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Clinical, Biochemical, and Histopathological Characteristics of Big Adrenal Masses: A Single-Center Retrospective Study

Büyük Adrenal Kitlelerin Klinik, Biyokimyasal ve Histopatolojik Özellikleri: Tek Merkez Deneyimi

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ABSTRACT

Introduction: Large adrenal tumors (≥8 cm) are associated with a high risk of malignancy, although their pathological distribution varies across institutions. Clarifying their clinical and biochemical features is essential for appropriate surgical decision-making. This study aimed to evaluate the clinical presentation, hormonal activity, surgical management, and histopathological outcomes of adrenal tumors ≥8 cm.

Methods: This retrospective study included patients who underwent adrenalectomy at a tertiary endocrine center and had a tumor size ≥8 cm on histopathology. Demographic data, hormonal evaluation, radiological findings, and follow-up outcomes were analyzed.

Results: Twenty-six patients (mean age 50.85 ± 13.04 years; 57.7% women) were included. Tumors were incidentally detected in 46.2% of cases. Hormonal hypersecretion was present in 46.2% of patients, most commonly catecholamine excess (34.6%). Pheochromocytoma was the most frequent diagnosis (38.5%), followed by adrenocortical carcinoma (15.4%). Overall, 46.2% of masses were malignant. Malignant tumors were significantly larger than benign ones (p = 0.041). Laparoscopic adrenalectomy was performed for smaller lesions than those treated by open surgery (p = 0.003). During follow-up, 58.3% of malignant cases developed metastases; two patients achieved remission.

CONCLUSION: Adrenal tumors ≥8 cm demonstrate marked clinical and pathological heterogeneity. Although tumor size is associated

ÖZ

Amaç: Büyük adrenal tümörler (≥8 cm), yüksek malignite riski ile ilişkilidir; ancak patolojik dağılımları merkezler arasında farklılık gösterebilmektedir. Uygun cerrahi karar verme süreci için bu tümörlerin klinik ve biyokimyasal özelliklerinin net olarak ortaya konulması önemlidir. Bu çalışmada, ≥8 cm adrenal tümörlerin klinik prezentasyonu, hormonal aktivitesi, cerrahi yönetimi ve histopatolojik sonuçlarının değerlendirilmesi amaçlandı.

Yöntemler: Bu retrospektif çalışmaya, üçüncü basamak bir endokrinoloji merkezinde adrenalektomi uygulanan ve histopatolojik incelemede tümör boyutu ≥8 cm olarak saptanan hastalar dahil edildi. Demografik özellikler, hormonal değerlendirme sonuçları, radyolojik bulgular ve takip verileri analiz edildi.

Bulgular: Çalışmaya 26 hasta (ortalama yaş 50,85 ± 13,04 yıl; %57,7 kadın) dahil edildi. Tümörler olguların %46,2'sinde insidental olarak saptandı. Hastaların %46,2'sinde hormonal hipersekresyon mevcuttu ve en sık görülen hormonal aktivite katekolamin fazlalığıydı (%34,6). En sık histopatolojik tanı feokromositoma (%38,5) olup, bunu adrenokortikal karsinom (%15,4) izledi. Tüm kitlelerin %46,2'si malign özellikteydi. Malign tümörler benign tümörlere göre anlamlı olarak daha büyüktü (p = 0,041). Laparoskopik adrenalektomi uygulanan lezyonların boyutu, açık cerrahi uygulananlara göre anlamlı derecede daha küçüktü (p = 0,003). Takip sürecinde malign olguların %58,3'ünde metastaz gelişirken, iki hastada remisyon sağlandı.

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ABSTRACT

with malignancy, the high prevalence of pheochromocytoma in referral centers highlights the importance of comprehensive biochemical evaluation. Management should be individualized using a multidisciplinary approach rather than relying solely on tumor size.

