MedCrave
Step into the World of Research

Journal of Cancer Prevention & Current Research

Possible Treatments in Metastatic Adrenocortical Carcinoma - Case Report

Abstract

The adrenocortical carcinoma (ACC) is a rare cancer of the adrenal cortex, affecting 0.5 to 2 cases per million inhabitants per year. The ACC is usually aggressive, with a 5-year survival of 25%. Most cases of ACC occur sporadically, but in some situations, this malignancy may be associated with a hereditary syndrome. The data in this case report was obtained through review of medical records of the patient and review of the literature using the PubMed portal of the MEDLINE database. It was reported the case of a 56 years old female patient, who initially presented with a mass in the upper pole of the left kidney, underwent to oncologic nephrectomy. Histopathological examination revealed adrenal cortex carcinoma. Initially, the treatment was mitotane, with the progression of the disease; it was initiated chemotherapy with doxorubicin, etoposide and cisplatin, associated to mitotane. After five cycles, the disease was stable, however, there was toxicity and limit dose of anthracycline, the treatment was followed with cisplatin, etoposide and mitotane for another five cycles. Upon new restaging there was an increase in the number and size of nodules, it was started treatment with capecitabine, gemcitabine and mitotane. The patient received seven cycles, with good tolerance to treatment. The third line treatment showed clinical benefit for the patient, with prolonged survival, and, with the palliative treatment, improving the quality of life. It is expected the emergence of new treatments grounded in the genetic and molecular profile, as well as predictor factors of response to the treatment.

Case Report

Volume 4 Issue 6 - 2016

CélioPereira Guércio*, Joaquim Dias da Costa Neto and Débora Bernardes Peixoto

Department of Medicine, Universityof Rio Verde, Brazil

***Corresponding author:** CélioPereira Guércio, Oncolive, Rua Tiradentes, n 822, Santo Agostinho, Rio Verde- GoiÃ¡s - Brazil, ZIP 75904-660; Tel: 556499552142; Email: celioguercio@hotmail.com

Received: April 23, 2016 | **Published:** May 17, 2016

Highlights

A. Three lines of systemic treatment for metastatic adrenocortical carcinoma.

B. Good quality of life, most impressive progression free survival in third line.

C. Warranty possible trial comparing first line options.

Introduction

Adrenocortical carcinoma (ACC) is a rare primary malignant tumor of the adrenal cortex affecting 0.5 to 2 people per million habitants per year [1]. There are two peaks of incidence, the first in children under 5 years of age, and the second in the fourth and fifth decades of life [2].

In the southern region of Brazil there is a high incidence among children of 2.9 to 4.2 cases per million per year, it is believed that this high incidence is associated with high prevalence of germline mutation TP53 R337H [3-4].

The ACC is commonly aggressive with a 25% 5-year survival rate among non-metastatic and metastatic cases [5]. Women are affected more, where approximately 60% of the patients have endocrine symptoms, and the most common form is the Cushing's syndrome (40%). Less frequently, it is observed pure hormonal syndromes of feminization in men and virilization in women [6].

Most cases ACC cases occur sporadically, but in some situations it may be associated with hereditary syndromes such as Li-Fraumeni syndrome, Beckwith-Wiedeman syndrome, multiple endocrine neoplasia type 1, congenital adrenal hyperplasia, and familial adenomatous polyposis [7].

This case report was carried out in order to demonstrate the difficulty of establishing new protocols for rare diseases in consequence of the lack of prospective clinical phase III studies, and the importance of giving value to data of smaller studies with promising results. Important advances with the personalized treatment directed by the genetic and molecular profile of the tumor are awaited, and it is expected more effectiveness and fewer side effects. But meanwhile these types of directed molecular treatment had poor outcomes.

Patients and Methods

The information in this case report were obtained by reviewing the full medical records of the patient and review of the literature using the portal database PubMed MEDLINE without time restriction until March 2015, using the following keywords individually or in combination, "adrenocortical carcinoma", "adrenocortical neoplasms," "adrenocortical tumor", "adrenocortical cancer," "treatment," "indications", "chemotherapy" and "survival." It was obtained the consent of the patient for the publication of information and images contained in this case report

Case Report

A 56 years old female patient, attended the Dr. Gordon Presbyterian Hospital of Rio Verde in March 2012 with a mass in the left upper pole of the kidney, with the dimensions of 12x9,5x10cm accessed by computed tomography. Because of the suspicion of tumor in renal area, left nephrectomy was performed. The histopathological examination revealed an adrenal cortex carcinoma. During the staging, the chest CT scan revealed multiple infracentimetric bilateral pulmonary nodules (Figure

1), the abdominal CT scan showed no other sites of disease, and the cranial MRI showed no disturbance, so it was diagnosed as an adrenal cortical carcinoma stage IV (T3N0M1).

