MANAGEMENT OF PNEUMONITIS POST-CONCURRENT CHEMORADIATION AND IMMUNOTHERAPY IN PATIENTS WITH ADVANCED LUNG CANCER: CASE REPORT AND LITTERATURE REVIEW

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Immune-related pneumonitis is a rare but serious complication in patients with non-small cell lung cancer (NSCLC) treated with durvalumab after concurrent chemoradiotherapy (CRT). We encountered a 61-year-old male with stage III non-small cell lung cancer (NSCLC) receiving concurrent chemoradiotherapy followed by durvalumab maintenance therapy. After 1 cycle of durvalumab treatment, he developed progressive dyspnea, dry cough, and low-grade fever. Chest CT scans revealed diffuse ground-glass opacities in both lungs, indicative of immune-related pneumonitis. Durvalumab was discontinued, and the patient was treated with high-dose corticosteroids and antibiotics. After one month, he fully recovered. Durvalumab was cautiously resumed under close monitoring without recurrence of pneumonitis. Conclusion: Early identification and management of immune-related pneumonitis are essential in NSCLC patients receiving durvalumab. Reintroducing durvalumab after recovery may be safe with vigilant monitoring.

Keywords: Non-small cell lung cancer, durvalumab, immune-related pneumonitis, chemoradiotherapy, immunotherapy rechallenge.

I. INTRODUCTION

Non-small cell lung cancer (NSCLC) in the locally advanced stage (stage III) accounts for approximately 30% of newly diagnosed lung cancer cases.[1] Concurrent chemoradiation (CRT) is the standard treatment for unresectable stage III NSCLC patients.[2] The addition of durvalumab, a monoclonal antibody targeting PD-L1, after definitive concurrent chemoradiation (dCRT) has significantly improved progression-free survival (PFS) and overall survival (OS) in stage III NSCLC patients.[3,4]

However, the use of durvalumab post-dCRT is associated with risks of immune-related pneumonitis (IRP) and radiation pneumonitis (RP).[5] Differentiating and managing these two complications present significant clinical challenges. We report a case of a stage III NSCLC patient who developed IRP after durvalumab treatment and subsequently resumed durvalumab therapy after recovery, aiming to discuss the diagnosis, treatment, and feasibility of immunotherapy rechallenge. This study aims to present a case of pneumonitis in a patient

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treated with concurrent chemoradiotherapy (cCRT) followed by durvalumab, focusing on the clinical manifestations, management strategies, and the implications for medical practice.

II. CASE REPORTS

A 61-year-old male with a 20 pack-year smoking history presented with persistent dry cough, chest pain, and dyspnea. Chest computed tomography (CT) revealed a large tumor in the right upper lung lobe invading the pleura and mediastinal lymph nodes (Figure 1). Transbronchial biopsy and histopathological results confirmed pulmonary adenocarcinoma. The patient underwent a PET-CT scan, which revealed a mass with increased FDG uptake in the right pulmonary hilum region involving all three lobes consistent with a primary malignant lesion, accompanied by several satellite nodules in the right lower lobe. Imaging also showed several lymph nodes with increased FDG uptake in the mediastinum and right pulmonary hilum, consistent with secondary regional lymphadenopathy. The patient's brain MRI results did not detect any secondary lesions. The patient was diagnosed with stage cT4N2M0 NSCLC according to the 8th edition of the TNM classification.[6]

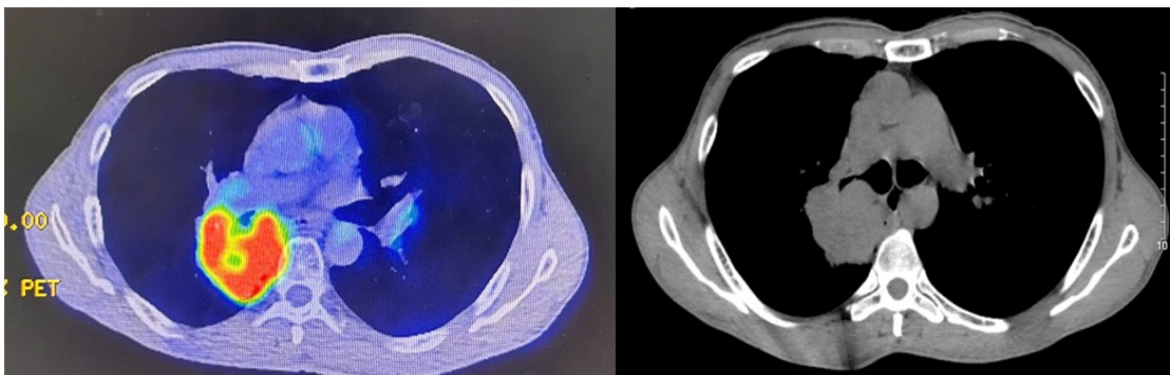

Figure 1. PET -CT and CT chest images before treatment

The patient underwent concurrent chemoradiotherapy (CRT) with weekly Paclitaxel – Carboplatin combined with radiotherapy at 60Gy in 30 fractions. After completing CRT, a re-evaluation showed a partial response (Figure 2), and he continued maintenance therapy with Durvalumab at 1500mg every 4 weeks.

