

Corticoadrenal carcinoma with bone, pulmonary and adrenal gland metastasis handled with surgery, chemotherapy, irradiation and mitotane

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INTRODUCTION

The corticoadrenal carcinoma represents the 0.05 % -0.2% of malignant neoplasms in the United States^[1]. In Colombia based on the information of the statistical yearbook of the National Cancer Institute, the corticoadrenal carcinoma represent 0.1 % of all new cases of cancer^[2]. This tumor has high risk of recurrence.

The main prognostic factor is the stadium, the 5-year overall survival is 82% for stage I, 61% for stage II, 50% for stage III and 13% for stage IV^[3,4].

This paper presents the case of a 47 year-old female patient with stage IV cortical-adrenal carcinoma, bone, pulmonary and adrenal gland metastasis handled with complete resection of the primary tumor, metastasectomy, mitotane, irradiation and chemotherapy. The patient showed complete tumor response and she achieved 50 months of overall survival.

DESCRIPTION OF THE CASE

I present the case of a 47 year-old female patient with 4 months of lumbar pain and sensation of mass in the right flank. A abdomen computed tomography scan revealed a right adrenal mass, 8 cm in diameter, suggestive of neoplasia.

The patient was scheduled for surgery, pathology

reported a neoplasm composed of epithelioid cells, with an eosinophilic cytoplasm and well-defined borders, cores with marked atypia and more than 6 mitoses per 50 CAP, the cells formed nests and trabeculae with nodular growth pattern and diffuse, with areas of fibrosis, osseous metaplasia and focal necrosis confluent. The proliferation index Ki67 was 2%.

The immunohistochemical study was positive for keratin AE1/AE3, Melan, Vimentin, Inhibin and synaptophysin. Was negative for S100, chromogranin, CD10 and CD117. It was not recognized lymphovascular invasion. The profile of immunohistochemistry and morphology corresponded to an adrenal cortical carcinoma

Chest CT scan and bone scan revealed a lesion suggestive of metastases to costal level, the CT scan of abdomen showed no signs of relapse/residue tumor. The costal biopsy that confirmed metastatic corticoadrenal carcinoma, by what surgical resection was performed in which was found a mass of 8x6x2 cm that destroyed the rib and committing the adjacent soft tissues, the the margins of section were negative for tumor .

The patient began treatment with mitotane 2000mg/day, she was asymptomatic. a year after a bone scan showed a metastatic lesion in left femur with high risk of fracture therefore, it was made of prophylactic osteosynthesis. The pathology confirmed corticoadrenal car-

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cinoma.

Mitotane dose was increased to 3000mg/day and the patient received radiation therapy in the left thigh with total dose of 3000 cGY. 18 Months later, a CT scan of the chest showed a metastatic lesion in left lower lobe, which was resected, the asymptomatic patient continued and in treatment with mitotane but at a dosage of 3500mg/day.

Six months after a CT scan of abdomen revealed a metastatic lesion in the left adrenal gland with ipsilateral kidney involvement; the patient was taken to nephrectomy and resection of the left adrenal gland, the pathology reported cortical adrenal carcinoma of 6 cm with signs of necrosis and 9 mitoses per high power field.

By the progression of the disease in spite of treatment with mitotane, presence of single kidney and that the metaiodobenzylguanidine glomerular filtration reported 72ml/min, the patient began treatment with chemotherapy: carboplatin AUC 5 day 1 and etoposide 100 mg/m² days 1 to 3. the patient completed 8 cycles of treatment with good tolerance. The CT scan of the chest, the CT scan of abdomen and bone scan control, showed no metastatic lesions.

At present, the patient shows no clinical evidence or imagenologic of relapse. She continues with mitotane treatment 3.5 gr/day, prednisolone 15 mg/day, fludrocortisone: 0.2 mg/day, levothyroxine 75 mcg/day, her overall survival is 50 months.

DISCUSSION

The corticoadrenal carcinoma is a rare and aggressive tumor. Most cases are sporadic in origin but can also occur in familial syndromes as multiple endocrine neoplasia (MEN) type 1, the syndrome of Li Li-fraumeni Syndrome, Beckwith-wiedemann syndrome Wiedeman, the Carney complex and congenital adrenal hyperplasia^[5,6].