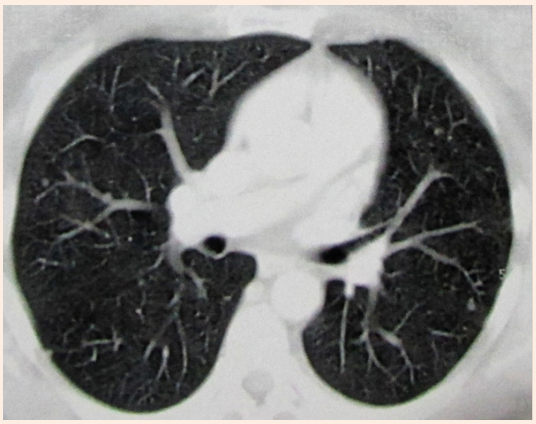

Figure 1: Chest CT scan showing multiple infra centimetric bilateral pulmonary nodules.

In April 2012 the patient reported only fatigue, scoring 0 on the scale of the Eastern Cooperative Oncology Group (ECOG 0), it was started treatment with mitotane in increasing doses up to 4 g / day without important toxicities. In June 2012 it was carried out the revaluation of the chest CT scan which found an increase in the size of pulmonary nodules. When the patient still was in ECOG 0-1 it was started chemotherapy with doxorubicin 40mg/ m^2 D1, etoposide 100mg / m^2 D2, D3 and D4, cisplatin 40mg / m^2 D3 and D4 every 28 days (CAE) associated with mitotane at lower doses (2g). After five cycles, in November 2012, it was the restaging performed, showing a stable disease, however, there was found toxicity (fatigue, anorexia, malaise, and hypotension). The treatment with cisplatin, etoposide and mitotane was continued for five more cycles with better tolerance.

In July 2013, in a new restaging, there was an increase in the number and size of nodules (up to 15 mm) on chest CT scans (Figure 2), with the patient being in ECOG 1. In August 2013 it was initiated a treatment with capecitabine 1500mg / day continuous, gemcitabine 800 mg / m^2 D1 and D8 every 21 days and mitotane 1g / day. The patient received seven cycles, and showed good tolerance to the treatment, remaining stable until March 2014.

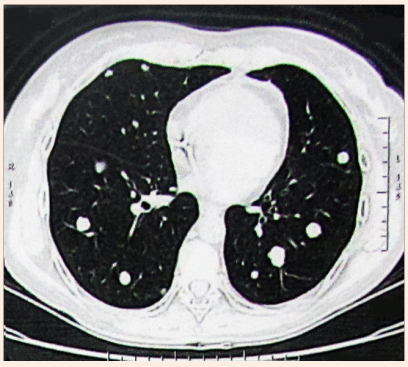

Figure 2: Chest CT scan showing multiple bilateral pulmonary nodules of up to 15mm.

In April 2014 it was performed a chest CT scan that showed an increase of pulmonary nodules and some confluents (Figure 3) and a abdomen CT that showed liver damage, not previously existing, in segment VII. At this time, the patient presented with ECOG 1-2, exclusive palliative care was started with consultations every 14 days and there was observed a progression of the disease with cough and slowly progressive dyspnea.

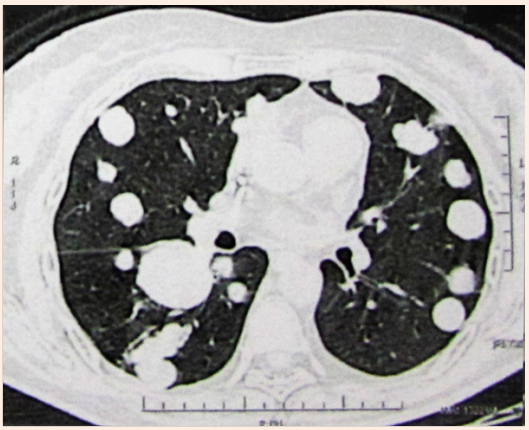

Figure 3: Chest CT scan showing bilateral increase in pulmonary nodules.

