genetic analysis, and advanced therapies such as targeted treatments, offers valuable insights into the clinical features, diagnostic pathways, and surgical management of these complex tumors, particularly in the Middle East, where such studies remain scarce.

What's New?

The current study findings underscore several key observations. Notably, a deviation from established epidemiological patterns was observed, with ACC predominating over pheochromocytoma in the current study cohort. Additionally, the unexpectedly high incidence of aldosterone-producing ACCs within the functioning tumor subgroup represented a distinctive finding that merits further investigation. The varied clinical presentations, from incidental detection to symptoms of mass effect or hormonal excess, highlighted the need for a high index of suspicion and thorough biochemical and imaging evaluation. The surgical outcomes were generally consistent with existing guidelines regarding the choice between laparoscopic and open adrenalectomy based on tumor size, while also demonstrating the necessity for conversion to open procedures in selected cases.

List of Abbreviations

ACC	adrenocortical carcinoma
CT	computed tomography
MRI	magnetic resonance imaging
MIBG	metaiodobenzylguanidine
PET/CT	positron emission tomography - computed tomography

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

None.

Consent for publication

Due permission was obtained from the patient/guardians of the patient to publish the case and the accompanying images.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report or research article.

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