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CASE REPORT

Giant Malignant Adrenocortical Tumor in a Young Male with Edema in Lower Extremities

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ABSTRACT

Adrenocortical carcinoma (ACC) is a rare tumor, with an annual incidence of 0.5-2/million. The incidence of ACC, which is seen slightly more in females, is increasing in children under the age of 5 years and in adults in their 4^{th}-5^{th} decades. ACC is seen as sporadic in the vast majority of cases. About half of ACCs are hormonally active. As cortisol is the most commonly secreted hormone in these tumors, patients present with rapid-onset Cushing's syndrome that often shows signs of virilization. In non-functional tumors, large intraabdominal mass and abdominal pain are the most common findings. Tumors can sometimes reach giant dimensions, often weighing 100-1000 g. ACC is a very aggressive tumor with a poor prognosis. Currently, surgical excision is considered as the only curative treatment. Due to the rarity of this entity, we present a young male patient with an ACC weighing 1200 g and 21 cm in diameter, which caused bilateral lower extremity edema.

Key words: *Adrenal glands, Adrenal cancer, Adrenocortical carcinoma*

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ÖZET

Genç Erkek Hastada Alt Ekstremite Ödemine Yol Açmış Dev Malign Adrenokortikal Tümör

Adrenokortikal karsinom (ACC), yıllık insidansı 0.5-2/milyon olan nadir bir tümördür. Kadınlarda biraz daha fazla görülen ACC'nin insidansı, 5 yaşın altındaki çocuklarda ve 4-5. dekaddaki yetişkinlerde artmaktadır. ACC'nin büyük çoğunluğu sporadik olarak görülmektedir. ACC'lerin yaklaşık yarısı hormonal olarak aktiftir. Kortizol, en fazla salgılanan hormon olduğu gibi, hastalar genellikle virilizasyon belirtileri gösteren hızlı başlangıçlı Cushing sendromu ile başvurur. Fonksiyonel olmayan tümörlerde büyük karın içi kitle ve karın ağrısı en sık görülen bulgulardır. Sıklıkla 100-1000 g ağırlığında olan ACC, bazen dev boyutlara ulaşabilen kötü prognozlu çok agresif bir tümördür. Günümüzde, cerrahi eksizyon tek küratif tedavi olarak kabul edilmektedir. Genç bir erkek hastada, 1200 g ağırlığında, 21 cm çapında ve bilateral alt ekstremite ödemine yol açmış bir ACC olgusunu, nadir görülmesi nedeniyle sunuyoruz.

Anahtar kelimeler: *Adrenal bezi, Adrenal kanser, Adrenokortikal karsinom*

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INTRODUCTION

Adrenocortical carcinoma (ACC) is a rare tumor, with an annual incidence of 0.5-2/million, and it is slightly more prevalent in females[1]. ACC shows bimodal age distribution with two peaks (under 5 years of age and in the 4^{th}-5^{th} decades of life)[2]. Cortisol is the most commonly secreted hormone in these tumors, and approximately half of the tumors are hormone-active. Hence, most of the patients present with Cushing syndrome, which has rapid onset and exhibits signs of virilization[3]. At the time of diagnosis, the majority of the patients are in advanced stages. Surgical excision is the unique curative treatment modality. ACC, which is an aggressive tumor, has a poor prognosis. The case reported herein presented with intraabdominal mass, abdominal pain and bilateral lower extremity edema. Computerized tomography (CT) revealed hepatic and pulmonary metastasis. The mass was totally resected. The pathology results of the mass, which measured 21 cm and weighed 1200 g, were reported as ACC.

