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Multidisciplinary Management of Advanced Mucinous Adenocarcinoma of the Lung: A Case Report

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Abstract

Managing advanced mucinous adenocarcinoma of the lung poses significant challenges, especially in patients lacking biomarkers for targeted therapies. This case illustrates the effectiveness of a multidisciplinary approach that integrates chemotherapy, immunotherapy, radiotherapy, and personalized treatment adjustments, leading to meaningful clinical responses in a patient with progressive disease.

Keywords: Mucinous adenocarcinoma of lungs, Double immunotherapy, Next generation sequencing, Multidisciplinary team

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Introduction

Lung cancer is the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) comprising about 80% of cases. Invasive mucinous adenocarcinoma, a subtype of NSCLC, presents unique diagnostic and therapeutic challenges due to its aggressive nature and limited response to conventional therapies [1-3]. While advancements in targeted therapies and immunotherapy have improved outcomes for some patients, managing advanced disease necessitates a tailored, multidisciplinary approach. This report details the successful treatment of a patient with advanced mucinous adenocarcinoma through dynamic treatment modifications guided by multidisciplinary team (MDT) discussions, highlighting the role of double immunotherapy in achieving favorable outcomes.

Case Presentation

A 32-year-old male non-smoker presented with a nine-month history (April 2023) of persistent cough and cold, along with Lichen planus under steroid treatment. His medical history was unremarkable. Initial investigations revealed significant lung abnormalities, including a large area of consolidation in the left upper lobe and multiple nodular lesions. Computed tomography (CT) guided lung biopsy confirmed a diagnosis of invasive mucinous adenocarcinoma, characterized by glandular spaces lined by pleomorphic tall columnar cells and extensive extracellular mucin pools. Immunohistochemistry analysis indicated the tumor was a "cold tumor," with positive for CK7 and negative of CK20, TTF1, Napsin A, CDX2, ALK and PDL1 expression (Dako, 22C3 clone).

Positron emission tomography-computed tomography (PET-CT) revealed an ill-defined consolidative lesion measuring 14.1 × 9.1 × 14.3 cm, affecting both the left upper and lower lobes. Additionally, a subpleural consolidative lesion of 6.5 × 2.8 cm was noted in the right upper lobe, accompanied by multiple discrete pulmonary nodules in the right upper and lower lobes, indicative of metastatic disease (Figure 1a). Enlarged lymph nodes were observed in the subcarinal, bilateral paratracheal, and left supraclavicular regions, measuring 1.7 × 12 cm. No distant metastases were detected in the liver, bones, or brain.

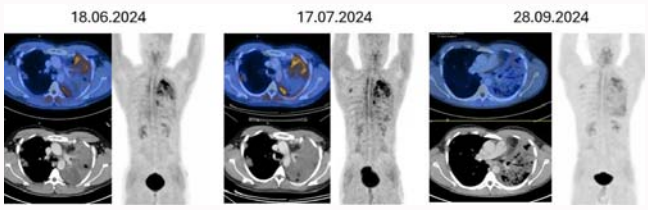

Figure 1a. Baseline PETCT scan at the time of presentation; **1b**. PET CT scan post chemotherapy with nivolumab; **1c**. PETCT scan post treatment with double immunotherapy and radiotherapy.

The patient started treatment with carboplatin and pemetrexed, adding nivolumab after the second cycle. An MRI after three cycles showed no focal lesions. Next Generation Sequencing (NGS) identified the STK11 p. Phe264ArgfsTer22 variant at 4.89% allele frequency, with negative results for mutations in several key genes. Low levels of Microsatellite Instability (MSI) and Tumor Mutation Burden (TMB) were noted. After four cycles, imaging indicated significant disease progression (Figure 1b), prompting a multidisciplinary team to recommend a new treatment plan with docetaxel, ramucirumab, and double immunotherapy for three more cycles.

The patient received the first cycle of Nivolumab (160 mg), Ipilimumab (50 mg), Ramucirumab (500 mg), and Docetaxel (100 mg) [4]. Due to grade 2/3 neutropenia, body ache and generalized fatigue following the first cycle, the docetaxel dose was reduced to 90 mg for the second cycle. An MDT discussion after the second cycle noted clinical improvement, leading to a PET-CT scan post-three cycles of chemo-immunotherapy, which demonstrated a partial response (Figure 1c) with significant reductions in lung lesions.

Radiotherapy was planned for the primary and metastatic sites. The patient underwent right intercostal drainage for pneumothorax during fiducial placement and received stereotactic body radiotherapy (SBRT) to the lung lesions. The patient tolerated the radiation well, and double immunotherapy continued from the fourth cycle onward. At the time of this report, the patient had completed the fourth dose of double immunotherapy without significant toxicities.

Discussion

Pulmonary mucinous adenocarcinomas have a distinct tumor microenvironment that affects T and B-Lymphocyte functionality. Mucin creates a barrier that hinders chemotherapeutic penetration and T-Cell contact with tumor cells, leading to immune evasion and increased metastatic potential. A high population of T-reg cells correlates with poor prognosis, as immune suppression occurs through various mechanisms, including the secretion of transforming growth factor-β (TGF-β) and interference in cell interactions.

This case underscores the complexity of managing advanced mucinous adenocarcinoma in the absence of actionable molecular targets. Initial disease progression (Figure 1b) following chemotherapy highlighted the necessity for adaptive treatment strategies guided by MDT discussions. The inclusion of ramucirumab, a VEGFR-2 inhibitor, with docetaxel likely improved disease control by targeting angiogenesis. Double immunotherapy may have enhanced anti-tumor activity by modulating the immune microenvironment, with studies indicating potential overall survival benefits in patients without actionable genomic signatures.

Comprehensive molecular profiling was crucial in excluding ineffective treatments and focusing on strategies tailored to the patient's disease characteristics. The patient's clinical improvement demonstrates the potential of integrating molecular diagnostics, MDT-driven decision-making, and personalized multimodal therapy in challenging cases.

Conclusion

Managing advanced lung cancer requires a multidisciplinary approach to navigate complex clinical scenarios. This case illustrates how MDT discussions, precision diagnostics, and adaptive treatment strategies can yield positive outcomes, even in challenging cases of mucinous adenocarcinoma. Regular follow-ups and collaboration among specialists were essential in improving the patient's condition, highlighting the potential of personalized care.

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