Keywords: Adrenal tumor, large adrenal mass, pheochromocytoma, adrenocortical carcinoma, adrenalectomy

ÖZ

Sonuç: ≥8 cm adrenal tümörler belirgin klinik ve patolojik heterojenite göstermektedir. Tümör boyutu malignite ile ilişkili olmakla birlikte, üçüncü basamak merkezlerde feokromositomanın yüksek prevalansı kapsamlı biyokimyasal değerlendirmenin önemini ortaya koymaktadır. Bu hastaların yönetimi yalnızca tümör boyutuna dayanılarak değil, multidisipliner bir yaklaşımla bireyselleştirilmelidir.

Anahtar Sözcükler: Adrenal tümör, büyük adrenal kitle, feokromositoma, adrenokortikal karsinom, adrenalektomi

INTRODUCTION

The widespread use of modern imaging techniques has led to a substantial increase in the incidental detection of adrenal lesions (1). Incidentally identified adrenal lesions are reported in approximately 4–10% of imaging studies, with even higher rates observed in autopsy series (2). Although most adrenal incidentalomas are benign, further radiological and biochemical evaluation of these lesions is essential to reach a specific diagnosis. When an incidental adrenal mass is detected, the patient's clinical features, imaging features for malignant/benign differentiation of the adrenal mass, and biochemical tests for functionality should be reviewed (3). The prevalence of adrenal tumors increases with age (4).

In determining the risk of malignancy of an adrenal tumor, imaging characteristics, especially the tumor size, are essential. Tumor size is considered one of the most important predictors of malignancy in adrenal lesions, with larger tumors carrying a higher probability of being malignant. Intermittent enlargement of adrenal masses is also considered an indicator of malignancy (2). However, the standard threshold for tumor size that indicates malignancy is unclear. While several guidelines suggest that any adrenal mass concerning radiographic characteristics and size ≥4 cm should be resected because of the increased risk of adrenal cancer, recent ones do not recommend a total tumor size for operation (5). Instead, newer guidelines suggest an individualized approach considering adrenalectomy in large tumors (5). Angeli et al. (6) reported a tumor size threshold of 4 cm for 80% sensitivity but 34% specificity for diagnosing a malignant adrenal mass. Sturgeon et al. (7) reported an estimated risk of malignancy with a specificity of 95% and a sensitivity of 77% for tumors larger than 8 cm. Based on this information, we aimed to examine the clinical and histopathological features of patients who underwent surgery for an adrenal mass larger than 8 cm.

MATERIALS AND METHODS

Study Design and Subjects

This retrospective study included patients with tumor size ≥8 cm on the histopathological examination after adrenalectomy, evaluated in the endocrinology outpatient clinic due to the detection of an adrenal mass at our tertiary care centre between 2010 and 2021. Demographic characteristics, clinical presentation, preoperative hormonal work-up, imaging results, surgical approach, pathology findings, and follow-up outcomes were retrieved from hospital records. The study protocol was approved by Ethics Committee of Gazi University (date: 28.06.2021 and no: 594).

Written informed consent was not required due to the retrospective design of the study.

Statistical Analysis

Commercial statistical software, Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA), was used for statistical analyses. The Shapiro-Wilk test was used to assess the conformity of continuous variables to the normal distribution, while the homogeneity of variance was evaluated using Levene's test. Continuous variables with a normal distribution were presented as the mean ± standard deviation. Continuous variables that were not normally distributed were presented as the median and interquartile range (25^{th}–75^{th} percentiles). Student's t-test was used for normally distributed continuous data, and the Mann–Whitney U test was used for non-normally distributed data. The relationships between variables that did not meet the assumption of normality were evaluated using Spearman's Rho correlation coefficient. The error rate ($\alpha = 0.05$) was set for all tests, and differences between groups were considered statistically significant when $p < 0.05$.

RESULTS

The study included 26 cases with adrenal masses larger than 8 cm; the mean age was 50.85 ± 13.04 years. Women comprised 57.7% (n = 15) of cases. 50% (13) of masses were located on the left, 46% (11) were on the right, and 3.8% (1) were bilateral. It was detected incidentally in 46.2% (12) of cases. The most prominent symptoms of the patients were abdominal pain, 38.5% (10); high blood pressure, 30.8% (8); and other symptoms, including back pain, fatigue, weakness, and palpitations.

