Oncology Case Reports Journal

Case Report
Published: 08 Aug, 2022

Hepatoidthymic Carcinoma: A Case Report of Response to Immune Checkpoint Inhibitor

Bindiya G Patel, Samantha Conlin, Syed Usman M Ehsanullah and Siddhartha Devarakonda*

Department of Hematology-Oncology, Washington University School of Medicine, USA

Abstract

Hepatoid Thymic Carcinoma (HTC) is a very rare subtype of thymic carcinoma with aggressive clinical course. HTC demonstrates polygonal tumor cells appearing like hepatocytes and expresses Hep-Par-1. In this case report, we describe a patient with HTC who responded to treatment with immune checkpoint inhibitor pembrolizumab after failing treatment with chemoradiation and targeted therapy with lenvatinib, a multiple kinase inhibitor. Next generation sequencing of the patient's tumor tissue demonstrated a mutation in *SMARCA4*. Review of relevant literature suggests that *SMARCA4* alteration maybe associated with higher likelihood of immune checkpoint inhibitor response.

Introduction

A 63-year-old African American man presented with progressive hoarseness and was eventually found to have left vocal cord paralysis. Imaging showed a large mediastinal mass encircling the left upper lobe pulmonary vein with involvement of the phrenic nerve leading to left hemi-diaphragmatic paralysis (Figure 1A). A biopsy of the mediastinal mass showed tumor cells that were positive for CK7, pankeratin, CD10, and Hepatocyte Paraffin 1 (HepPar1) by immunohistochemistry. The tumor cells were negative for PSA, NK, TTF-1, and CD117, Alpha Fetoprotein (AFP), CK20, CD5, OCT3/4, CD30, PLAP, RCC, PAX8, D240, S100 and NKX 3.1. These features suggested a diagnosis of thymic carcinoma with hepatoid differentiation (HTC). Based on radiographic imaging features, the cancer was staged cT3N0M0 (stage IIIA) and treatment with concurrent chemoradiation with carboplatin and paclitaxel was pursued as surgical resection was not felt to be feasible. Unfortunately, despite excellent initial response, progression of disease was noted in the left adrenal gland and C5 vertebral body (Figure 1B). Radiation to the metastatic sites was pursued. However, within a month of completing radiation, imaging revealed progressive disease involving the lungs and kidneys. Next generation sequencing performed on tissue collected at first progression failed to reveal readily targetable alterations, and showed somatic mutations in TP53 p.P128fs (Variant Allele Frequency (VAF) 27.2%), *MAX* p.R60L (VAF 17.7%), and *SMARCA4* p.E1603fs (VAF 15.7%). Tumor mutational burden was 18.4 m/MB. After discussing chemotherapy and treatment with lenvatinib, based on data from the REMORA study, a collective decision was made to start treatment with lenvatinib [1]. Imaging studies performed to investigate worsening right arm pain and numbness within five weeks of initiating treatment showed progressive worsening of disease involving the C4-C6 vertebral bodies with epidural extension of the previously irradiated tumor at this location, which prompted urgent surgical intervention. With limited treatment options and rapidly progressive disease that failed to respond to several treatment modalities, treatment with pembrolizumab 200 mg every 3 weeks was eventually initiated. Post-treatment scans showed a favorable treatment response (Figure 1C1-2C2). Treatment was well tolerated. To date, 16 cycles of pembrolizumab have been administered with durable disease control.