In August 2014, the patient was in ECOG 2-3, with worsening of anorexia, fatigue, and use of home supplementation of oxygen. During clinical examination it was noticed mild rhonchi in auscultation, distended abdomen with mass of approximately 12cm bulging the mesogastrium. Other imaging tests weren't requested, because it wouldn't change the course of the disease. In October, there was a worsening of dyspnea, severe abdominal pain, so, the patient was hospitalized for control of symptoms, progressing to death from multiple organ failure.

Discussion

Facing a rare neoplasia, and one of the most aggressive endocrine tumors that exist, with median survival of twelve months or less in metastatic cases, usually little responsive to cytotoxic chemotherapy like other endocrine tumors. The conducting of phase III prospective studies is limited, difficulting the advance in the treatment of this disease, and causing the existence of fewer protocols listed as standard therapy [8-11].

Until the publication of the study Combination Chemotherapy in Advanced Adrenocortical Carcinoma (FIRM-ACT) in June 2012 by Fassnacht et al. [8] there were only treatments based monoterapy with mitotane or chemotherapy CAE, without randomized studies. It was considered a major breakthrough the results of this phase III randomized trial with 304 patients, which compared mitotane associated with streptozotocin or with CAE in the first-line treatment of metastatic cases, with better response rate (23.2 % vs. 9.2%, P <0.001), longer 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) in the mitotane associated with the CAE group, a trend towards higher overall survival in patients who received subsequent therapy (14.8 months vs 12.0 months; hazard ratio, 0.79; 95% CI, 0.61 to 1.02; P = 00:07) and

better overall survival in patients not receiving second line (17.1 months vs 4,7 months).

The patient began treatment after the first progression along with the publication of the clinical trial FIRM-ACT presenting progression of lung disease after thirteen months of this protocol of treatment, still with good performance status. At the time, there was the need of basing the treatment on a nonrandomized phase II study, published by Alfredo Berruti et al., in 2010, with 28 patients using fluorouacil or capecitabine 1500mg continuously and gemcitabine 800 mg / m^2 D1 and D8 (CG) every 21 days, on the second or third line of therapy, which showed an impressive 46.3% rate of clinical benefit including a patient with complete response.

The patient benefited from the third line treatment with capecitabine and gemcitabine with good tolerance and nine months of progression-free survival. This case report is a good example of improvement and extension of survival with palliative chemotherapy for an aggressive disease, and at the same time, an opportunity to discuss new possibilities for randomized clinical trials comparing CG versus CAE, both associated with mitotane for the first line of palliative chemotherapy, thus, comparing the efficacy and toxicity.

It is also expected, the emergence of new treatments grounded in the genetic and molecular profile, as well as predictors of treatment response. It's known the presence of IGF2 / IGFR1, VEGF, mTOR, Wnt / b-catenin routes, with the possible development of monoclonal antibodies against factors and receptors, tyrosine kinase inhibitors and other small molecules.So far, the result of such approaches were disappointing, indicating the necessity of a better knowledge about the disease, the interactions between signaling pathways and the predictive factors for better predictions of therapeutic success [12-20].

The third line palliative chemotherapy treatment, based on a phase II non-randomized study, brought clinical benefits to the patient, providing prolonged survival and improving the patient's quality of life. Thus, it was demonstrated the importance of giving value to smaller studies' data with promising results, there is, however, the need to create future randomized trials for less toxic first-line and subsequent palliative chemotherapy.

The lack of protocols and therapeutic options lead to believe that the emergence of new studies and treatments based on the genetic and molecular profile of the disease, are essential to obtain treatments with greater efficacy and fewer side effects, thus increasing the survival and quality of life of the patients.