Preoperative biochemical tests were completed for all but one emergency case. Fourteen masses (53.8%) were non-functional; the remaining masses demonstrated hormonal hypersecretion, most commonly of catecholamines [34.6% (9)], followed by hypercortisolism [7.7% (2)], and one case of aldosterone-cortisol co-secretion.

Open surgery was performed in 76.9% of cases, typically for larger tumors, while the remaining cases were performed laparoscopically. Median tumor size was 10.25 cm (8–18 cm). Pheochromocytoma was the most common diagnosis [38.5% (10)], followed by ACC [15.4% (4)], myelolipoma [11.5% (2)], cavernous hemangioma, cysts, cortical hyperplasia, schwannoma, pleomorphic sarcoma, sarcomatoid carcinoma, diffuse large B-cell lymphoma (DLBCL), and renal cell carcinoma (RCC) metastasis (Table 1). Fourteen masses (53.8%) were benign; the remainder were malignant.

Of the cases evaluated as malignant, 33.3% (4) were pheochromocytoma, 33.3% (4) were adrenocortical carcinoma (ACC), and the remaining cases were pleomorphic sarcoma, sarcomatoid carcinoma, DLBCL, and RCC metastasis. During follow-up, metastasis occurred in 58.3% (7) of malignant cases, and the patients died. Of these, 25.0% (3) were metastatic; they received medical treatment, and two patients (one DLBCL, one pheochromocytoma) remained in remission.

Among pheochromocytomas, three were incidental findings. Catecholamine excess was detected in all but one emergency case, which had a tumour diameter of 110 cm in the left adrenal gland, had metastases to the spleen, kidney, and liver, and presented with severe abdominal pain. Forty per cent of cases were classified as malignant pheochromocytoma because of metastasis to non-adrenal organs. Preoperative alpha-blocker treatment was administered to all cases except the case taken for emergency surgery; no intraoperative complications were identified.

The median tumour diameter in benign lesions (9.25 cm; range 8–12 cm) was lower than that in malignant lesions (11.25 cm; range 8–18 cm) (p = 0.041). The median tumour diameter for those who underwent laparoscopic [9 (8–9.5) cm] was lower than that for open surgery [11 (8–18] cm) (p = 0.003). The tumour diameters of non-functional masses [9.55 (8–15) cm] and functional masses [11 (8–18) cm] were similar (p = 0.297) (Table 2). No correlation was found between tumour diameter and age at diagnosis.

Table 1. Histopathological distribution of adrenal tumors ≥8 cm.

Pathological diagnosis	% (n)
Pheochromocytoma	5 (10)
Adrenocortical carcinoma	4 (4)
Myelolipoma	5 (3)
Cavernous hemangioma	7.7 (2)
Benign cyst	3.8 (1)
Cortical hyperplasia	3.8 (1)
Schwannoma	3.8 (1)
Pleomorphic sarcoma	3.8 (1)
Sarcomatoid carcinoma	3.8 (1)
Diffuse large B-Cell lymphoma	3.8 (1)
Renal cell carcinoma metastasis	3.8 (1)

Table 2. Tumor size differences by pathology, functional status, and surgical technique.

Feature	Size	p-value
Benign	9.25 cm (8–12)	0.041
Malign	11.25 cm (8–18)	
Non-functional	9.55 cm (8–15)	0.297
Functional	11 cm (8–18)	
Laparoscopic surgery	9 cm (8–9.5)	0.003
Open surgery	11 cm (8–18)	

DISCUSSION

In this single-center retrospective study, we evaluated the clinical, biochemical, surgical, and pathological characteristics of 26 patients with adrenal tumors ≥8 cm. Although large adrenal masses are frequently reported as malignant in the literature, pheochromocytoma was the most common histopathological diagnosis in our study, which likely reflects referral bias at a tertiary endocrine center. Tumor size was significantly larger in malignant lesions and in those managed with open surgery, whereas functional status was not associated with tumor diameter.

Large adrenal masses pose a significant diagnostic challenge; the likelihood of malignancy increases with tumor size, while the histopathological distribution varies considerably among centers. Previous literature consistently reports ACC as the predominant diagnosis in tumors ≥8–10 cm (8). In contrast, pheochromocytoma was the most common pathology in our cohort, followed by ACC. This difference likely reflects referral bias, as our tertiary endocrine center manages a high proportion of hormonally active adrenal tumors, particularly those suspected of secreting catecholamines.

