Endocrinology Polikliniğine Başvuran Adrenal İnsidentaloma Olgularımızın Retrospektif Değerlendirilmesi

Amaç: Bu çalışmada, farklı şikayetler nedeniyle yapılan görüntülerele adrenal insidentaloma saptanılan hastaların hormonal durumlarını, tedavi verilerini ve histopatolojik tanılarını gözden geçirme amaçlamaktayız.

Hastalar ve Yöntem: Çalışmaya 2015-2018 yılları arasında farklı şikayetler nedeniyle yapılan görüntülerele adrenal insidentaloma saptanılan hastaların hormonal durumlarını, tedavi verilerini ve histopatolojik tanılarını gözden geçirme amaçlamaktayız.

Bulgular: Olguların değerlendirildirildiğiinde, 180’i (%83) nonfonksiyonel, 37’i (%17) fonksiyonel olarak değerlendirildi. Fonksiyonel olarak değerlendirilen 37 hastanın; 10’unda (%4.6), feokromositoz, 9’unda (%3.4), Cushing endromu, 13’ünde (%2.3) primer hiperaldosteronizm saptandı. Nonfonksiyonel olarak değerlendirilen 180 hastanın; 7’inde metastatik hastalık, 3’ü küçük hücreli büyük hücreli karsinom, 1’i meme karsinomu, 1’i prostat karsinomu ve 2’i primer bilimin Meydenin kanser, 4’ü myelolipom, 1’i ganglionobrom, 1’i kisthidatik, 2’inde adrenokortikal karsinom saptandı.

Sonuç: Bu çalışmanın sonucuna göre adrenal insidentalomalı hastalarda hormonal olarak aktif olma durumu nadir değildir. Bazı adrenal kitleler malign özellik taşıyabilme riski vardır. Bu nedenle adrenal insidentalomalı hem fonksiyonel olup olmadığı hem de malign-benign lezyon ayırma açısından tespit edilmesi gereken bir durumdur.

Anahtar Kelimeler: Adrenal insidentaloma, feokromositoz, Cushing endromu, hiperaldosteronizm

Abstract

Aim: The aim was to review the hormonal status, treatment and histopathological diagnosis of patients admitted to our endocrinology outpatient clinic with the diagnosis of adrenal incidentaloma.

Patients and Methods: Between 2015-2018, 217 patients with adrenal incidentaloma who were admitted to the endocrinology outpatient clinic were included in the study. A mg overnight dexamethasone suppression test (DST), 24 hour urine free cortisol, 24-hour urine methanephrine and normetanephrine levels were evaluated in all patients. Patients who also have hypertension or hypokalemia were screened for the plasma aldosterone/renin activity ratio. CT or MRI imaging properties of adrenal incidentalomas were screened.

Results: In the evaluation of cases; 180 (83%) of the masses were evaluated as non-functional and 37 (17%) as functional. Of the 37 patients evaluated as having functional adrenal mass; 10 (4.6%) had pheochromocytoma, 5 (2.3%) Cushing’s syndrome, 9 (4.1%) subclinical Cushing’s syndrome and 13 (6%) primary hyperaldosteronism were detected. In 180 patients who were evaluated as having non-functional adrenal mass; metastatic disease in 7 (3 non-small cell lung cancer, 1 breast cancer, 1 prostate carcinoma and 2 unknown primary cancer), myelolipoma in 4, ganglioneuroma in 1, hydatid cyst in 1, adrenocortical carcinoma in 2 patients were detected.

Conclusion: According to the results of this current study, adrenal incidentalomas do not seem to be functional. Some adrenal masses may have malignant features. For this reason, adrenal incidentaloma is a condition that should be examined both in terms of functionality and malignancy potential.

Key words: Adrenal incidentaloma, pheochromocytoma, Cushing’s syndrome, hyperaldosteronism

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INTRODUCTION
An adrenal incidentaloma is an adrenal mass that is found in an imaging examination performed for other reasons, typically without the suspicion of any adrenal disease. Radiological studies report that the incidence is 3% in the 5th decade and increases up to 10% with age (1-2). Approximately 80% of adrenal incidentalomas are non-functional adrenal adenomas. Studies reported the prevalence of subclinical Cushing’s syndrome to be 5%, pheochromocytoma as 5%, adrenocortical carcinoma as 5%, adrenal metastases as 2.5%, and primary hyperaldosteronism as 1% in patients with adrenal incidentaloma. Other causes are benign cysts, ganglioneuroma, myelolipoma, etc (3-4). Computed tomography (CT) and Magnetic Resonance Imaging (MRI) are the main imaging modalities for adrenal incidentalomas. An attenuation coefficient of 10 HU or less in a non-contrast CT and rapid washout of the contrast agent after 10 or 15 minutes are important indicators for the detection of benign lesions (5). In MRI, adenomas are seen as hypo or isointense in T1-weighted images and hyper or isointense in T2-weighted images (6-7).

