Clinical Oncology: Case Reports

Case Report

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Impressive Response to Immunotherapy in a Patient with Metastatic Adrenocortical Carcinoma

Lindsey Addington*, Hagman Thomas, Hawk, Nicole CMA and Pablo Bedano

Abstract

ACC incidence is 1 to 2 cases per million making randomized clinical trials difficult to conduct. The current standard first line treatment for metastatic ACC showing tumor response and improved progression free survival (PFS) is etoposide-doxorubicin-cisplatin (EDP) plus mitotane. Multiple efforts to find a targeted treatment for ACC have not shown impressive responses. Immunotherapy agents such as checkpoint inhibitors programmed cell death – 1 receptor (PD-1) and programmed cell death-ligand 1 have shown significant responses in multiple malignancies including melanoma, non-small-cell-lung cancer, Hodgkin's lymphoma to name a few. We present a case of a female patient with metastatic ACC involving the lungs, lymph nodes, and liver who progressed after EDP-mitotane, then had a significant decrease in tumor burden with anti-PD-1 agent pembrolizuamb.

Keywords

Metastatic adrenocortical carcinoma; Immunotherapy; Pembrolizumab

Introduction

ACC has a poor prognosis with limited effective treatment options especially in the metastatic setting where survival is 13% at five years [1,2]. The only approved first line treatment for stage IV ACC is EDP + mitotane; although response rates are dismal at 23% and median PFS of 5 months [3-5]. The rarity of ACC makes it difficult to conduct clinical trials to develop more effective treatments. We present a stage IV ACC patient with metastases to the lungs, lymph nodes and liver that had a dramatic response to anti-PD-1 agent, pembrolizumab.

Case Presentation

A 59 year old female presented with fatigue, hypertension, hyperglycemia, nausea, and vomiting. She underwent a left adrenalectomy of a 14 x 8.7 cm mass. Pathology was consistent with adrenocortical carcinoma. One of one lymph node was positive for metastatic disease and margins were positive.

She completed adjuvant radiotherapy and then initiated adjuvant mitotane. Four months after resection, she presented with a persistent cough, and shortness of breath requiring oxygen therapy. A CT of chest revealed increase size and number of pulmonary nodules with new mediastinal and bilateral hilar adenopathy, as well as, evidence of hepatic metastases (Figure 1).

From September to February of 2018, six cycles of EDP + mitotane were administered. Within the first month of treatment, a CT of chest, abdomen, and pelvis demonstrated evidence of interval increase of pulmonary nodules and hepatic metastases. She was referred to a local university for consideration of clinical trial but there were none available for her.

Immunotherapy with pembrolizumab was initiated in March, 2018. A CT scan of the chest, abdomen, and pelvis on week 10 revealed dramatic decrease in size of pulmonary nodules and

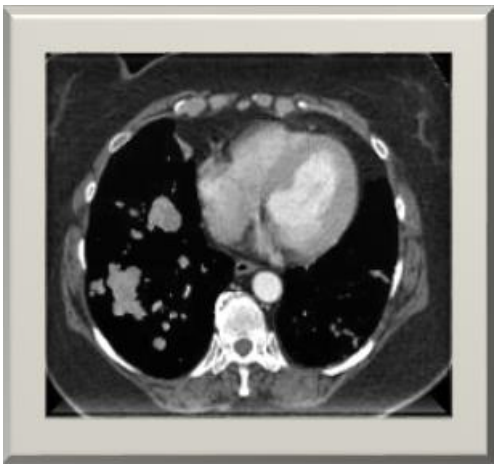

Figure 1a: CT of chest and abdomen with increased size of innumerable pulmonary nodules with largest nodule in right lower lobe measuring 4.0 cm x 2.7 cm. multiple hepatic masses ranging up to 1.9 cm in size.