CASE REPORT

A 27-year-old male patient presented with abdominal pain, weight loss and gradually increasing swelling in both legs for an extended period. On his physical examination, a mass with indefinite margin was detected in the right upper quadrant together with the signs of mild virilization. Blood analysis showed elevated serum levels of DHEA-S (938.6 μg/dL). Abdominal ultrasonography demonstrated a 145 × 115 mm hypoechoic, heterogeneous solid lesion containing calcifications in the right adrenal gland. CT revealed a 10 × 13 × 13 cm lesion depressing the right kidney inferiorly, the margins of which could not be clearly distinguished from the liver and inferior vena cava (IVC); the lesion was close to the right renal vein, contained millimetric calcifications, and became heterogeneously opaque with intravenous contrast substance (Figure 1). In addition, two lesions of 15 mm and 22 mm, consistent with metastasis, were observed in the posterior segment of the right liver lobe. On thoracic CT, a few nodules in both lungs, < 10 mm and considered to be metastatic, attracted attention. Moreover, a few lymph nodes (the largest of which measured 22 × 12 mm) located in the right paratracheal region were observed in the mediastinum, and hypodense thrombus that was likely associated with the tumor was observed in the segmental branches of the inferior lobe pulmonary arteries. After the Trucut biopsy was reported as adrenocortical tumor, the patient was considered as metastatic adrenocortical cancer and was consulted with the medical oncology department. Considering the large tumor size and young age of the patient, surgical resection was offered as the first-line therapeutic option. Exploration demonstrated a giant adrenal mass seen to push the right kidney inferiorly and extend to the hepatic veins behind the liver in the superior aspect. In the medial aspect, the mass was seen to compress the IVC. The mass was totally excised (Figure 2). The patient was discharged from the hospital without complication on postoperative day 6. Microscopic examination of the mass showed tumor cells with eosinophilic cytoplasm and a large nucleus, showing remarkable pleomorphism and atypia. Extensive coagulation necrosis foci were observed inside the tumor. On immunohistochemical examination, negative staining was observed with chromogranin A, CD57 and S100 protein, but extensive positive cytoplasmic staining was observed with synaptophysin and CD56. While areas consistent

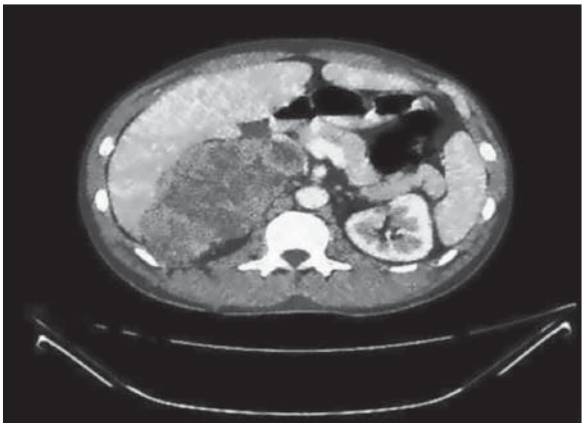

Figure 1. The appearance of the giant adrenal mass on CT.

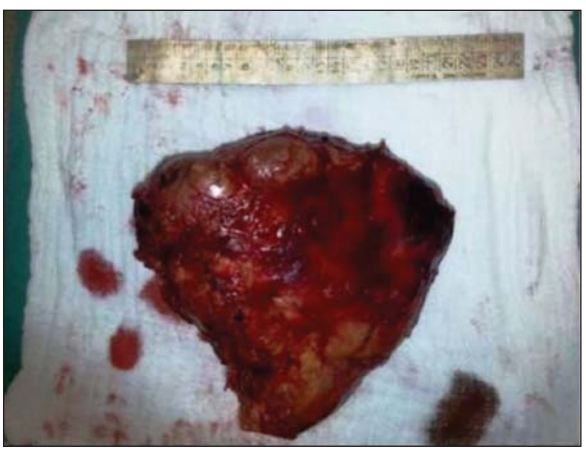

Figure 2. The totally excised adrenal tumor.

with invasion of blood vessel and lymphatic vessel were observed, no capsule invasion was determined (Figure 3).

