Exp Oncol 2018
40, 3, 251–253

CASE REPORT

Experimental ONCOLOGY

A CASE REPORT OF LATE LOCAL RELAPSE OF ADRENOCORTICAL CARCINOMA 18 YEARS AFTER ADRENALECTOMY

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Adrenocortical cancer is an extremely rare tumor presenting with extensive locoregional spread at the time of diagnosis. Due to the diagnostic difficulties preoperatively and a lack of effective treatment options, patients have poor prognosis. Patients succumb to metastases within a couple of months. Only 20 cases have been so far reported in the literature with a medium disease-free survival up to 2 years. We present a case of a locoregional recurrence of adrenocortical cancer 18 years after left adrenalectomy.
***Key Words*: adrenocortical carcinoma, local relapse, adrenalectomy, long-term survival, nephrectomy.**

Adrenocortical carcinomas (ACC) are rare neoplasms that occur in 0.5–2 cases per million people per year [2, 11]. ACC has a female predominance [20]. Adrenal masses are usually found incidentally during radiological examinations performed for indications other than adrenal diseases. Incidental adrenal masses are reported as 8.7% of the adrenal cancer cases [10]. In 50% cases tumor cells release one of adrenocortical gland hormones, what makes for special manifestations of this pathology including virilism and clinical symptoms of hyperadrenalismus. In most cases ACC are exceeding 20 cm in diameter and have a strong tendency to invade the adrenal vein, vena cava. Metastases to regional and periaortic nodes are common, as is distant hematogenous spread to the lungs and other viscera. The median survival is about 2 years [11]. ACC is a very rare malignant tumor and to date there were only 20 cases reported in the literature and to the best of our knowledge there have been no cases with the disease-free survival more than 5 years [9, 10, 12, 18]. The majority of those patients succumbed to disease within a year due to local recurrence or metastases [20]. Here, we report about a patient who was admitted with left-sided adrenal mass and diagnosed with recurrence of adrenal cortical carcinoma after left adrenalectomy 18 years ago.

CASE REPORT

A 35-year-old female was admitted to the surgical department of State Scientific Institution "Scientific-Practical Centre of Preventive and Clinical Medicine", State Administration of Affairs, Kyiv, Ukraine, due a headache, and hypertension crisis resistant to medical therapy. She had a remarkable medical history: 18 years ago she underwent left adrenalectomy for an ACC. The tumor exceeded 18 cm in diameter. Histopathological examination of the adrenalectomy specimen revealed left high-grade adrenal carcinoma. The final pathological diagnosis was left ACC pT3N0M0, stage III, 3rd clinical group. After the surgery the patient quarterly underwent follow-up for cancer, urine steroids tests, abdominal radiography and ultrasound, magnetic resonance imaging (MRI). She was observed by oncologist, gynecologist, endocrinologist and was prescribed the substitution cortisol therapy. The patient became pregnant on the 12th year postoperatively. After the delivery she discontinued all the recommendations and prescriptions because of good state of health. She started feeling worse 18 years after the left adrenalectomy, therefore she consulted the same doctor.

Upon physical examination blood pressure was 220/130 mm Hg and her pulse was 88/min. Her body mass index was 35.1. The signs and symptoms of adrenal hormone oversecretion were proven with laboratory oversecretion of 11-deoxycorticosterone and dehydroepiandrosterone (DHEA). Serum cortisol and the aldosterone to renin ratio were normal. Ultrasonography showed heterogeneous and hypoechoic lesion of left arenal gland 6.3 × 5.4 × 2.9 cm with non-defined borders (Fig. 1). Abdominal computed tomography (CT) scan with intravenous contrast showed 7.1 × 5.3 × 3.8 cm soft-tissue mass with irregular borders in the left adrenal bed with abnormal postoperative cellular tissue. Vena renalis sinistra was strangulated by a neoplasm, luminal narrowing is 0.5 cm (Fig. 2).

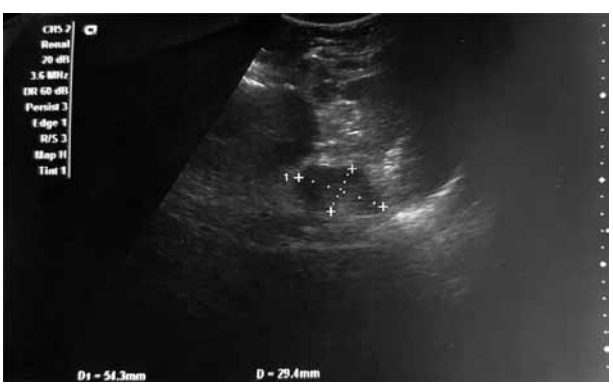

Fig. 1. Results of ultrasound of the adrenal bed

Submitted: July 16, 2017.
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Abbreviations used: ACC – adrenocortical carcinomas; CT – computed tomography; DHEA – dehydroepiandrosterone; MRI – magnetic resonance imaging.