The malignancy rate in the present study aligns with earlier findings that large adrenal tumors are associated with a substantial risk of malignancy. Abdel-Aziz et al. (9) reported an 84% ACC rate in tumors >8 cm, whereas Cichocki et al. (10) found ACC in 63% of tumors >10 cm. However, more recent multicenter cohorts suggest slightly lower malignancy rates and emphasize the importance of imaging rather than size alone. The 2023 ENSAT update stresses that although size is a strong predictor, it should not be used in isolation for surgical decision-making when imaging and biochemical features are benign (11). Importantly, we found that malignant tumors had significantly larger diameters than benign tumors. Malignant tumors were significantly larger, reinforcing tumor diameter as an important predictor; however, considerable overlap between benign and malignant lesions limits its discriminatory value. Functional status was not linked to malignancy, consistent with recent evidence showing that hormonal hypersecretion—other than androgen excess—does not reliably distinguish malignant from benign disease (11,12).

The high malignancy rate among pheochromocytomas is notable. Malignant pheochromocytoma is difficult to predict preoperatively, as tumor size and catecholamine profile do not reliably differentiate benign from malignant disease (13). Moreover, recent evidence suggests that increasing tumor size itself is associated with a higher likelihood of metastatic behavior in pheochromocytoma and paraganglioma, highlighting the role of tumor diameter as a risk factor for aggressive disease (14).

Regarding surgical management, laparoscopic adrenalectomy was performed for tumors with significantly smaller diameters than those selected for open surgery. This pattern is consistent with current recommendations favoring open adrenalectomy for large or radiographically suspicious masses due to concerns about capsular disruption, incomplete resection, and oncologic upstaging (15,16). Nevertheless, recent evidence indicates that minimally invasive adrenalectomy may still be safely performed in carefully selected patients with pheochromocytomas larger than 5 cm, with comparable perioperative outcomes despite longer operative times (17).

Study Limitations

Strengths of this study include detailed biochemical evaluation, histopathological verification, and long-term outcome data. Limitations include the retrospective design, single-center setting, and relatively small sample size, which may restrict generalizability.

CONCLUSION

Our study shows that adrenal tumors ≥8 cm are pathologically heterogeneous and should not be assumed to represent ACC. The high frequency of pheochromocytoma in our cohort reflects referral patterns and highlights the importance of thorough preoperative endocrine evaluation and perioperative management. These findings support an individualized approach to large adrenal masses that integrates biochemical testing, imaging features, and multidisciplinary decision-making rather than relying on tumor size alone.

Ethics

Ethics Committee Approval: The study protocol was approved by Ethics Committee of Gazi University (date: 28.06.2021 and no: 594).

Informed Consent: Written informed consent was not required due to the retrospective design of the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.C., M.M.Y., B.B., B.A., M.A., M.F.A., A.B., A.E.A., M.A., A.K., S.S., A.P., F.B.T., Concept: M.C., M.M.Y., B.B., B.A., M.A., M.F.A., A.B., A.E.A., M.A., A.K., S.S., A.P., F.B.T., Design: M.C., M.M.Y., B.B., B.A., M.A., M.F.A., A.B., A.E.A., M.A., A.K., S.S., A.P., F.B.T., Data Collection or Processing: M.C., M.M.Y., B.B., B.A., M.A., M.F.A., A.B., A.E.A., M.A., A.K., S.S., A.P., F.B.T., Analysis or Interpretation: M.C., M.M.Y., B.B., B.A., M.A., M.F.A., A.B., A.E.A., M.A., A.K., S.S., A.P., F.B.T., Literature Search: M.C., M.M.Y., B.B., B.A., M.A., M.F.A., A.B., A.E.A., M.A., A.K., S.S., A.P., F.B.T., Writing: M.C., M.M.Y., B.B., B.A., M.A., M.F.A., A.B., A.E.A., M.A., A.K., S.S., A.P., F.B.T.

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