The 40-60% of patients with corticoadrenal carcinoma don't have symptoms but can have them for mass effect on nearby structures with tumors greater than 10cm, some patients have abdominal distention, vomiting, fever, anorexia and weight loss^[7,8]. The diagnosis is incidental up to 8% of the cases and reaches up to 11% when the tumor is larger than 4 cm. Imaging studies of choice are magnetic resonance imaging and computed tomography scan.

The value of attenuation in computed tomography expressed in Hounsfield units (HU) has been shown to have good diagnostic yield to differentiate between benign and malignant lesions, a value < 10 HU suggests that the lesion is benign with sensitivity of 96-100% and a specificity of 50-100%. The percentage of 'washing' contrast in images of the late 10-15 minutes allows you to differentiate adenomas of malignant masses since the 'washing' is faster in adenomas, the cortical carcinoma-adrenal usually shows an absolute percentage of washing (APW) < 60% and a relative percentage of washing (RPW) < 40^[9,10].

When the results of these studies are equivocal, the use of FDG-PET has shown about 95% accuracy to distinguish between injury cortical-benign and malignant adrenal, however, is not able to establish if it is primary or metastatic lesion^[11,12].

The histological diagnosis of cortico-adrenal carcinoma is based on the scale of Weiss that evaluates 9 characteristics: high mitotic rate (>5 per 50 fields), which is an important criterion for distinguishing between benign and malignant tumors and predicts aggressiveness; atypical mitosis, high nuclear grade, low percentage of clear cell necrosis, diffuse tumor architecture, vascular invasion, venous and sinusoidal^[10,13].

Treatment strategies include the control of hormone secretion, surgical resection, chemotherapy, and radiation therapy. The radiofrequency ablation and chemoembolization are alternatives for the management of the liver metastases and lung smaller than 5 cm in patients with high risk of surgical complications^[14,15]. The therapeutic options for the treatment of hypercortisolism in functional tumors are the mitotane, ketoconazole, metyrapone and etomidate.

Mitotane is the chemotherapeutic agent more effective for the treatment of cortical carcinoma-adrenal, should be initiated at a dose of 1-2 g/day and perform daily increments of 1-2 grams every 1-2 weeks; usually a dose of 3-6 g/day is sufficient^[16].

The surgery (open adrenalectomy) is the only potentially curative treatment is always to achieve the complete removal of the tumor. The surgical treatment is a option of management for metastasis and/or local relapses, especially in symptomatic patients, with good status performance and completely resectable lesions^[1,3,10,11,17].

The 80% of the patients treated with radical resec-

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tion experience relapses local and distance in the first 6- 24 months, by this should be considered adjuvant treatment with mitotane, which shows benefit in decline in the rate of recurrence and increase overall survival^[18].

The recommended schedules as first-line treatment for cortical carcinoma-adrenal are unresectable streptozotocine plus mitotane or etoposide, doxorubicin and cisplatin (EDP) plus mitotane which show overall response rates of 36% and 49% respectively^[3,8,10,11,19].

The Firm-ACT trial showed that for first-line therapy, patients in the EDP-mitotane group had a significantly higher response rate than those in the streptozocin-mitotane group (23.2% vs. 9.2%, $P < 0.001$) and longer median progression-free survival (5.0 months vs. 2.1 months; hazard ratio, 0.55; 95% confidence interval [CI], 0.43 to 0.69; $P < 0.001$); there was no significant between-group difference in overall survival (14.8 months and 12.0 months, respectively; hazard ratio, 0.79; 95% CI, 0.61 to 1.02; $P = 0.07$)^[20].

The adjuvant radiation therapy in the tumor bed is recommended in patients with high risk of recurrence (> 8 cm tumors, Ki 67 $> 20\%$ presence of invasion and lympho-vascular), for patients with histologically incomplete resection (R1) or indeterminate (Rx) and in stage III disease^[3,8,21].

In addition the radiation therapy is useful in the management of local recurrences and from bone metastases by reducing the pain, the risk of neurological complications and fractures, can also be used for the management of brain metastases and the superior vena cava syndrome^[8,15,22].

This case shows how the multimodal treatment (surgery, radiation therapy, chemotherapy and mitotane), may improve the survival of patients with corticoadrenal metastatic carcinoma.

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