



Neoadjuvant and Adjuvant Approach Treatment of B-RAF Positive Limited Metastatic Melanoma

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Abstract

In the present case study, we describe a 44 year old male with BRAF-V600 mutated metastatic melanoma treated with neoadjuvant targeted therapy, resection of all sites of disease and adjuvant immunotherapy. He received combination dabrafenib and trametinib therapy as neoadjuvant treatment for stage IV metastatic melanoma. He suffered from multiple pyrexia events during neoadjuvant therapy and also again when adjuvant targeted therapy was begun. Because of this complication the adjuvant treatment was changed to nivolumab. During treatment a total body CT scan was performed and showed a complete clinical response that was ultimately achieved, till now (10/2020) the patient remains in remission. We present, to the best of our knowledge, the first reported case of a patient with metastatic melanoma treated as neoadjuvant with targeted therapy, followed by surgery and treated as adjuvant with immunotherapy in which the patient gain a clinical complete response after a complete resection of the tumour.

Keywords: Melanoma; Dabrafenib; Trametinib; Nivolumab; BRAF-V600; Mutations

Introduction

The BRAF gene encodes a RAS-regulated kinase that regulates the transduction kinase pathway responsible for cell growth and malignant transformation. A mutated version of this regulatory gene, BRAF-V600, plays an important part in the pathogenesis of human cancers. There are activating BRAF mutations in over 60% of melanomas as well as some other cancers [1]. For patients with advanced melanoma harboring the BRAF V600 mutation, BRAF/MEK inhibitors (BRAFINIB/MEKINIB) have proven to be successful targeted therapies [2-4]. Immune checkpoint inhibitors (ICI) are also FDA-approved for these patients and some studies have found immunotherapy to achieve better survival rates than BRAF/MEK therapy [5]. Additionally, immunotherapy has been noted to have lower rates of resistance than their biological therapy counterparts [6].

Case Story

A 42-year old, male, was referred for a biopsy of a mass in the right axillary area in October 2018 by a primary care physician. He had no history of disease and chronic medications. There was no family history of cancer.

He complained of a right axillary lump with pain that had persisted over the last two months and which didn't improved with antibiotics. He was admitted to the hospital for further evaluation, and had an excisional biopsy of the lump, with histopathologic findings of metastatic malignant melanoma. Molecular testing showed BRAF V600E -mutated.

Positron emission tomography– computed tomography (PET-CT) was performed in November 2018 and showed hyper-metabolic uptake of right axillary lymph nodes (with 14 mm as the largest diameter and a pulmonary nodule (diameter of 4 mm) in the right upper lobe (RUL) of the lung. The presumptive clinical diagnosis was malignant melanoma TX N1b M1b, stage IV (Figures 1 and 2).

A multidisciplinary conference including an oncologist, surgeons, and radiologist came to the conclusion that the patient should start

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SUNTEXT REVIEWS

with combination of BRAF and MEK inhibitors as neoadjuvant target therapy. TAFINLAR® (dabrafenib) 150mg twice daily and MEKINIST® (trametinib) 2mg once daily were administered for 8 weeks during the treatment period the patient suffered alternately from pyrexia events.



Figure 1: Shows the hyper-metabolic uptake of the pulmonary nodule in the right upper lobe (RUL) of the lung (red circle) (PET-CT selections from November 2018).



Figure 2: Shows the hyper-metabolic uptake of right axillary lymph nodes (red circle) (PET-CT selections from November 2018).

In January 2019 the patient underwent a PET-CT scan showing a good radiological response, with subsequently right axillary lymph node dissection and wedge resection of RUL of the lung were performed.



Figure 3: Shows a good radiological response to the treatment, before the wedge resection of RUL of the lung was performed (red circle) (PET-CT selections from January 2019).

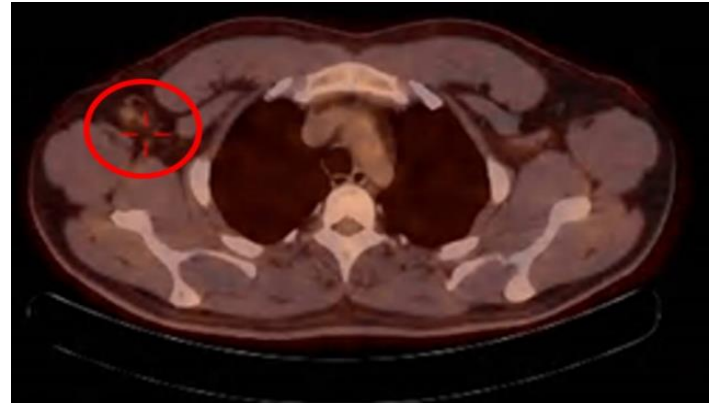


Figure 4: Shows a good radiological response before the subsequently right axillary lymph node dissection (red circle) (PET-CT selections from January 2019).

