

Case Report

A Giant Metastatic Adrenal Cortical Carcinoma Case Presented with Rapid Progression

Hızlı İlerleyen Dev Metastatik Adrenal Kortikal Karsinom Olgusu

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ABSTRACT

Adrenocortical carcinoma (ACC) is an uncommon and aggressive tumor. Despite the current treatment options commonly used in ACC, the prognosis is poor. No risk factors have been identified except for genetic predisposition. The most important factors affecting the prognosis are the stage at the time of diagnosis and the resectability of the primary tumor. Here, we present a metastatic ACC case of a 29-year-old woman presented with symptoms of swelling in her feet, abdominal striae, and mild abdominal pain for three months. The abdominal computed tomography scan revealed a 14 cm mass in the right adrenal gland, indistinguishable from the liver and right kidney. Clinicians should consider primary ACC, which has limited treatment options, in the differential diagnosis in the presence of findings such as edema, obesity, and striae.

Keywords: Adrenocortical carcinoma, case study, chemotherapy, metastatic, mitotane

ÖZET

Adrenokortikal karsinom (AKK) nadir görülen, agresif bir tümördür. AKK'de yaygın olarak kullanılan mevcut tedavi seçeneklerine rağmen prognoz kötüdür. Genetik yatkınlık dışında herhangi bir risk faktörü tanımlanmamıştır. Prognozu etkileyen en önemli faktörler, tanı anındaki evre ve primer tümörün rezektabilitesidir. Bu yazıda, üç aydır ayaklarda şişlik, karında çizgilenme ve hafif karın ağrısı şikayetleri ile başvuran 29 yaşındaki kadın hastada metastatik AKK olgusu sunulmaktadır. Bilgisayarlı tomografide sağ böbreküstü bezinde karaciğer ve sağ böbrekten ayırt edilemeyen 14 cm'lik kitle saptandı. Tedavi seçenekleri kısıtlı olan primer AKK; ödem, obezite, stria gibi bulguların varlığında ayırıcı tanıda düşünülmelidir.

Anahtar kelimeler: Adrenokortikal karsinom, olgu sunumu, kemoterapi, metastatik, mitotan

Introduction

Adrenocortical carcinoma (ACC) is an uncommon and aggressive tumor. The annual incidence is reported as 0.5-2 cases per million, and it is more common in women than men. A bimodal age distribution is seen, as under the age of five years and in the fifth decade [1]. Currently, except for genetic predisposition, no risk factors have been identified. While most of the patients present with symptoms related to excessive hormone production; the remaining cases are detected incidentally or as a result of complaints related to tumor size. In adrenocortical carcinomas, computed tomography (CT) and magnetic resonance imaging (MRI) are the preferred imaging modalities both for the localization of the tumor and detection of distant metastases. 25% of the cases has metastatic disease at the time of diagnosis, mostly to liver, lung, lymph nodes, and bone [2]. While 5-year survival rate is 60-80% in tumors confined to the adrenal gland, it is decreased to 0-28% in metastatic stage [3]. The most important factors affecting the prognosis are stage at the time of diagnosis and the resectability of primary tumor. In addition, advanced age, tumor size, presence of hormone-secreting tumor, high Ki-67 index (>10%) and mitotic activity, and tumor necrosis may be related to poor prognosis in ACC. Currently, the only curative approach is surgical resection. Palliative therapy is just limited to patients with unresectable or metastatic ACC [4]. Here, it was aimed to present a metastatic ACC case that passed away rapidly after the initiation of systemic treatment.

Case Report

A 29-year-old woman referred to our clinic with symptoms of swelling in her feet, abdominal striae, and mild abdominal pain that has begun three months ago. Medical history of the patient was remarkable for obesity (BMI: 43), type-2 diabetes mellitus, hypothyroidism, and thalassemia minor. The

medications were levothyroxine sodium, metformin, and insulin aspart. Alopecia, acne, aphthous stomatitis, striae on the abdomen and feet, and bilateral pretibial edema were found in the physical examination at referral. Initial laboratory findings showed hyperglycemia, elevated liver function tests including total bilirubin, direct bilirubin, indirect bilirubin, alkaline phosphatase, gamma glutamyl transferase, aspartate transaminase, alanine transaminase, and INR (international normalized ratio) levels. Ejection fraction was more than 60% without significant pathology in Echocardiography. No thrombus formation was detected with bilateral lower extremity doppler ultrasound screening. Further investigation was planned due to the Cushingoid appearance and abnormal laboratory results.

