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Ongoing response of metastatic thymic carcinoma after completion of two years of pembrolizumab immunotherapy: A case report

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Abstract

Purpose: Thymic epithelial tumors are rare malignancies of thymic epithelial cells, and approximately 500 new cases are diagnosed each year in the USA. Thymic carcinomas are the most aggressive subtype of thymic epithelial tumors and constitute just over 10% of thymic epithelial tumors. They are associated with a shorter overall survival than thymomas and are often non-resectable and tend to metastasize to many locations. The recommended treatment of localized disease is surgery, whenever possible, and radiation with or without chemotherapy. For unresectable and metastatic thymic carcinomas, the standard treatment is chemotherapy, although the proportion of patients who achieve a response is less than 50%. Immunotherapy with checkpoint inhibitors has been a new option for the treatment of several malignancies in the past few years. Thymic carcinomas have a high expression of PD-L1, which in other malignancies correlates with a better response to PD-1 and PD-L1 antibodies in several studies. Preliminary research also suggests checkpoint inhibitors can induce responses in this disease.

Patient Presentation: We present the case of a 65-year-old male who presented with a mediastinal mass found incidentally on a chest radiograph after a fall. The patient was asymptomatic and had no remarkable findings on exam. He was ultimately diagnosed with stage IV metastatic thymic carcinoma and treated with pembrolizumab immunotherapy. He is experiencing a partial response that has been ongoing for more than 2 years even after stopping therapy.

Conclusion: Our report further underscores the potential for a novel approach to treating thymic carcinomas with immunotherapy. There have been no previous case reports of patients with metastatic thymic carcinoma having long-term remissions with this therapy.

Keywords

Thymic carcinoma; immunotherapy; pembrolizumab.

Abbreviations

CT: Computerized tomography; IHC: Immunohistochemistry; FDG: Fluorodeoxyglucose; PET-CT: Positron emission tomography/computed tomography; MRI: Magnetic resonance imaging.

Introduction

Thymic epithelial tumors are rare malignancies of thymic epithelial cells, and approximately 500 new cases are diagnosed each year in the USA [1]. Thymic carcinomas are the most aggressive subtype of thymic epithelial tumors and constitute just over 10% of thymic epithelial tumors [2]. They are associated with a shorter overall survival than thymomas and are often non-resectable and tend to metastasize to many locations. The recommended treatment of localized disease is surgery, whenever possible, and radiation with or without chemotherapy. For unresectable and metastatic thymic carcinomas, the standard treatment is chemotherapy with cisplatin, doxorubicin, and cyclophosphamide, or carboplatin and paclitaxel, although the proportion of patients who achieve a response is less than 50% [3]. Immunotherapy with checkpoint inhibitors has been a new option for the treatment of several malignancies in the past few years [4]. Thymic carcinomas have a high expression of PD-L1, which in other malignancies correlates with a better response to PD-1 and PD-L1 antibodies in several studies [5,6]. Preliminary research also suggests checkpoint inhibitors can induce responses in this disease [7].

We present the case of a patient with metastatic thymic carcinoma treated with pembrolizumab, experiencing a partial response that has been ongoing for more than 2 years even after stopping therapy.

Case presentation

A 65-year-old male former smoker (4 pack-year history, quit 1997) with a history of renal cell carcinoma treated with nephrectomy in 2012, chronic renal dysfunction and alcohol abuse presented in February of 2017 with a mediastinal mass detected incidentally on a chest radiograph after a fall. The patient was initially asymptomatic and had no remarkable findings on exam. Computerized Tomography (CT) imaging showed a 7 x 5.4 cm soft tissue mass in the right paratracheal station partially occluding the superior vena cava. Contact with the trachea, right mainstem bronchus and aorta was also noted. A 2.8 x 3.6 cm mass was also found on the right adrenal gland. The biopsy of the mediastinal mass had limited tissue but revealed polygonal epithelioid cells arranged in sheets and cords in a background of predominantly small, mature polyclonal lymphocytes, plasma cells and fibrotic stroma. Immunohistochemistry (IHC) was positive for OSCAR among the epithelioid cells. Diagnosis was consistent with thymic neoplasm. Since cytologic atypia and increased mitotic activity were not unequivocally identified, and with the absence of CD5 staining among the epithelial cells, thymoma was favored.