It is recommended that all adrenal incidentaloma patients should be evaluated for Cushing’s syndrome and pheochromocytoma to determine whether they are functional in terms of hormone secretion, and patients who also have hypertension or hypokalemia should be evaluated for primary hyperaldosteronism. In patients with adrenal incidentaloma, 24-hour urine fractionated metanephrines are used as a screening test for pheochromocytoma. 1 mg overnight dexamethasone suppression test (DST), free cortisol levels in 24-hour urine, metanephrine-normetanephrine levels in 24-hour urine, and plasma aldosterone and plasma renin activity levels in patients with hypertension were recorded for all patients from files. Imaging characteristics of the patients evaluated by CT or MRI were recorded from the files. The treatments and the histopathological diagnoses of adrenal incidentaloma in patients subjected to adrenalectomy were recorded from the files.

RESULTS
Of the 217 patients included in the study, 143 (65.9%) were female and 74 (34.1%) were male. The mean age was 54.8 ± 12.6 years. The mean mass size was 26.8 ± 14.8 mm. Of the 217 cases, 105 (48.4%) had a mass on the left, 85 (39.2%) on the right, and the masses of 27 (12.4%) patients were bilateral.
Of 217 patients, 52 (24%) had hypertension (Table 1). In functional evaluation of 217 patients; adrenal incidentalomas were non-functional in 180 (83%) patients and functional in 37 (17%) patients. Of the 37 patients who were evaluated as having functional adrenal mass, 10 (4.6%) had pheochromocytoma, 5 (2.3%) had Cushing's syndrome, 9 (4.1%) had subclinical Cushing's syndrome, and 13 (6%) had primary hyperaldosteronism (Table 1).

Of the 180 patients evaluated as having non-functional adrenal incidentaloma; 7 (3.2%) had metastatic disease (3 non-small cell lung carcinoma, 1 breast cancer, 1 prostate carcinoma and 2 cancer of unknown origin), 4 (1.8%) had myelolipoma, 1 (0.4%) had ganglioneuroma, 1 (0.4%) had cyst hydatid, 2 (0.9%) had adrenocortical carcinoma (Table 1).

**DISCUSSION**

Adrenal incidentaloma is the general name of lesions detected during imaging studies performed for other reasons to people who do not have any adrenal gland related complaints or physical examination findings. Generally, lesions with a diameter of 10 mm or greater are considered adrenal incidentaloma. Development of imaging techniques, aging, presence of metabolic syndrome, white race origin, frequency of hospital admission and female gender are seen as major factors increasing the incidence of adrenal incidentaloma. In a study conducted by Çömlekçi et al., with 376 adrenal incidentaloma patients, it was found that the mean age was 54.7 ± 13.1 and it was seen more frequently in women (70%) (10). In our study, the mean age was 54.8 ± 12.6 years in accordance with the literature. Likewise, it was found to be more frequent in women (65.9%). Approximately 50-60% of adrenal masses are located in the right adrenal gland, 30-40% in the left adrenal gland, and 10-15% in both adrenal glands. However, when ultrasonography is used as an imaging modality, adrenal masses are observed more frequently in the right adrenal gland due to insufficient imaging of the left adrenal gland compared to CT (11-13). In a study conducted by Kutbay et al. (14), it was found that 51.3% of adrenal masses were on the left, 38.5% were on the right and 10.2% were bilateral. In our study, the localization of the adrenal incidentalomas was made by CT and MRI and 48.4% of the masses were on the left, 39.2% on the right and 12.4% were bilateral.