References

1. Fassnacht M, Berruti A, Baudin E, Demeure MJ, Gilbert J, et al. (2015) Linsitinib (OSI-906) versus placebo for patients with locally advanced or metastatic adrenocortical carcinoma : a double-blind , randomised , phase 3 study. Lancet Oncol 16(4): 1-10.
2. Terzolo M, Daffara F, Ardito A, Zaggia B, Basile V, et al. (2014) Management of adrenal cancer: A 2013 update. J Endocrinol Invest 37(3): 207-217.
3. Xu YZ, Zhu Y (2013) Conventional chemotherapy and emerging targeted therapy for advanced adrenocortical carcinoma. Anticancer Agents Med Chem 13(2): 248-253.
4. Else T, Kim AC, Sabolch A, Raymond VM, Kandathil A, et al. (2014) Adrenocortical carcinoma. Endocr Rev 35(2): 282-326.
5. Erickson L, Rivera M, Zhang J (2014) Adrenocortical carcinoma: review and update. Adv Anat Pathol 21(3): 151-159.
6. Griffin AC, Kelz R, LiVolsi VA (2014) Aldosterone-Secreting Adrenal Cortical Carcinoma. A Case Report and Review of the Literature. Endocr Pathol 25(3): 344-349.
7. Berruti A, Baudin E, Gelderblom H, Haak HR, Porpiglia F, et al. (2012) Adrenal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 23(suppl7): Vii131-138.
8. Fassnacht M, Terzolo M, Allolio B, Baudin E, Haak H, et al. (2012) Combination Chemotherapy in Advanced Adrenocortical Carcinoma. N Engl J Med 366(23): 2189-2197.
9. Fay AP, Elfiky A, Teló GH, McKay RR, Kaymakcalan M, et al. (2014) Adrenocortical carcinoma: The management of metastatic disease. Crit Rev Oncol Hematol 92(2): 123-132.
10. Fulawka L, Patrzalek D, Halon A (2014) Adrenal cortical carcinoma with extension into the inferior vena cava - case report and literature review. Diagn Pathol 9: 51.
11. Germano A, Rapa I, Volante M, Lo Buono N, Carturan S, et al. (2014) Cytotoxic activity of gemcitabine, alone or in combination with mitotane, in adrenocortical carcinoma cell lines. Mol Cell Endocrinol 382(1): 1-7.
12. Naing A, Lorusso P, Fu S, Hong D, Chen HX, et al. (2013) Insulin growth factor receptor (IGF-1R) antibody cixutumumab combined with the mTOR inhibitor temsirolimus in patients with metastatic adrenocortical carcinoma. Br J Cancer 108(4): 826-830.
13. Maluf DF, de Oliveira BH, Lalli E (2011) Therapy of adrenocortical cancer: present and future. Am J Cancer Res 1(2): 222-232.
14. Ronchi CL, Kroiss M, Sbiera S, Deutschbein T, Fassnacht M (2014) Current and evolving treatment options in adrenocortical carcinoma: Where do we stand and where do we want to go? Eur J Endocrinol 171(1): R1-R11.
15. Subramanian C, Zhang H, Gallagher R, Hammer G, Timmermann B, et al. (2014) Withanolides are potent novel targeted therapeutic agents against adrenocortical carcinomas. World J Surg 38(6): 1343-1352.
16. Ribeiro TC, Jorge AA, Almeida MQ, Mariani BMDP, Nishi MY, et al. (2014) Amplification of the Insulin-Like Growth Factor 1 Receptor Gene Is a Rare Event in Adrenocortical Adenocarcinomas: Searching for Potential Mechanisms of Overexpression. Biomed Res Int 2014: 936031.
17. Poli G, Ceni E, Armignacco R, Ercolino T, Baroni G, et al. () 2D-DIGE proteomic analysis identifies new potential therapeutic targets for adrenocortical carcinoma. Oncotarget 6(8): 5695-706.
18. Gordon BL, Finnerty BM, Aronova A, Fahey TJ (2015) Genomic medicine for cancer diagnosis. J Surg Oncol 111(1): 24-30.
19. Kerkhofs TMA, Derijks LJJ, Ettaieb H, Hartigh J Den, Neef K, et al. (2015) Development of a Pharmacokinetic Model of Mitotane : Toward Personalized Dosing in Adrenocortical Carcinoma. Ther Drug Monit 37(1): 58-65.
20. Kirschner LS (2015) Inhibition of IGF-1R in adrenocortical carcinoma. Lancet Oncol 16(4): 356-357.

Citation: Guércio CP, Neto JDC, Peixoto DB (2016) Possible Treatments in Metastatic Adrenocortical Carcinoma - Case Report. J Cancer Prev Curr Res 4(6): 00143. DOI: 10.15406/jcpcr.2016.04.00143