Discussion

Thymic carcinomas are aggressive and extremely rare tumors that account for 5% of all thymic neoplasms [2]. Thymic carcinoma cells exhibit cytologic atypia and histologic features not specific to the thymus [2]. HTC is a rare subtype of thymic carcinoma, and only a few cases of HTC have been reported to date in the literature [3-5]. In these reports, HTC cells have been described as mimicking hepatoid adenocarcinoma cells morphologically and expressing Hep-Par-1 but staining negative for AFP4. Microscopically, HTC demonstrates polygonal tumor cells forming solid sheets and trabecula appearing like hepatocytes [3,4]. As observed in our patient, HTCs have been described as aggressive. Most patients with HTC present with an anterior mediastinal mass and lymph nodes,

OPEN ACCESS

Correspondence:
Bindiya G Patel, Department of Hematology-Oncology, Washington University School of Medicine, 660 S, Euclid Avenue, Saint Louis, MO, 63110, USA, Tel: 314-305-2272; E-mail: b.g.patel@wustl.edu

Received Date: *15 Jul 2022*
Accepted Date: *03 Aug 2022*
Published Date: *08 Aug 2022*

Citation:
Patel BG, Conlin S, Ehsanullah SUM, Devarakonda S. Hepatoidthymic Carcinoma: A Case Report of Response to Immune Checkpoint Inhibitor. Oncol Case Report J. 2022; 5(1): 1044.

ISSN: 2641-9173

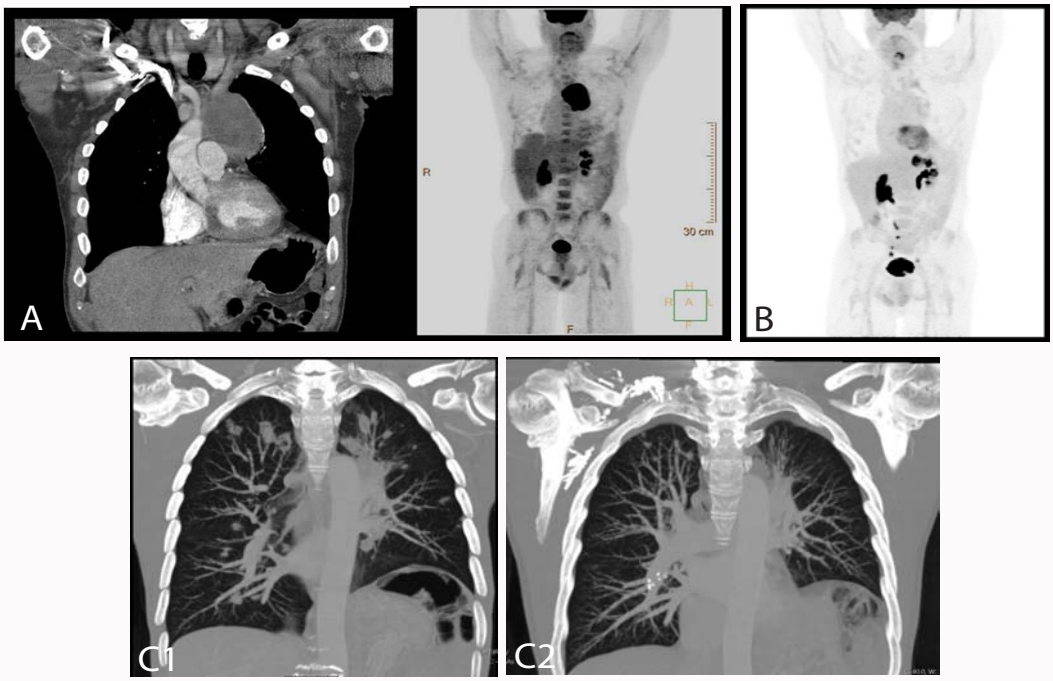

Figure 1: CT and PET images of SW. A: Mediastinal mass at diagnosis. B: Progression to adrenal gland after chemoradiation. C1: Representative lung metastatic lesions prior to starting pembrolizumab. C2: Representative lung metastatic lesions on most recent imaging on pembrolizumab therapy.

thyroid, gastrointestinal tract, lung, and genitourinary tract have been described as metastatic sites. Thorough immunochemical staining is often necessary to exclude cancers of lung, prostate, hepatic, renal, mesothelial and germ cell origin. The optimal treatment approach for HTCs is unclear given the extreme rarity of HTC and lack of clinical data. Since thymic carcinomas are radiosensitive [6], neoadjuvant or adjuvant radiation can be considered with surgery [3-5]. Responses to cisplatin-containing chemotherapy regimens have been described [3].