| All Population n=217 (%) |
|--------------------------|
| **Gender**               |
| Female                   | 143 (65.9)  |
| Male                     | 74 (34.1)   |
| **Age (year)**           | 54.8 ± 12.6 |
| **Hypertension**         |
| Yes                      | 52 (24)     |
| No                       | 165 (76)    |
| **Tumor size (mm)**      | 26.8 ± 14.8 |
| **Tumor localization**   |
| Left                     | 105 (48.4)  |
| Right                    | 85 (39.2)   |
| Bilateral                | 27 (12.4)   |
| **Functional evaluation**|
| Non-functional           | 180 (83)    |
| Functional               | 37 (17)     |
| **Non-functional adrenal mass evaluation** | 180 (83) |
| **Non-Functional adrenal adenom** | 165 (76) |
| **Metastatic disease**   | 7 (3.2)     |
| **Myelolipoma**          | 4 (1.8)     |
| **Ganglioneuroma**       | 1 (0.4)     |
| **Cyst hydatid**         | 1 (0.4)     |
| **Adrenocortical carcinoma** | 2 (0.9) |
| **Functional adrenal mass evaluation** | 37 (17) |
| **Pheochromocytoma**     | 10 (4.6)    |
| **Cushing's syndrome**   | 5 (2.3)     |
| **Subclinical Cushing's syndrome** | 9 (4.1) |
| **Primary hyperaldosteronism** | 13 (6) |
If Cushing’s syndrome is left untreated, 50% of patients will die within five years, especially for vascular reasons. In cases with Cushing’s syndrome, infections and thromboembolic events are more common than in the normal population. Despite treatment, cardiovascular risk may persist. In patients with persistent moderate hypercortisolemia, mortality rate increases by 3.8-5 times compared to normal population (15). Pheochromocytoma is a potentially curable cause of hypertension and, if not detected, poses a high risk of morbidity and mortality, particularly during surgical procedures and pregnancy. Pheochromocytoma is seen in 0.2-0.6% of the hypertensive population (16-17). It is seen in 2-4% of young hypertensive population (18). Malignant pheochromocytomas constitute 8-12% of pheochromocytomas. 5-year survival in malignant pheochromocytoma is 30-60% (19-21).

Primary hyperaldosteronism is seen in 1.3-10% of hypertension patients and is a potentially curable cause of secondary hypertension. Primary hyperaldosteronism patients have higher cardiovascular morbidity and mortality than essential hypertension patients with the same age, sex and blood pressure values (22-23). Adrenocortical carcinoma is a rare and highly malignant tumor with a poor prognosis. 20-30% of adrenocortical carcinomas are detected as an incidental adrenal mass. While the 40-month survival rate is 50% in patients without metastasis, this rate is 10% in metastatic patients (24). Adrenal gland is one of the most common metastatic sites of malignant tumors. Adrenal metastasis was detected in 13-17% of autopsy series of metastatic tumors. Adrenal metastasis is most commonly seen in lung and kidney tumors (25-27).

In the management of patients with adrenal incidentaloma, the differential diagnosis of malignant, metastatic and hormone-releasing functional masses from benign and non-functional masses should be made because of their serious effects on morbidity and mortality. In a study conducted by Mantero et al. with 1004 adrenal incidentaloma cases, 83% of the adrenal incidentalomas were evaluated as non-functional, 17% as functional (5.28% pheochromocytoma, 9.96% hypercortisolemia, and 1.75% primary hyperaldosteronism) (11). In our study, functional evaluation of 217 patients; 180 (83%) were non-functional and 37 (17%) were functional. Of the 37 patients who were evaluated as having functional adrenal lesion, 10 (4.6%) had pheochromocytoma, 5 (2.3%) had Cushing’s syndrome, 9 (4.1%) had subclinical Cushing’s syndrome, and 13 (6%) had primary hyperaldosteronism. Of the 180 patients evaluated as having non-functional adrenal incidentaloma; 7 (3.8%) had metastatic disease (3 non-small cell lung carcinoma, 1 breast cancer, 1 prostate carcinoma and 2 cancer of unknown origin), 4 (2.2%) had myelolipoma, 2 (1.1%) had adrenocortical carcinoma, 1 had ganglioneuroma and 1 had cyst hydatid. The data we obtained as a result of our study were found to be compatible with previous studies on this subject.

Our study has some limitations. This is a single-center study and the sample size is relatively small. The results of our study were consistent with previous studies in the literature, but primary hyperaldosteronism was detected at a higher rate. According to the results of this study, it is not uncommon for adrenal incidentalomas to be functional. In addition, some adrenal masses may be malignant. Therefore, adrenal incidentaloma is a condition that should be examined in terms of both functionality and malignant-benign lesion distinction.

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