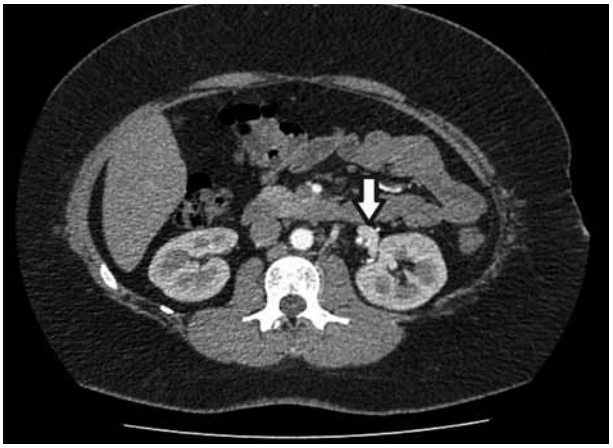

Fig. 2. CT of abdomen showing large left-sided adrenal mass (arrow)

Mammography, upper gastrointestinal system endoscopy, thorax CT, liver function tests including ALT and AST were performed to exclude metastasis from other organs to adrenals, which gave normal results.

We set up the following preoperative diagnosis: Ca suprarenal gland sinister T3NxMx stage III. State post adrenalectomy (1999). Progression of the disease: relapse of adrenal cortical carcinoma.

The patient went on to have a total resection of local relapse of adrenal tumor and nephrectomy for the underlying lesion.

On gross examination specimen removed from the bed of the left adrenal measured 6 × 5 × 3 cm (Fig. 3). The mass was found to be a grey-yellow-pink tumor with a humpy surface. On cut surface, there are green-grey, yellow-grey colored areas with focuses of malaxing and necrosis within the mass. The left kidney and vena renalis sinistra were adhered to tumor and involved in tumorous mass. The interface between the kidney and the mass was examined carefully by close serial sectioning. On the excision axis, the tumor spreads to the vena renalis wall.

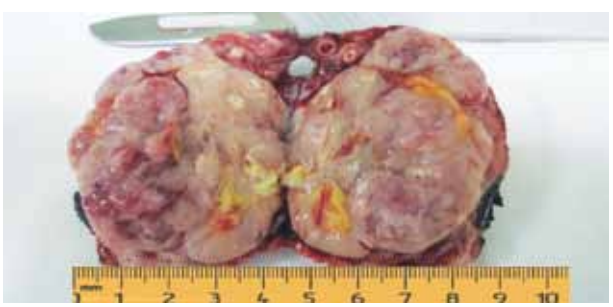

Fig. 3. Specimen of the mass removed from the bed of the left adrenal gland

On microscopic examination the tumor of left retroperitoneal space showed atypical cells with evidence foci of necrosis (Fig. 4). There was hyperchromatic cells with epithelial and spindle cell morphology, and nuclear atypia. It could point to discomplectation of structure — the widely-spread parts of carcinoma do not contain stromal cells. Tumor spreads to the adventitia and media of vena renalis wall.

Based on the histologic profile, the tumor was diagnosed as high-grade ACC, with necrosis areas, invasion of left renal vein.

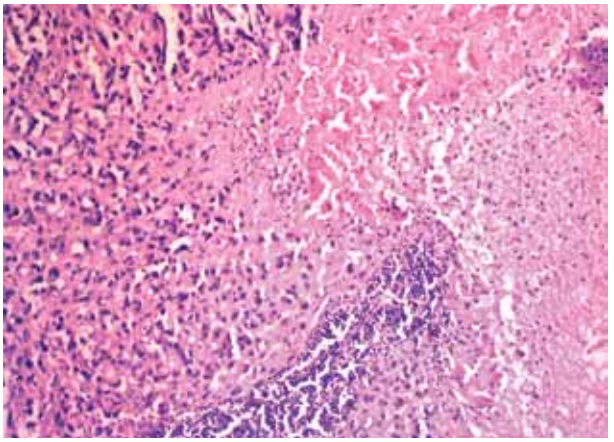

Fig. 4. Histopathology section showing extensive necrosis of tumor. Hematoxylin-eosin, original magnification, × 200