PD-L1 is highly expressed in thymic epithelial tumors [7]. Durable responses have been seen in patients with previously treated advanced thymic carcinomas with pembrolizumab, with a response rate of 22.5%, and mediation duration of response of 2.99 years [8]. Given the rarity of HTCs, there is no data on the efficacy and safety of treatment of these tumors with Immune Checkpoint Inhibitors (ICIs). Notably, NGS of tumor tissue in our patient demonstrated a mutation in *SMARCA4* (or BRG1). *SMARCA4* is a tumor suppressor gene that encodes the catalytic subunit of the chromatin remodeling switch sucrose non-fermentable SWI/SNF complex. Although presence of *SMARCA4* alteration has been observed to have negative prognostic impact, better ICI response has been seen compared to *SMARCA4* wild-type tumors [9]. Pan-cancer analysis of *SMARCA4* alterations across various tumors showed positive correlation with expression of immune checkpoint genes suggesting a higher likelihood of ICI response in *SMARCA4* altered malignancies [10]. *SMARCA4* has been found to be recurrently mutated (~4%) in thymic epithelial tumors [10]. Here we describe, to the best of our knowledge, the first case report of successful treatment of a *SMARCA4* mutated HTC with ICI. The importance of reporting clinical outcomes in patients with such rare malignancies cannot be emphasized enough given the sparse available literature.

References

1. Sato J, Satouchi M, Itoh S, Okuma Y, Niho S, Mizugaki H, et al. Lenvatinib in patients with advanced or metastatic thymic carcinoma (REMORA): A multicentre, phase 2 trial. Lancet Oncol. 2020;21(6):843-50.
2. Rosai J, Sobin LH. Histological typing of tumors of the thymus: Springer Berlin Heidelberg; 1999.
3. Franke A, Ströbel P, Fackeldey V, Schäfer R, Göller T, Becker HP, et al. Hepatoid thymic carcinoma: Report of a case. Am J Surg Pathol. 2004;28(2):250-6.
4. Jeong JS, Kang HJ, Jo U, Song MJ, Nam SY, Song JS. Hepatoid thymic carcinoma: A case report of a rare subtype of thymic carcinoma. J Pathol Transl Med. 2021;55(3):230-4.
5. Lee JH, Kim H, Chae YS, Won NH, Choi JS, Kim CH. Hepatoid thymic carcinoma: A case report. Korean J Pathol. 2009;43(6):562-5.
6. Surmei-Pintilie E, Narducci F, Farre I, Kolesnikov-Gauthier H, Boulanger T, Petit S, et al. Asymptomatic pelvic metastasis from thymic carcinoma: A case report. Case Rep Oncol. 2014;7(2):422-5.
7. Owen D, Chu B, Lehman AM, Annamalai L, Yearley JH, Shilo K, et al. Expression patterns, prognostic value, and intratumoral heterogeneity of PD-L1 and PD-1 in thymoma and thymic carcinoma. J Thorac Oncol. 2018;13(8):1204-12.
8. Giaccone G, Kim C. Durable response in patients with thymic carcinoma treated with pembrolizumab after prolonged follow-up. J Thorac Oncol. 2021;16(3):483-5.
9. Schoenfeld AJ, Bandlamudi C, Lavery JA, Montecalvo J, Namakydoust A, Rizvi H, et al. The genomic landscape of *SMARCA4* alterations and associations with outcomes in patients with lung cancer. Clin Cancer Res. 2020;26(21):5701-8.
10. Peng L, Li J, Wu J, Xu B, Wang Z, Giamas G, et al. A pan-cancer analysis of *SMARCA4* alterations in human cancers. Front Immunol. 2021;12:762598.