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Reduction of Pericardial Effusion in Patients with Advanced Non-Small Cell Lung Cancer Treated by Nivolumab

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Abstract

Nivolumab is an immune checkpoint inhibitor used to treat various advanced malignancies including metastatic non-small cell lung cancer. The side effects of immunotest inhibitors are different from traditional cytotoxic chemotherapy and pericardial effusion is one of the adverse effects of immunotherapy. However, here we present a 59-year-old male with advanced non-small cell lung cancer (NSCLC) treated with nivolumab who successfully managed reduction of pericardial effusion in patients treated by Nivolumab after 11 cycles. During the treatment, he underwent only one pericardial puncture and drainage of pericardial effusion.

Keywords: Pericardial effusion; Lung cancer; Nivolumab

Introduction

Nivolumab is a fully human immunoglobulin G4 monoclonal antibody, also directed against PD-1. The activation of T-cells and cell-mediated immune responses against the tumor are enhanced by blocking the activation of PD-1 by its ligands programmed cell death ligand 1 (PD-L1)-overexpressed on certain cancer cells-and programmed cell death ligand 2 (PD-L2), which is primarily expressed on antigen-presenting cells. Nivolumab inhibits the interaction between the programmed cell death-1 (PD-1) receptor and its ligands (PD-L1 and PD-L2) and restores antitumor immunity [1].

Any drug that treats a disease at the same time will always have adverse reactions. The adverse response to immunotherapy has its own uniqueness, such as rashes, itching, diarrhea, interstitial pneumonia, and even myocarditis. We present a 59-year-old patient with metastatic squamous cell carcinoma of the lung who suffered progress of disease after chemotherapy and targeted treatment secondary to treatment with nivolumab.

Case Presentation

A 59-year-old male with a history of 48-pack-year cigarette smoking was diagnosed of Patients with stage 4 lung adenocarcinoma. He progressed through chemotherapy and targeted treatment was eventually started on nivolumab. After 2 cycles of permitracycline combined with cappatin chemotherapy, the patient's genetic test indicated that KRAS mutation and MET mutation, and oral kozoltinil was re-evaluated as disease progression one month later Plasma and TMB values were 13.9 and 9.9, respectively. Nivolumab therapy was then initiated for the patient (3 mg/kg every 2 weeks) as a third-line therapy.

After chemotherapy and targeted treatment, Nivolumab starting from 2018-9-6, 200 mg drops once for 14 days. The patient's chest CT examination before immunotherapy suggested that the right lung lung tumor blocked the right lung lower bronchial tube and entered the middle bronchial tube mediastinal invasion, mediastinal multiple lymph node metastasis, at the same time, combining with obstructive pulmonary dysplasia in the lower right lung. At that time, the symptoms were shortness of breath and intermittent fever (Figure 1). After 7 2 cycles of treatment, he presented to our hospital. Chest CT revealed that the right pulmonary emphysema is smaller than before, especially in the middle bronchi, the lung is not open in the middle of the upper right lung, and the mediastinal lymph nodes are not significantly changed compared with the preceding. The symptoms are obviously relieved. The right pulmonary valve mass and mediastinal lymph nodes decreased significantly (Figure 1).

A small amount of pericardial effusion before and after the first cycle of immunotherapy (Figure 2) after 3 cycle of immunotherapy, the patient suffered from dyspnea, Heart color ultrasound suggests a lot of pericardial effusion. (Figure 2) and symptoms are relieved after immediate cardiac puncture operation of drainage effusion. During the subsequent treatment, the median pericardial effusion was reviewed twice. Echocardiography shows no separate liquid region in pericardial cavity 4 months after nivolumab administration. So far, except for a small amount of skin rash (Figure 3), there have been no adverse reactions such as immuno-related pneumonia and myocarditis. At present, the patient has no obvious symptoms. He is on vacation and his quality of life has improved significantly.