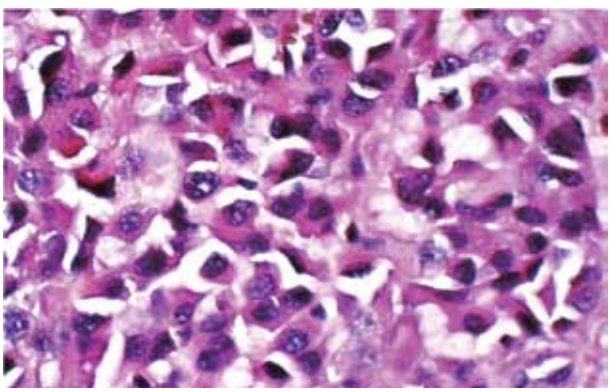

Fig. 5. Histopathology section showing cells with epithelial and spindle cell morphology, and nuclear atypia. Hematoxylin-eosin, original magnification, × 400

At the time of writing, 11 months postoperatively, the patient remained alive and underwent the follow-up visits to the endocrine surgeon, oncologist and gynecologist.

DISCUSSION

ACC is a rare and highly malignant endocrine neoplasm accounting for an estimated 0.02% of all cancer cases [5, 6]. The majority of adrenal tumors are mostly sporadic and unilateral but some of them are associated with Li — Fraumeni syndrome, type-1 multiple endocrine neoplasia, Beckwith — Wiedemann syndrome and Carney complex [10, 13]. ACC typically metastases to the lung, liver, peritoneum and pleura, lymph nodes and bones [11, 20]. Prognosis is considerably poor, and the 5-year overall survival rate of ACC is less than 30% [3]. Even with favorably performed radical resections, the majority of patients succumb to local recurrence or *de novo* metastases [8].

Although remarkable medical history of left adrenalectomy 18 years ago, we initially carried out a diagnostic workup to exclude metastasis from extra-adrenal organs and suspected the potentially malignant adrenal incidentaloma. The primary cancers that mostly spread to the adrenal gland are those of kidneys, lungs, colon, liver and breast [8]. In this context we performed mammography, colonoscopy, upper gastrointestinal system endoscopy, thorax CT, all of which were normal. The initial diagnosis we could

make was the recurrence, local relapse of adrenal cortical carcinoma. According to the recent guidelines adrenal biopsy is not an option for the patients with such an initial diagnosis because of risk of tumor dissemination [6]. Postoperative histopathological examination of the total removal of local relapse of adrenal tumor specimens revealed left-sided high-grade ACC with vena renalis sinistra invasion.

Based on the data collected from the previous cases ACC is more frequent in women than in men (ratio 1.5:1) [6]. In twelve cases reported in the world literature the patients died within 2 days to 30 months after the initial diagnosis [10, 20]. Our case was a middle-aged woman who survived 18 years after the left adrenalectomy performed for ACC. At the 11-months follow up after the removal of local relapse of ACC the patient was free of disease progression.

ACCs tend to be aggressive, and patients often present with extensive locoregional spread at diagnosis [20]. A detailed preoperative endocrine assessment is essential to establish the origin of the tumor that is why in all cases of adrenal mass a comprehensive hormonal analysis is strongly recommended [2]. Moreover, urine steroid metabolomics revealed an early-stage steroidogenesis in ACC that performed well in differentiating malignant neoplasms from adrenal adenomas [1]. Cases of ACC with adrenal hormone production have been reported previously; there was a significant urine steroids overproduction in our case as well [4]. Previous studies demonstrated that CT and MRI are effective modalities for diagnosis and tumor location confirmation [6, 7, 20].

After surgical excision, including complete metastatic resection, adjuvant chemotherapy is indicated. Our patient avoided receiving any chemotherapy. But there are some data with controversial effects of chemotherapy postoperatively [16, 20]. Additional research is required in order to confirm the significant effect of chemotherapy. Mitotane induces adrenal cortex degeneration and necrosis, and in combination with chemotherapy tends to be more effective than chemotherapy alone [17].

ACC is rare tumor with an aggressive and unpredictable behavior. Due the diagnostic difficulties preoperatively and a lack of effective treatment options, patients have poor prognosis. Mostly, only postoperative immunohistochemical examination may provide a definitive diagnosis. The only effective option for tumors at present is adrenal surgery. In case of advanced adrenal cortex cancer adjuvant chemotherapy is considered ineffective. To the best of our knowledge, our case is the first case of 18-years surveillance after the adrenalectomy because of ACC reported in the literature [10, 14, 15, 19, 20]. The possible diagnosis of ACC should be considered during the management of adrenal masses. Therefore, additional research is required in order to explore targeted therapy for management of advanced and metastatic ACC.

CONFLICT OF INTERESTS

The authors declare that they have no competing interest.

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