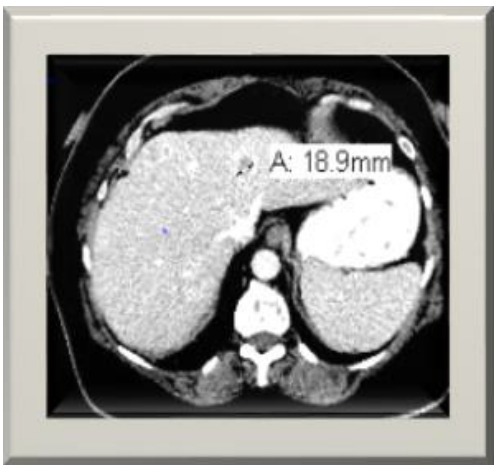

Figure 1b: CT of chest and abdomen with increased size of innumerable pulmonary nodules with largest nodule in right lower lobe measuring 4.0 cm x 2.7 cm. Multiple hepatic masses ranging up to 1.9 cm in size.

***Corresponding author:** Lindsey Addington, Community Hospital Cancer Center South 1440 East County Line Road Indianapolis, IN 46227, USA, Tel: 3175072666; E-mail: lindsmyoung79@gmail.com

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lymphadenopathy with dominant nodule decreasing from 4 x 2.7 cm to 1.6 x 1 cm. As well as interval improvement of hepatic metastases. Mitotane was discontinued in June, 2018 due to undesirable side effects of hypotension, hypercalcemia, memory loss and acute kidney injury (Figure 2).

The patient's clinical status improved and her persistent cough resolved. She no longer needed oxygen therapy and she was also able to enroll in an exercise program. A CT scan at week 18 showed continued improvement in pulmonary metastases with near resolution of several nodules. There was also decrease size and number of hepatic lesions. Pembrolizumab was tolerated well with only a grade I rash to arms (Figure 3).

Interestingly this patient's tumor was PD-L1 negative. Tumors that express PD-L1 are felt to have better response to therapies that target PD-L1 function by blocking PD-L1 from inhibiting T-cells that attack cancer cells. [6,7].

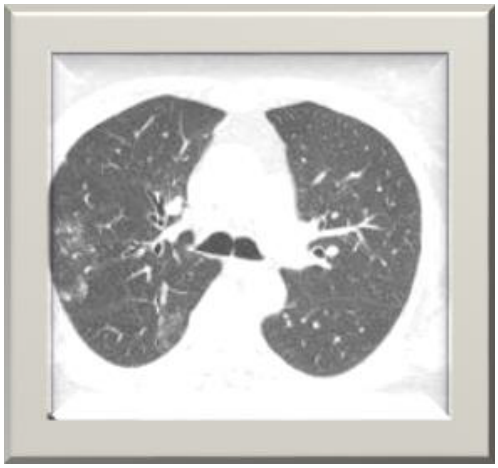

Figure 2a: CT of chest and abdomen showed interval improvement in pulmonary nodules with largest decreasing in size from 4 cm x 2.7 cm to 1.6 cm x 1 cm. Improvement in hepatic masses with left lobe mass decreasing from 19 mm to 15 mm.

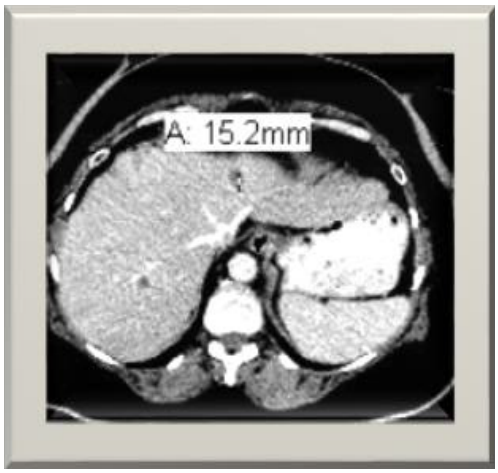

Figure 2b: CT of chest and abdomen showed interval improvement in pulmonary nodules with largest decreasing in size from 4 cm x 2.7 cm to 1.6 cm x 1 cm. Improvement in hepatic masses with left lobe mass decreasing from 19 mm to 15 mm.