Initially, the patient delayed consultation with oncology. A repeat CT in April of 2017 showed a 7.6

x 7.6 x 8.2 cm mass with superior vena cava invasion and possible invasion of the right brachiocephalic vein. The right adrenal mass had grown and was measured at 5.0 x 3.8 cm. 18F-fluorodeoxyglucose (FDG) Positron Emission Tomography/Computed Tomography (PET-CT) revealed uptake up to 20.5 SUV in the mediastinal mass and 14.26 SUV in the adrenal mass and did not reveal any additional metastatic disease (Figure 1). Magnetic Resonance Imaging (MRI) of the brain with contrast did not suggest any brain involvement.

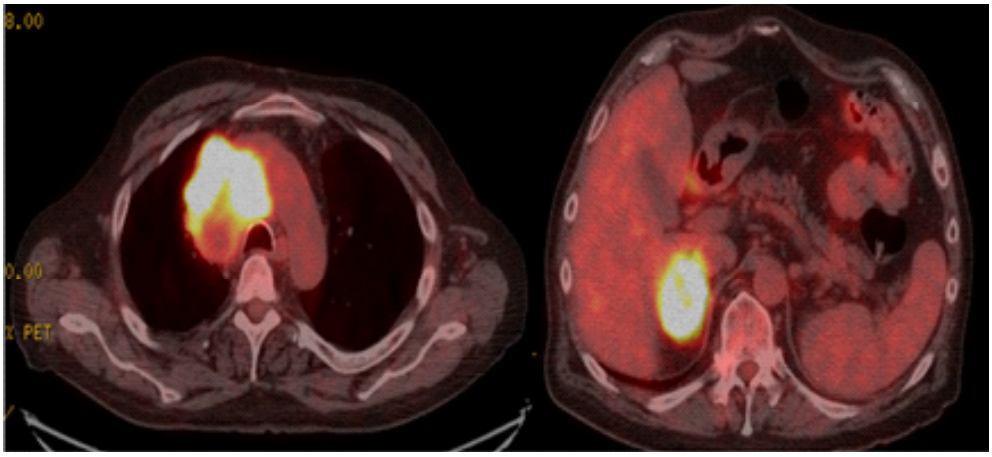

Figure 1: PET-CT imaging prior to initiating treatment with pembrolizumab.

In May of 2017, the adrenal gland biopsy was consistent with poorly differentiated non-small cell carcinoma with patchy labeling for CD10 and vimentin and with negative CK7, CK20, ERG, CD31, p40, PAX8, TTF1 and napsin-A. On further review, the histologic sections from both specimens demonstrated similar findings. PD-L1 IHC 22C3 staining revealed 95% expression. Based on clinical presentation and pathologic staining, stage IV thymic carcinoma was favored.

The patient began treatment with 3 cycles of carboplatin/paclitaxel. However, CT imaging after 3 cycles showed evidence of progression by increase in the size of the right adrenal mass and slight increase in the portion of the mediastinal mass extending into the superior vena cava. Other chemotherapy regimens were considered, and hospice was entertained at that point because of declining condition. Given that his cancer was refractory to chemotherapy and that there is no standard second-line option, pembrolizumab therapy was discussed and planned. Soon after administration of the first dose the patient developed worsening face swelling and was diagnosed with superior vena cava syndrome that was treated with 30Gy/10 fractions of radiation. However, his condition later improved and imaging after 3 months of therapy showed significant size decrease in the superior mediastinal mass and right adrenal mass. Repeat FDG-PET-CT a year after starting pembrolizumab showed a decrease in size of both masses with SUV uptake of 1.4 and 2.4 in mediastinal mass and adrenal mass, respectively. Repeat FDG-PET-CT after two years showed evidence of stable disease compared to a year prior with SUV uptake of 1.5 and 1.6 in mediastinal and adrenal mass, respectively (Figure 2).