Pathological specimens revealed metastatic melanoma in one of the 12 resected lymph nodes with negative margins and microscopic residual metastatic melanoma (Figures 3 and 4).

The combination targeted therapy was restarted as adjuvant, but after 2 weeks of treatment the patient was admitted to the in-patient oncology department because of persistent fever (39c) of 3 days duration. He had a total body CT scan which showed a pulmonary nodule and no apparent aetiology of the pyrexia. The treatment was changed to OPDIVO® (nivolumab) 3mg/kg every two weeks. While on the adjuvant immunotherapy, the patient developed acute pancreatitis and grade III colitis. Treatment had to be interrupted several times and oral prednisone administered (2mg/kg). In August, 2019 after 12 cycles of immunotherapy the patient underwent total body CT scan which showed no evidence of disease. He remains in remission till the moment (October 2020) (Figure 5).

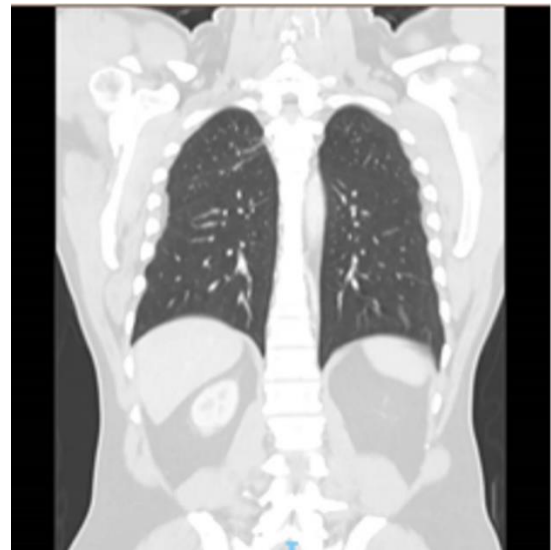


Figure 5: Shows the patient's remission till the moment (CT selections (chest part) from October 2020).

Discussion and Conclusion

We have described a patient who had a metastatic melanoma stage IV, which was treated in an unusual fashion, with both targeted therapy (neoadjuvant) and immunotherapy (adjuvant). We showed that a patient with BRAF 600 mutated melanoma need not be subjected to severe side effects from anti BRAF/MEK therapy, since the immunotherapy option for treatment can also be effective. Especially due a development and improvement role in the new era of treatments such as targeted and immunotherapy therapy for treating melanoma. Treatment by neoadjuvant targeted therapy need not be followed by the same type of adjuvant therapy and can be changed to immunotherapy with favourable results.

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Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

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References

1. Marcia SB, Volpe P, Feldman M, Kumar M, Rishi I, Gerrero R, et al. BRAF and RAS mutations in human lung cancer and melanoma. *Cancer Res.* 2002; 62.
2. Chapman PB, Hauschild A, Robert C, Haanen JB, Ascierto P, Larkin J, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. *N Engl J Med.* 2011; 364: 2507-2516.
3. Larkin J, Ascierto PA, Dreno B. Combined vemurafenib and cobimetinib in BRAF-mutated melanoma. *N Engl J Med.* 2014; 371: 1867-1876.
4. Dummer R, Ascierto PA, Gogas HJ, Arance A, Madala M, Liskay G, et al. Encorafenib plus binimetinib versus vemurafenib or encorafenib in patients with BRAF-mutant melanoma (COLUMBUS): a multicentre, open-label, randomised phase 3 trial. *Lancet Oncol.* 2018; 19: 603-615.
5. Moser JC, Chen D, Hu-Lieskovan S, Patel S, Colonna SV, Ying J, et al. Real-world survival of patients with advanced BRAF V600 mutated melanoma treated with front-line BRAF/MEK inhibitors, anti-PD-1 antibodies. *Cancer Med.* 2019; 8: 7637-7643.
6. Sharma P, Hu-Lieskovan S, Wargo JA, Ribas A. Primary, adaptive, and acquired resistance to cancer immunotherapy. *Cell.* 2017; 168: 707-723.