After consultation with department of endocrinology, hypercortisolemia (midnight level: 46,6 µg/dL), and low ACTH levels (5 pg/mL) were detected. 1 mg dexamethasone suppression test was compatible with hypercortisolemia. Aldosterone to renin ratio, catecholamine and sex-hormone levels were in normal range. The Pituitary MRI showed no significant finding. Abdominal CT scan revealed a 14 cm mass in the right adrenal gland, indistinguishable from the liver and right kidney, and multiple parenchymal liver masses with the largest diameter 10 cm. (Figure 1, 2, 3). No pathological lesion was detected in thorax CT. The histopathological and immunohisto-chemical analysis of liver tru-cut biopsy was reported as the metastasis of primary adrenal cortex carcinoma. And, positive staining for synaptophysin, inhibin, melan A, vimentin and p53 was detected in the pathology specimen. A hypermetabolic mass with intense 18-FDG (18-fluorodeoxyglucose) uptake in the right surrenal region with tendency to coalesce in the liver was detected in 18-FDG positron emission tomography-computerized tomography (18-FDG PET-CT). A similarly heterogeneous

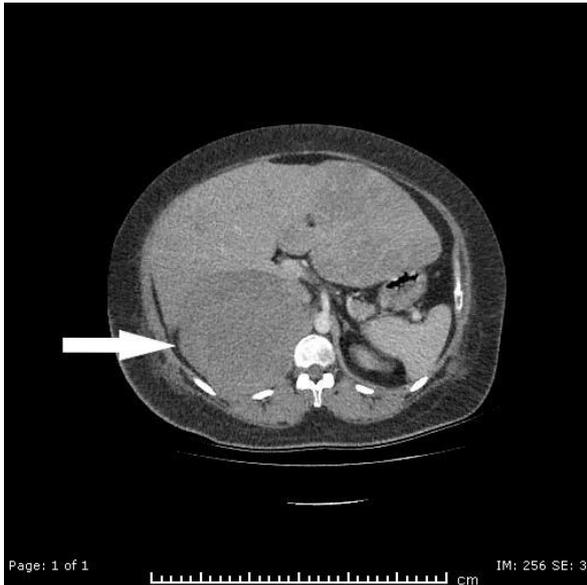


Figure 1. Contrast-enhanced CT image in the axial plane: Hypodense mass filling the right adrenal lodge and indenting the liver. Heterogeneously enhancing hypodense mass lesions in the liver parenchyma.

pattern of 18-FDG uptake was also demonstrated in the liver metastases. (Figure 4).

Surgery was not considered due to widespread liver metastasis, and systemic chemotherapy consisted of cisplatin and etoposide was immediately initiated with daily mitotane therapy. However, neutropenic sepsis occurred four days after the completion of first-cycle of chemotherapy, and no further chemotherapy could be given. The patient had hepatic failure and was in a state of visceral crisis at the time of admission and presented with serious signs and symptoms. In the follow-up, severe renal and liver impairment developed. Moreover, the mental status of the patient worsened progressively, and status epilepticus occurred. General condition of the patient deteriorated rapidly due to high disease burden, visceral crisis and sepsis. It was a chain of events that resulted in infectious manifestations and multiorgan failure on the basis of uncontrolled aggressive malignancy in the patient. The patient passed away on the 23rd day of the diagnosis. Hence,

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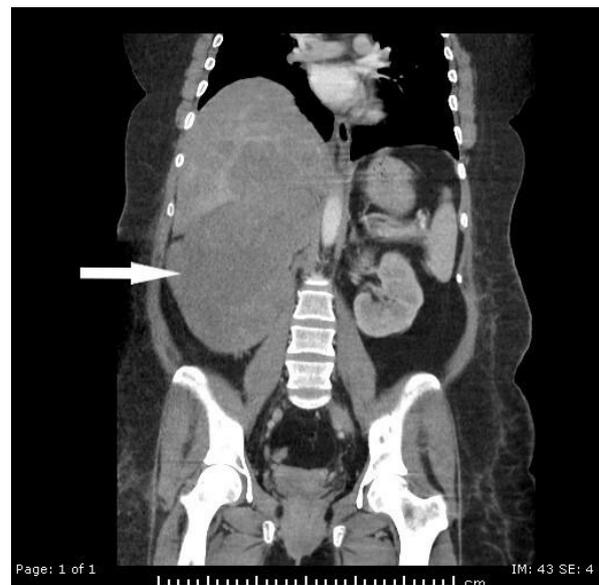


Figure 2 and 3. Contrast-enhanced CT image, coronal and sagittal section: A lobulated contoured hypodense mass filling the right adrenal lodge and extending inferior. The mass has a component on the superior part that erases the liver contours and invades the liver. It is seen that the mass depresses the right kidney downwards.

informed consent was obtained from the next kin of the patient for publication of this case report and related images.

