Oncology Case Reports Journal

Case Report
Published: 15 Nov, 2022

Targeting the Oncogenic Driver BRAF V600E Mutation in Metastatic Symptomatic Multiagent Refractory Papillary Thyroid Cancer Done Successfully Using Dabrafenib and Trametinib: Case Report and Literature Review

Morrison DG*, Castellon C, Cuadras A, Ortega A and Lopez J

Department of Hematology and Oncology, The Oncology Institute of Hope and Innovation, USA

Abstract

Radioactive iodine refractory metastatic papillary thyroid cancer is usually managed with lenvima. Other small molecule inhibitors are used when it fails. Many papillary thyroid cancers have BRAF V600 mutations. We report the successful use of dabrafenib and trametinib after multiple agents have failed. A unique tumor flare response was observed.

Keywords: BRAF V600; Thyroid Cancer; Drug

Introduction

A 65-year-old lady diagnosed in 2008 with papillary thyroid cancer by thin needle biopsy. She did not have a family history suggesting her thyroid cancer was anything but a sporadic event. Total thyroidectomy completed without complications. TSH maximally suppressed with levothyroxine replacement therapy from this time onward. Recurrent disease noted at base of left neck, and this was managed with surgical resection (November 16th, 2013) and then RAI times three as well as external beam radiation treatment. Treatments were associated with mild lymphedema of upper left neck, dense radiation fibrosis, left shoulder pain with reduced mobility and left cranial nerve XI palsy. Pulmonary metastases, multiple level II and III left neck nodes and left palatine tonsil involvement noted 5/2016. She received Lenvatinib as a single agent. She did require dose reductions due to adverse event of difficult to control hypertension. Her disease was well controlled without tumor related symptoms and near complete remission until July 19th, 2021. She then received sorafenib starting November 29th, 2021. After 8 weeks no symptomatic or objective response was observed. At that time, she experienced left neck pain at the site of her visible and readily palpable recurrence on her left neck, 3.5 cm rock hard, tender and immobile mass, and severe left facial edema causing her difficulty swallowing, speaking and the inability to open her left eye.

Methods & Case Presentation

In view of rapid failure of sorafenib and presence of a targetable lesion, BRAF V600E, dabrafenib and trametinib were obtained from the drug manufacturer on a compassionate basis. These agents are not yet approved for this indication by Medicare. In less than 2 weeks from starting this drug combination the tender, hard, immobile enlarged nodes at the base her left neck resolved as did her facial edema. Subcutaneous hemorrhage was observed at the prior site of malignant adenopathy at the base of her left neck (Figure 1). While her response is ongoing it is only partial (complete by physical exam (Figure 2) but radiographic studies only indicate partial response) but all her symptoms have resolved. She experienced grade 2 pyrexia managed by forcing ice cold nonalcoholic fluids and oral antipyretics, acetaminophen and ibuprofen.

Results and Discussion

BRAF V600E mutations can be targeted with the drug combination used for this patient. Successful treatment of cancers bearing these mutations such as hairy cell leukemia, Merkel cell carcinoma, non-small cell lung cancer, anaplastic thyroid cancer and melanoma have been reported elsewhere (reviewed in depth in current NCCN guidelines for these cancer types) [1]. Literature search for the use of these 2 drugs in papillary thyroid cancer revealed no data regardless of the starting point of the search (e.g., thyroid cancer, papillary thyroid cancer, BRAF V600E, dabrafenib

OPEN ACCESS

Correspondence:
David G Morrison, Department of Hematology and Oncology, The Oncology Institute of Hope and Innovation, 11480 Brookshire Street, Suite 309, Downey, CA 90241, USA, Tel: 504-655-3390; E-mail: davidmorrison@theoncologyinstitute.com

Received Date: *26 Oct 2022*
Accepted Date: *11 Nov 2022*
Published Date: *15 Nov 2022*

Citation:
Morrison DG, Castellon C, Cuadras A, Ortega A, Lopez J. Targeting the Oncogenic Driver BRAF V600E Mutation in Metastatic Symptomatic Multiagent Refractory Papillary Thyroid Cancer Done Successfully Using Dabrafenib and Trametinib: Case Report and Literature Review. Oncol Case Report J. 2022; 5(2): 1048.

