



Induction of stable disease with combination of immunotherapy plus chemotherapy in metastatic Non-Small Cell Lung Cancer: A Case Report

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General Note

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ABSTRACT

Programmed death ligand 1 (PD-L1) is part of an inhibitory checkpoint that helps protect against autoimmunity by acting as negative regulators of activated T cells. We reported a metastatic non-small cell lung cancer (NSCLC) case to received monoclonal immunotherapy with nivolumab plus chemotherapy with a stable disease for more than six months. A 46-year-old female with bone metastatic adenocarcinoma of the lung, a history of chronic cough and hemoptysis referred to the Clinic. The computed *tomography* (CT) scan showed an increased irregular pleural thickness in mediastinal and parietal pleura and liver metastasis. She received erlotinib as the first line treatment and switched to paclitaxel/carboplatin plus bevacizumab and then maintenance therapy. The CT scan showed us better result after nivolumab plus pemetrexed therapy for eight cycles rather than before the policy of treatment. In conclusion, nivolumab-pemetrexed *combination* therapy can improve survival and reduced progression in metastatic NSCLC patients. But considering to epidermal growth factor receptor mutation and the PD-L1 percentage can be very important in a selected protocol of treatment and improvement of survival of the patient.

Keywords: non-small cell lung cancer, metastasis, PDL-1, nivolumab

Abbreviation:

PD-L1: programmed death ligand 1

NSCLC: non-small cell lung cancer

CT: computed tomography

PD-1: programmed death 1

EGFR: epidermal growth factor receptor gene

TKI: tyrosine kinase inhibitors

ALK: anaplastic lymphoma kinase

TTF-1: thyroid transcription factor-1

1. INTRODUCTION

Lung cancer is the most common cause of cancer death worldwide with an annual mortality rate of more than 1.3 million worldwide [1]. Lung cancer is divided into two main histological types; where non-small cell lung cancer (NSCLC) comprises around 85% of the cases and small-cell lung cancer, the remaining 15% of the cases [2]. Immune checkpoint blockade has been recently studied in various cancers. Programmed death 1 (PD-1) receptor on T-cell surfaces and programmed death ligand 1 (PD-L1) are part of an inhibitory checkpoint that helps protect against autoimmunity by acting as negative regulators of activated T-cells [3]. The standard of care for non-small cell lung cancer (NSCLC) has changed with the introduction of immune checkpoint modulators such as nivolumab; a monoclonal antibody which binds to PD-1 receptor expressed on T-cells [4]. Nivolumab is currently authorized in both European Union and the USA for the therapy of the NSCLC [5].

We reported a metastatic NSCLC case to bone and liver treated with monoclonal immunotherapy by nivolumab plus chemotherapy (combination therapy) to had stable disease more than six months.

2. CASE REPORT

A 46-year-old female with bone metastatic adenocarcinoma of the lung and a history of chronic cough and hemoptysis was referred to the Clinic of Oncology in February 2014. Immunohistochemistry analysis showed CDX2, CK 5/6, calretinin, anaplastic lymphoma kinase (ALK), estrogen receptor and progesterone receptor were negative, but the epidermal growth factor receptor gene (EGFR), CK7 and thyroid transcription factor-1 (TTF-1) were positive and PD-L1<1%. The computed tomography (CT) scan showed increased irregular pleural thickness in mediastinal and parietal pleura. In the right lung parenchyma, the sporadic lens of atelectasis could be seen and decreased the relative volume of the right half of the thoracic. The left lung was normal. In mediastinum, several lymph nodes with a maximum diameter of 17 mm were evident (Figure 1). Hence, she received erlotinib as the first line treatment for 18 months and had good response with decrease in the size of the lesions. Then she switched to paclitaxel/carboplatin plus bevacizumab for six cycles. In June 2016 after the first line chemotherapy, she was treated with the maintenance therapy including pemetrexed plus bevacizumab for 8 cycles. The CT scan showed infiltration into mediastinal pleural space with a multitude of lymph nodes was seen in 8 to 14 mm of mediastina. Right diaphragm solcus were occupied by the masses. The findings are associated with

changes in the right lung parenchyma, especially the lower section of the middle lobe with reducing the size of the right lung February 2017 (Figure 2) with liver metastasis. In March 2017, she was treated with nivolumab plus pemetrexed for 8 cycles (combination therapy). After this period in May 2017, the CT scan did not show specific changes over before (Figure 3). She was in stable disease phase until September 2017 with good clinical condition. An informed consent was obtained from the patient to report the case.