Discussion

ACC is an uncommon tumor with a five-year overall survival (OS) rate less than 50%. The well-established prognostic factors are age, disease stage, distant metastasis, Ki-67 index,

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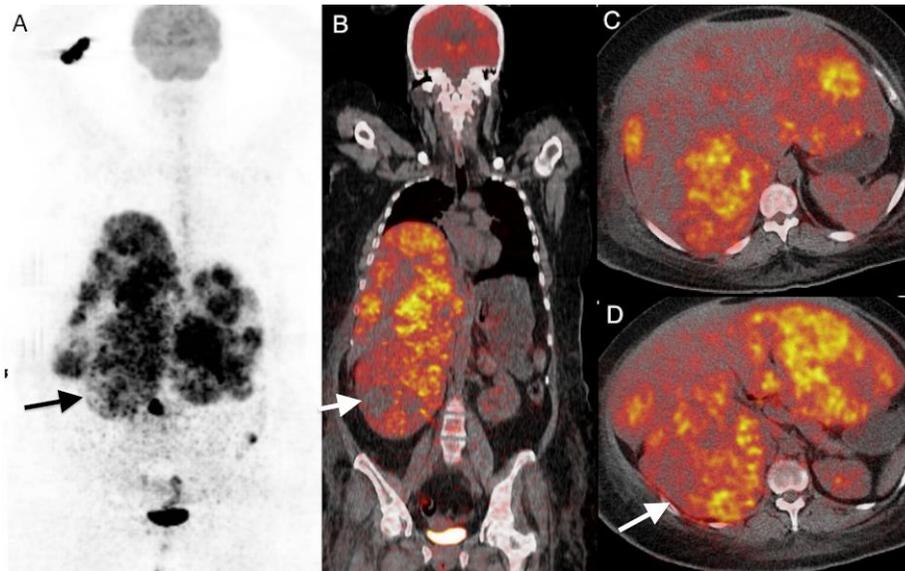


Figure 4. The primary mass was indicated with an arrow on maximum intensity projection (MIP) PET scan (figure A), coronal fusion image (figure B), axial fusion images (figure C and D).

hormone production status, and complete resection of the mass [5]. Surgery is the preferred treatment option and is recommended even in the presence of distant metastasis [6]. Despite resection, recurrence and metastasis rates are high for ACC. ACC can be functional or non-functional depending on hormone secretion. While functional carcinomas are usually detected early because of the symptoms related to excessive hormone production; nonfunctional carcinomas may not be diagnosed until the tumor has compression on adjacent tissue and organs or it may be detected incidentally in imaging [2].

For functional ACC; obesity, hypertension, Cushing's syndrome can be seen in cortisol-secreting masses; virilization in androgen-secreting masses; hypertension, muscle weakness, and hypokalemia due to aldosterone secreting tumors; gynecomastia in tumors that secrete estrogen [6]. In the present case, there were not any complaints due to the hormone excess despite hypercortisolism. Abdomen CT scan findings were consistent with typical characteristics of ACC. Furthermore, 18-FDG PET-CT showed high uptake in the right adrenal primary mass and in liver metastases.

Chemotherapy regimen consisting of cisplatin, doxorubicin, and etoposide in combination with mitotane therapy is usually given in the adjuvant, unresectable, and metastatic settings [7,8]. Moreover, radiotherapy can be applied for symptom palliation in patients with metastatic ACC [9].

Despite the current treatment options commonly used in ACC, the prognosis is poor. A rapid progression of the disease is also common in this patient group. Therefore, more effective and less toxic new treatment options such as immunotherapy and multi-kinase inhibitors are needed for advanced disease [10]. In our case, despite administration of one cycle of cisplatin and etoposide in combination with daily mitotane therapy, the disease progressed rapidly and the patient passed away in a few weeks.

Conclusion

In conclusion, we aimed to present a young patient with diagnosis of metastatic ACC with aggressive clinical course and mortal outcome. The presence of long-standing nonspecific symptoms precluded suspicion for clinical diagnosis, and the patient who lost

the chance of early diagnosis was diagnosed in the metastatic stage. Rapidly initiated systemic treatments did not yield results and the patient passed away in a short time. Clinicians should consider primary ACC,

which has limited treatment options, in the differential diagnosis in the presence of findings such as edema, obesity, and striae in the lower extremities.

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