Discussion

Checkpoint inhibitors such as pembrolizumab and nivolumab have revolutionized the treatment of metastatic malignant melanoma and NSCLC. Nivolumab's adverse reactions include myocarditis, but with the extension of the treatment cycle, there was no adverse heart reaction and the pericardial effusion completely disappeared, Among the symptoms of pericardial inflammation, pericardial effusion is one of the common clinical manifestations. A study also showed that patients treated with nivolumab plus chemotherapy had a significant longer PFS than those treated with only nivolumab. (HR=0.43, 95% CI: 0.194-0.953, p,0.05) and showed that nivolumab with chemotherapy had longer PFS than nivolumab only. However, in our study, PD-L1 status seems to have an apparent effect on the patient. In the process of clinical diagnosis and treatment, repeated puncture fluid is often required, but during the puncture with the larger risk, if there is a slight carelessness, it is very likely to lead to arrhythmias and organs. Damage, even death.

The pericardial effusion has been in the middle to large amount

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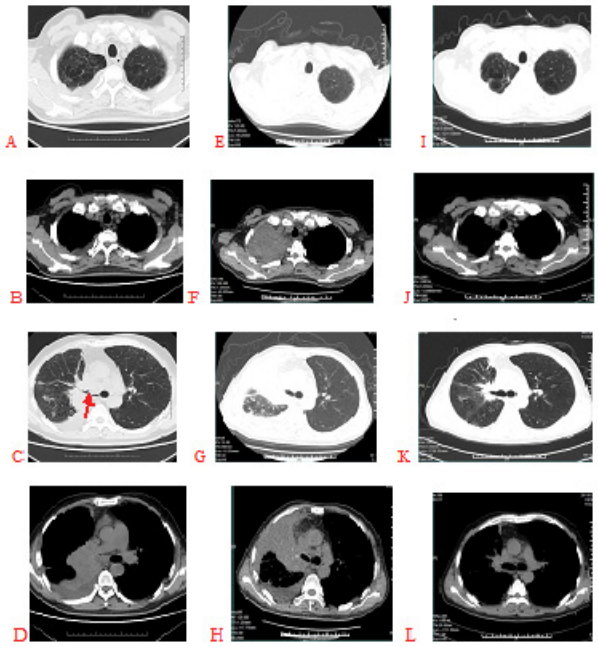

Figure 1: (A-D) Lung and mediastinal windows of computed tomography (CT) before nivolumab administration shows right pulmonary portal mass and right pulmonary dissection; (E-H) computed tomography (CT) after 2 cycles of nivolumab administration shows tumor reduction; (I-L) Computed tomography (CT) after 4 cycles of nivolumab administration shows significant reduction of tumor and mediastinal lymph nodes.

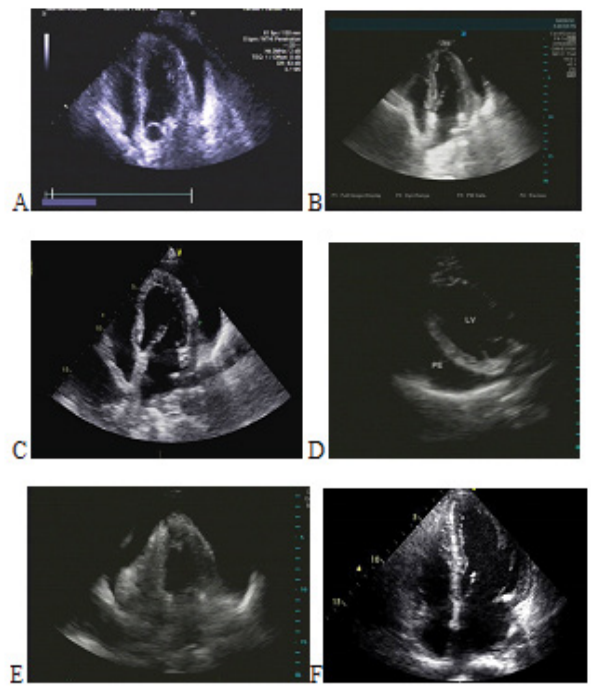

Figure 2: (A) Echocardiography indicated less pericardial effusion before nivolumab administration; (B) A small amount of pericardial effusion is detected after 1 cycles of nivolumab administration; (C) Mass pericardial effusion after 3 cycles of nivolumab administration; (D) shows Medium pericardial effusion 2 months after nivolumab administration; (E) shows Medium pericardial effusion 3months after nivolumab administration; (F) Echocardiography shows no separate liquid region in pericardial cavity 4 months after therapy.