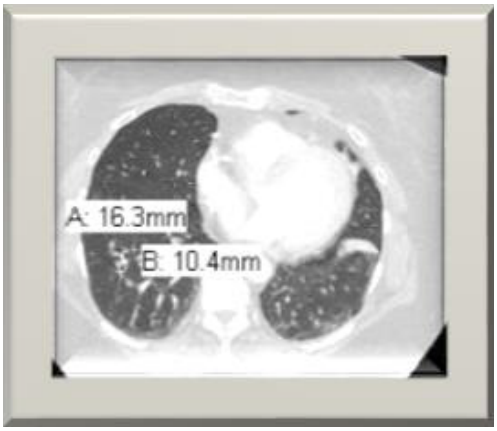

Figure 3a: CT of chest and abdomen with improvement in pulmonary nodules with several nodules in the right lower lobe nearly resolved. Improvement in size and number of liver masses with discrete nodule decreasing from 15 mm to 11 mm.

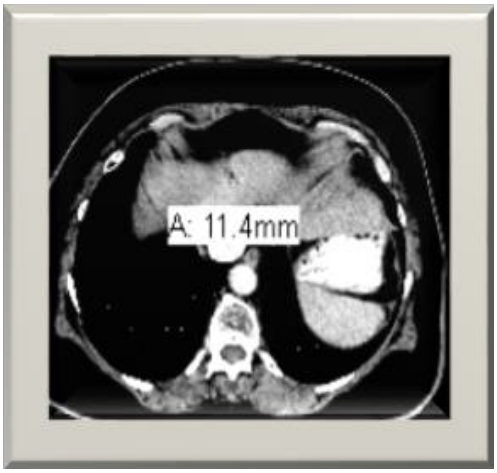

Figure 3b: CT of chest and abdomen with improvement in pulmonary nodules with several nodules in the right lower lobe nearly resolved. Improvement in size and number of liver masses with discrete nodule decreasing from 15 mm to 11 mm.

Discussion

Metastatic ACC has limited treatment options and poor prognosis. The FIRM-ACT trial was the largest, randomized clinical trial to establish standard treatment for advanced disease. The results of this study showed EDP + mitotane had a 23% objective tumor response, median PFS of 5 months but failed to improve overall survival [3]. This chemotherapy regimen has the potential of serious adverse effects including myelosuppression, infection, thrombosis, neuropathy and decline in overall health [4].

The advancement of genomic molecular testing has shown ACC is biologically and genetically a heterogeneous cancer. Multiple early phase clinical trials to target the signaling of these genes have not demonstrated a significant clinical response [8]. Studies using immunotherapy have been recently completed in the setting of metastatic ACC (NCT02720484, NCT 0267333). Immunotherapy with anti-PD-1, PD-L1, and CTLA-4 (pembrolizumab, nivolumab, ipiluzumab) have shown efficacy in multiple advance cancers

including melanoma, non-small-cell-lung cancer, and urothelial carcinoma [9-11]. New approvals and indications are occurring at a rapid rate. According to clinicaltrial.gov there are hundreds of open trials for immunotherapy and several that may affect how ACC is treated in the future [12]. Immunotherapy is in general well tolerated with majority of toxicities being grade 1 or 2 [13].

Conclusion

In summary, we present a case in which anti-PD-1 treatment with pembrolizumab made a dramatic impact on this patient's tumor burden and rapidly improved her clinical status as well as her quality of life. This shows that anti-PD-1 immunotherapy may be effective treatment in metastatic ACC despite no expression of PD-1.

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Author Affiliations Top

Community Hospital Cancer Center, 1440 East County Line Road Indianapolis, IN 46227, USA

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