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Case Report
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A Patient with BRAF^{V600E} - Mutant Lung Adenocarcinoma Responding to Dabrafenib and Trametinib

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Abstract

BRAF is a gene that encodes a protein belonging to the RAF family of protein kinases. This protein transduces signals via the mitogen-activated protein kinase pathway to the nucleus of receptive cells. We report another case of BRAF^{V600E}-mutant lung adenocarcinoma responding to dabrafenib and trametinib treatment.

Introduction

BRAF is a gene that encodes a protein belonging to the RAF family of protein kinases. This protein transduces signals via the Mitogen-Activated Protein Kinase (MAPK) pathway to the nucleus of receptive cells. Mutations in this gene lead to constitutive kinase activity, favoring cancer cell proliferation and survival [1].

BRAF activating mutations are amongst the most frequent cancer-causing mutations in melanoma and have also been identified as oncogenic drivers contributing to the pathogenesis of lung cancer. They are rare, but nevertheless present in about 2% to 4% of non-small cell lung cancer, with about 50% of these being the V600E mutation (point mutation leading to the substitution of thymine with adenine resulting in a change in the amino acid on position 600 from valine to glutamate) [2,3].

Until recently, treatment options for patients with BRAF mutations were limited, with lower response rates to platinum-based chemotherapy and poor outcomes. Nowadays, multiple BRAF inhibitors are available, with a specific affinity for the V600E mutation and thus better responses than non-V600E mutations [1-4]. A recent phase 2 trial [2] tested the combination of dabrafenib and trametinib in patients with untreated BRAF^{V600E} mutant metastatic Non-Small-Cell Lung Carcinoma (NSCLC) which proved to have clinically meaningful antitumor activity. As data in this subject is emerging, we here report another case of BRAF^{V600E}-mutant lung adenocarcinoma responding to dabrafenib and trametinib treatment.

Case Presentation

A 69-year-old man was admitted to the hospital with a history of dyspnea and right pleural effusion. He was a former smoker with ischemic cardiomyopathy and type 2 diabetes and was treated by allopurinol, glucophage, irbesartan, asaflow, bisoprolol and atorvastatine. As the

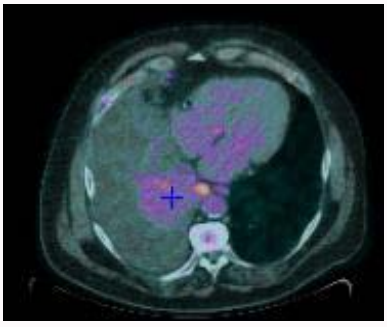

Figure 1A: PET-CT (07/11/2018): Intensely hyper metabolic right posterior and paramedian thoracic lesion, infrahilar, accompanied by an intensely sub carinal hyper metabolic adenopathy. Large right pleural effusion, not hyper metabolic.

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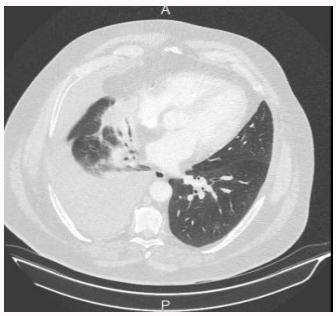

Figure 1B: First pulmonary Computed Tomography (CT) scan of (10/2018).

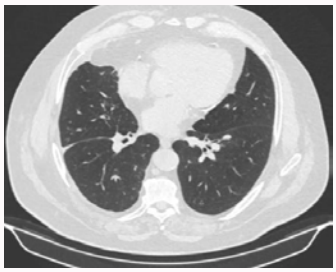

Figure 1C: Tumor regression after 6 months of treatment (05/2019).

echocardiography was reassuring and computed tomography scan did not show any abnormal mass, drainage of pleural effusion was performed. The cytology being inflammatory, a pleuroscopy was done showing an aspect of pleural carcinomatos is and was followed by talc pleurodesis. The Positron Emission Tomography-Computed Tomography (PET-CT) confirmed a right para-hilar mass with hilar and homo lateral mediastinal lymph nodes (staging cT1bN2M1a, Figure 1A and 1B). Laboratory investigations from the pleuroscopy confirmed pleural carcinomatos is of lung adenocarcinoma with 35% PD-L1 (or programmed death-ligand 1) expression, and direct sequencing showed the presence of $BRAF^{V600E}$ mutation.

The patient entered a Medical Need Program and benefited of a first line therapy by Trametinib (Mekinist®) 150 mg twice a day and Dabrafenib (Tafinlar®) 2 mg once a day. Only 6 months after therapy started, the tumoral mass and pleural effusion almost completely disappeared (Figure 1C). The patient maintained a good quality of life and did not suffer any inconvenient adverse effects. One year after treatment initiation, the oncologic response is still maintained.

Conclusion

Although $BRAF^{V600E}$ mutations are rare in NSCLC and the prognostic implications remain unclear, the significant antitumor activity resulting from dabrafenib and trametinib therapy is enough to encourage the testing of this mutation in all NSCLC to help therapeutic decision.

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