ISSN: 2641-9173

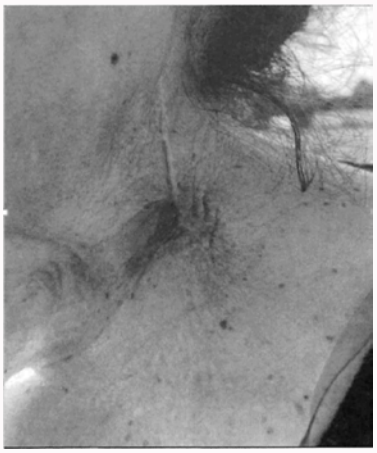

Figure 1: Malignant adenopathy at the base of her left neck.

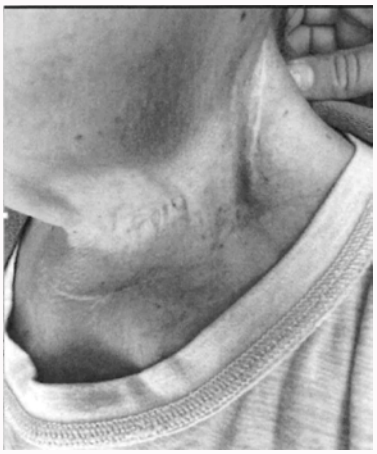

Figure 2: Complete by physical exam.

or trametinib etc.). Requests from the drug maker for any data on this application of these agents in thyroid cancer revealed little published data to support or refute their use [1]. Over the years this patient's insurance coverage changed multiple times requiring her to see new providers. Her medical oncologist prior to our seeing her ordered a Solid Tumor Core Profile. BRAF V600E testing is part of this profile. Her archived tumor specimen harbored this mutation. Papillary thyroid cancers very frequently harbor this mutation [2]. This observation again high lights the ongoing role for oncogenic driver testing and the role of agents that target these mutations even in patients with malignancies with these targets not previously reported to be sensitive to these novel agents. Screening for targets for agents such as these and the use of targeted agents in papillary thyroid cancer refractory to multiple tyrosine kinase inhibitors is endorsed by current NCCN guidelines [3,4]. However, the lack of published data on the use of dabrafenib and trametinib in metastatic papillary thyroid cancer bearing the BRAF V600E mutation is part of the reason for this case report. Hemorrhage at the site of the tumor occurred early after starting treatment. Hemorrhage has also been seen with other small molecular inhibitors. This patient's response was quite vivid (Figure 1).

Conclusion

Oncogenic driver mutations should be screened for upon RAI resistance being confirmed. Dabrafenib and trametinib are an effective palliative treatment for BRAF V600 mutation papillary thyroid cancer. The hemorrhagic response after starting this combo is best viewed as a tumor flare response.

Acknowledgement

Special thanks to Rachael Salazar and Edith I barra for coordinating completion of this manuscript.

References

1. White PS, Anita P, Lee SL, Eaton O. Intermittent dosing of dabrafenib and trametineb in metastatic BRAF^{V600E} mutated papillary thyroid cancer: Two case reports. Thyroid. 2017;27(9):1201-5.
2. Wang JR, Zafereo ME, Dadu R, Ferrarotto R, Busaidy NL, Lu C, et al. Complete surgical resection following neoadjuvant dabrafenib plus trametinib in BRAF^{V600E}–mutated anaplastic thyroid cancer. Thyroid. 2019;29(8):1036-43.
3. My Cancer Genome. Content Alteration. braf-v600e.
4. Haddad RI, Bischoff L, Ball D, Bernet V, Blomain E, Busaidy NL, et al. Thyroid carcinoma, Version 2.2022. J Natl Compr Canc Netw. 2022;20(8):925-51.