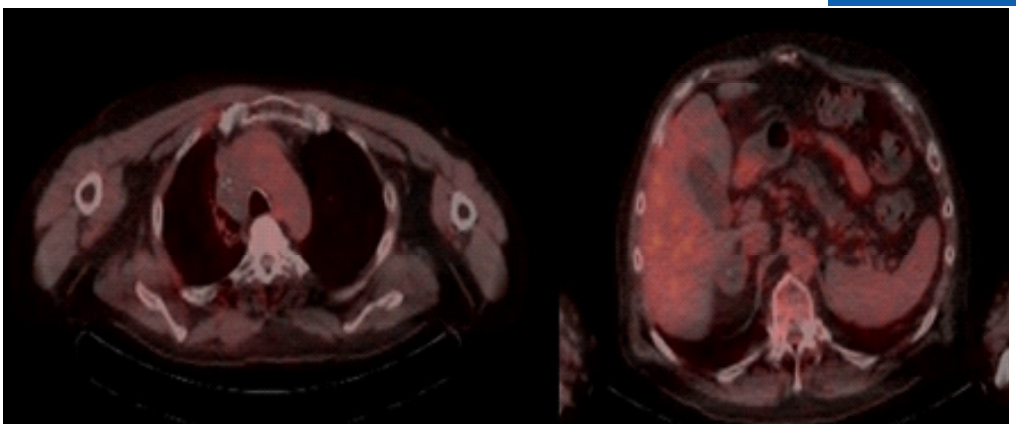

Figure 2: FDG-PET-CT imaging after 2 years of pembrolizumab immunotherapy.

After completing 2 years of pembrolizumab, the benefits and risks of continuing immunotherapy were discussed with the patient. Financial toxicity also became a relevant factor in the discussion. Surgical resection of adrenal gland and radiation therapy to the adrenal gland were also entertained. After considering all these options the patient opted for surveillance without additional therapy and received his last dose of pembrolizumab on 06/21/2019. He has ongoing follow up in our clinic for surveillance, and his last clinic visit and FDG-PET-CT on 06/17/2020 did not reveal any evidence of progression with mediastinal and adrenal SUV uptake below mediastinum (Figure 3). The patient was seen again in clinic on 10/29/2020 and continues to feel well.

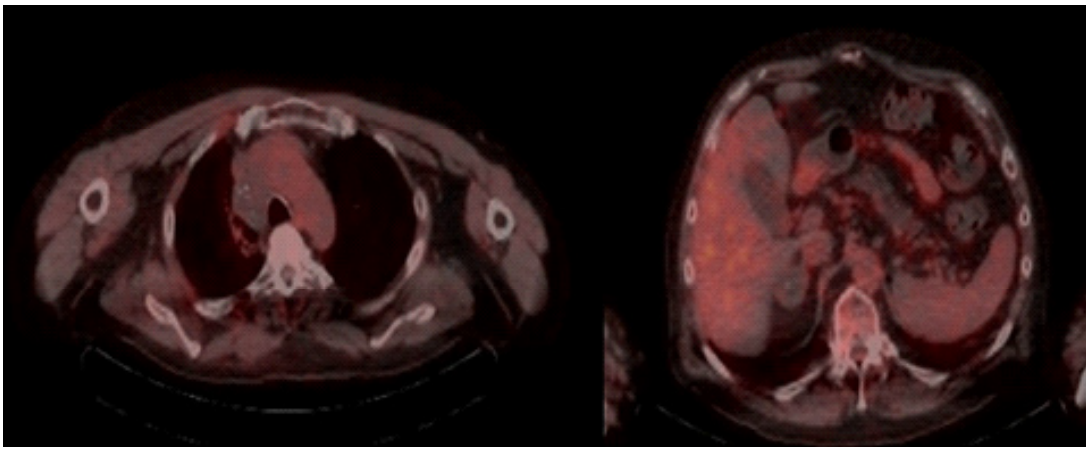

Figure 3: FDG-PET-CT imaging 1 year after treatment cessation.

Discussion

Our case is a presentation of metastatic thymic carcinoma with partial response to immunotherapy with ongoing remission after completing 2 years of pembrolizumab immunotherapy and discontinuing therapy for one year. Thymic carcinomas have a high expression of PD-L1, which in other malignancies correlates with a better response to PD-1 and PD-L1 antibodies in several studies. Preliminary research also suggests checkpoint inhibitors can induce responses in this disease. In a single-arm phase 2 study of pembrolizumab in 40 patients with recurrent thymic carcinoma who had progressed after at least one line of chemotherapy, it was found that one patient achieved a complete response, eight patients achieved partial responses, and 21 patients achieved stable disease [7]. Our report further underscores the potential for a novel approach to treating thymic carcinomas with immunotherapy. There have been no previous

case reports of patients with metastatic thymic carcinoma having long-term remissions with this therapy. One limitation associated with this case report is that our patient has been followed for just one year after treatment cessation. We will continue to follow this patient and hope for continued remission. Our report provides evidence to suggest that it would be feasible to attain long term remission of this disease even after treatment cessation.

Declarations

Consent for publication

The authors have obtained consent to publish from the participant to report individual patient data.

Authors' contributions

JH saw and treated the patient. SS and JH reviewed the patient's medical history and treatment course. SS and JH equally contributed to the writing of the case report. All others read and approved the final manuscript.

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