Figure 1 The CT scan of lung in February 2014



Figure 2 The CT scan of lung in February 2017

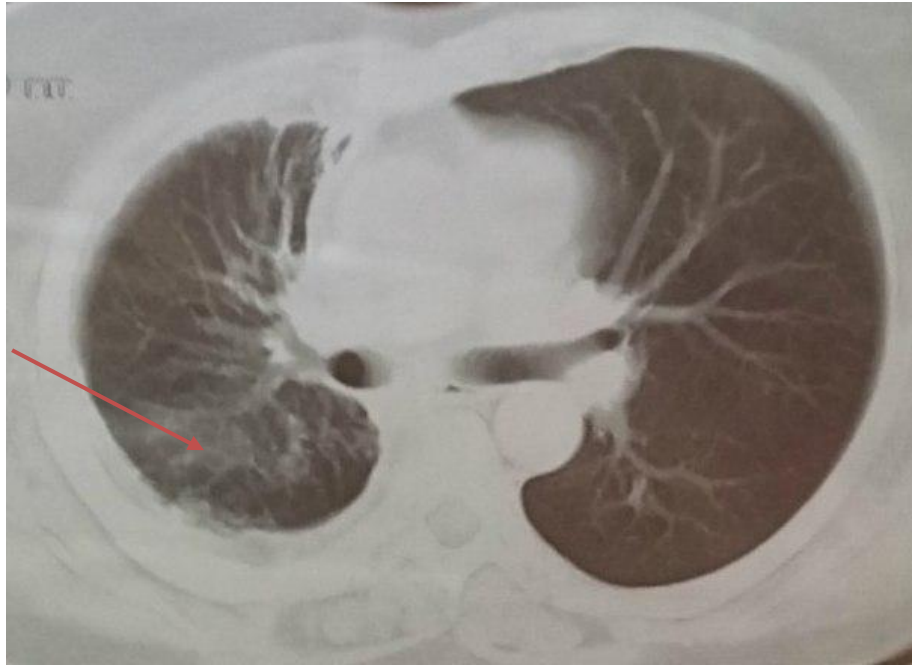


Figure 3 The CT scan of lung in May 2017

3. DISCUSSION

This case shows that the immunotherapy with nivolumab combined with chemotherapy can improve progression and survival in metastatic NSCLC patient with EGFR mutation-positive and PD-L1<1%. Nivolumab, a PD-1 immune-checkpoint-inhibitor antibody, inhibits the PD-L1/PD-1 anti-immune pathway and restores the immune response of the cytotoxic T-cells [6]. PD-1/PD-L1 inhibitors have been rapidly integrated into the standard of care for NSCLC and increasing numbers of other cancer types [7]. There was no significant change in the CT scans during three different times; because the CT scans don't show acceptable reasons about worse condition expect decreasing size of right lung and few lymph nodes during time.

Several trials were compared the efficacy and safety of nivolumab with the second-line chemotherapy agents such as docetaxel in advanced NSCLC. The data showed that nivolumab was able to improve the overall survival and to interfere with disease progression without major safety issues in NSCLC [5]. The results of a meta-analysis by Zhao et al. [8] showed that immunotherapy may be more efficacious in advanced NSCLC patients. Two trials [9,10] reported that combinations of immunotherapy and chemotherapy may be more efficacious in metastatic NSCLC that probably chemotherapy could promote an immune response to cancer and hence be synergistic with immune therapy. In the present case, the patient for around 6 months after combination therapy (nivolumab plus pemetrexed) was in a stable disease phase and good clinical condition compared with chemotherapy or target therapy alone has been done before combination therapy. One trial [11] reported that nivolumab was not associated with significantly longer progression-free survival than chemotherapy among patients with previously untreated stage IV or recurrent NSCLC with a PD-L1 expression level of 5% or more. PD-L1 expression level was reported as predictive marker of response in immune checkpoint inhibitors, such as nivolumab and pembrolizumab [12].

Constitutive signaling through the EGFR pathway can also promote tumor escape via activation the PD-1/PD-L1 pathway [13]. The efficacy of PD-1 blockade in EGFR mutation-positive NSCLC patients with different mechanisms of acquired resistance to EGFR tyrosine kinase inhibitors (TKI) is unknown [14]. Recently has been reported that EGFR mutations can be a possible unfavorable marker of response to immune checkpoint inhibitors [14-16] concluded that T790M-negative patients with EGFR mutation-positive NSCLC were more likely to benefit from nivolumab after EGFR-TKI treatment, possibly as a result of a higher PD-L1 expression level, than are T790M-positive patients. The present metastatic NSCLC case with regard to EGFR mutation-positive and PD-L1<1%, had a good overall survival and progression-free survival.

4. CONCLUSION

Combination therapy with nivolumab plus pemetrexed can improve survival and reduced progression in metastatic NSCLC patients. EGFR mutation and the PD-L1 percentage can be very important for selecting appropriate treatment protocol and improvement of survival of the patient.

CONFLICT OF INTEREST

The authors have declared that there was no conflict of interest.

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