DISCUSSION

Although ACC is particularly more common in children under the age of 5 years and in adults in the 4^{th}-5^{th} decades of life, the present case was a 26-year-old male[2]. ACC, the majority of which are sporadic, is known to be associated with familial cancer syndromes such as Li-Fraumeni and Beckwith-Wiedemann[4]. Familial history in terms of cancer was negative in the present case, who was otherwise healthy. Fifty to sixty percent of adrenocortical tumors are functional, and the most common clinical presentation is Cushing syndrome, due to excessive cortisol secretion[3]. Virilization may sometimes accompany this clinical presentation. The presented case had only elevated serum DHEA-S level, which caused mild virilization. Other adrenocortical tumors are non-functional and usually present with abdominal pain, weight loss and intraabdominal mass. The present patient also admitted to our clinic with abdominal pain and swelling in both lower extremities. These tumors may cause pressure on the IVC and sometimes thrombus when they reach larger sizes[5]. Abdominal CT revealed compression of the IVC by the tumor, despite the absence of tumoral invasion into the IVC. Although 90% of the adrenal tumors > 6 cm are malignant, the size alone is not a criterion of malignancy. Heterogeneity of the tumor, irregular margin, bleeding, and presence of lymphadenopathy or liver metastases on CT are the signs suggestive of malignancy. The CT of the present case showed a 13 cm mass that displaced the right kidney inferiorly and compressed the right renal vein. Moreover, metastatic lesions were detected in the liver and lungs. Complete surgical resection is the only curative treatment modality and is the only promising method in the long term. Nevertheless, ACC has high relapse rates[6]. Surgical resection, which forms the basis of treatment in ACC, is recommended also in selected stage 4 patients because of favorable effects on survival[7,8]. Debulking may facilitate the efficacy of other therapeutic options while reducing the symptoms associated with excessive hormone secretion[9]. Conversely, Allolio et al. suggested mitotane therapy as the first-line therapeutic option in stage 4 ACC[10]. Clinical response to mitotane, which has been used for years in the medical treatment of ACC, is quite variable. With a narrow therapeutic range, mitotane leads to severe adverse events such as neurological toxicity. In recent years, new therapeutic regimens have been developed using mitotane in combination with streptozotocin or etoposide/doxorubicin/cisplatin[11]. Despite all, surgery, especially en-bloc resection together with invaded adjacent tissues and organs, remains as the basic therapy for ACC. Cases with a tumor size up to 26 cm have been reported in the literature[12]. The tumor of the present case measured 1200 g and 21 cm. Tumor stage and the adequacy of surgery are the main factors that determine survival [13]. Various staging systems have been suggested in the past. Today, the staging system offered by the European Network for the Study of Adrenal Tumors (ENSAT) is usually used[14]. While the 5-year life expectancy is 84% for stage 1 tumors < 5 cm, it is

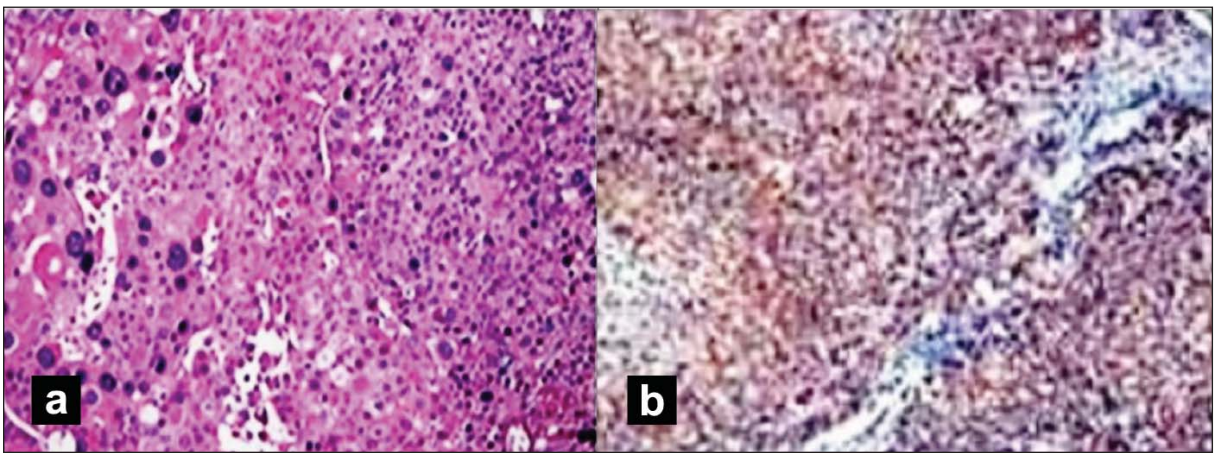

Figure 3. Conventional adrenocortical carcinoma composed of pale eosinophilic cells arranged in a trabecular to solid pattern with bizarre atypical cells (H&E stain x200) (a), diffuse cytoplasmic reactivity with synaptophysin (b).

about 10% in stage 4 tumors, which is defined as the presence of adjacent organ involvement, fixed lymphadenopathy and distant organ metastasis[4].

In conclusion, adrenocortical cancer is a rare, aggressive malignancy with poor prognosis. It may rarely reach larger sizes. Giant tumors are usually non-hormone-active malignancies. Surgery remains the first-line therapeutic option in the treatment of ACC as it provides longer survival, even in patients presenting with advanced stage tumor.

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