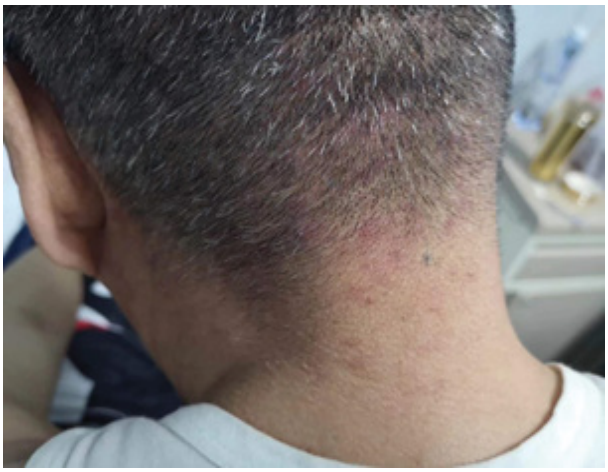

Figure 3: A small amount of rash scattered around the neck and face during the treatment.

during the patient's single drug immunotherapy. If the patient will benefit from the intermittent puncture drainage effusion, combined with the patient's condition, the pericardial effusion disappears, and immunotherapy improves the patient's symptoms. At the same time, pericardial effusion can be obviously controlled. This case brings us to the question of whether the presence of medium to large pericardial effusion during immunotherapy must be alleviated as soon as possible. In addition to a small amount of skin rash on the head and face, the patient also had a rash in the past using Peimethasar chemotherapy. There were no adverse reactions such as interstitial pneumonia and myocarditis. IrAEs are thought to arise from immunologic enhancement causing autoimmune inflammation of non-targeted organ systems, resulting in side effects like pneumonitis, hepatitis, nephritis, and endocrinopathies [2]. Tumor mutation burden (TMB) is an emerging biomarker with utility in predicting response to immunotherapy [3,4]. The increase in TMB is thought to lead to an increase in the production of new sites, attracting infiltration of tumor lymphocyte, The plasma and tissue TMB of the patients in this study were 12.16 Muts/Mb and 9.99 Muts/Mb, respectively, the symptoms and signs improved significantly after treatment and the quality of life improved significantly.

Most series demonstrated an increase of PD-L1 expression after chemotherapy and radiotherapy, particularly when platinum-based regimen was used, but some other works reported a decrease of PD-L1 expression after neoadjuvant chemotherapy [5-10] The use of tyrosine kinase inhibitors including osimertinib, could decrease the level of PD-L1 expression in EGFR mutated tumors [11,12], but conversely, when those tumors acquire gefitinib resistance, they seem to express more strongly PD-L1. The patients in this study were met-mutations, which developed rapidly after oral xazolinib, and more studies are expected on the relationship between met-mutations and pd-L1.

So far, although there are no obvious adverse reactions in the patients in this report, due to the heterogeneity of the tumor and the unique individual immune system, the related toxicity of immunotherapy and the effect of later treatment still require careful observation and evaluation.

Conclusion

Pericardial effusion often occurs during lung cancer, and

appropriate treatment is given according to the patient's symptoms and the amount of pericardial effusion, such as pericardiocentesis drainage fluid. Adverse reactions to immunotherapy include myocarditis. However, in combination with this case, in the course of immunotherapy, with the regular use of drugs, there is no occurrence of myocarditis, and pericardial effusion may gradually be absorbed. We, therefore, suggest that in similar cases, deciding of pericardial effusion during the treatment may improve the outcome of NSCLC patients by allowing continuation of nivolumab therapy.

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