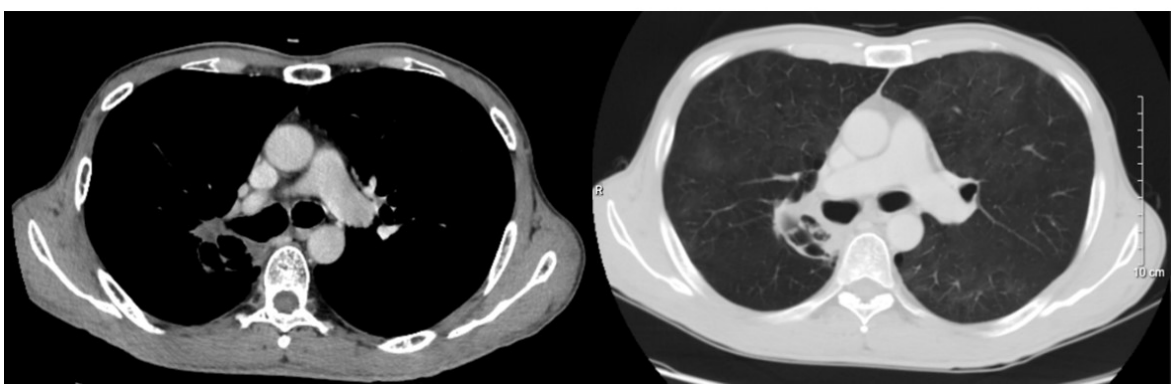

Figure 2. CT chest image after CRT

Three weeks after the first cycle of treatment with Durvalumab, the patient developed progressively worsening dyspnea, dry cough, and low-grade fever (37.8°C). Physical examination revealed bilateral crackles upon auscultation. Chest CT showed diffuse ground-glass opacities in both lungs, especially in the peripheral regions, not confined to the irradiated areas (Figure 3). Blood tests indicated normal white blood cell counts and mildly elevated C-reactive protein (CRP). Pulmonary function tests showed decreased lung function compared to pre-durvalumab treatment (FEV1 decreased from 80% to 65%). Blood tests indicated normal white blood cell counts and mildly elevated high-sensitivity C-reactive protein (hs-CRP) at 5.8 ng/mL, while Procalcitonin was low at 0.05 ng/mL. The patient underwent blood cultures from both arms to identify bacteria and rapid tests to rule out influenza and COVID-19, which were all negative.

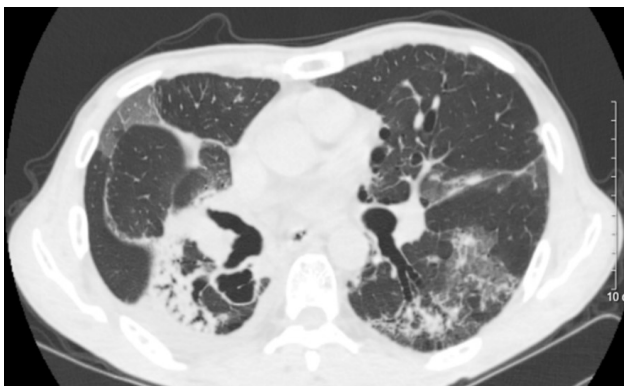

Figure 3. CT chest images after concurrent chemoradiotherapy and 1 cycle of durvalumab

Based on the patient's clinical condition, which did not exhibit clear signs of infection despite declining respiratory function, and after thorough consultations with radiologists and respiratory and infectious disease specialists, we excluded other causes of pneumonia and diagnosed as immune-related pneumonitis. Durvalumab was discontinued, and the patient was hospitalized with a suspected diagnosis of grade 2 immune-related pneumonitis.[7] He was treated with intravenous methylprednisolone at 1 mg/kg/day and antibiotics with levofloxacin 500 mg/day, twice a day to infection prophylactic. Supplemental oxygen via nasal cannula was provided, and vital signs were closely monitored.

After 48 hours of treatment, the patient's clinical symptoms improved significantly, with reduced dyspnea and cough. After one month of treatment, a follow-up chest CT after 30 days showed a marked reduction of inflammatory lesions (Figure 4), respiratory symptoms did not recur, and pulmonary function tests returned close to baseline levels. We decided to discontinue prophylactic antibiotics and continue tapering the corticosteroid therapy to complete a total of eight weeks.

Following careful assessment and weighing of risks and benefits, durvalumab was reinitiated with close monitoring. During subsequent treatment, the patient did not experience recurrence of pneumonitis and continued durvalumab according to the treatment schedule.

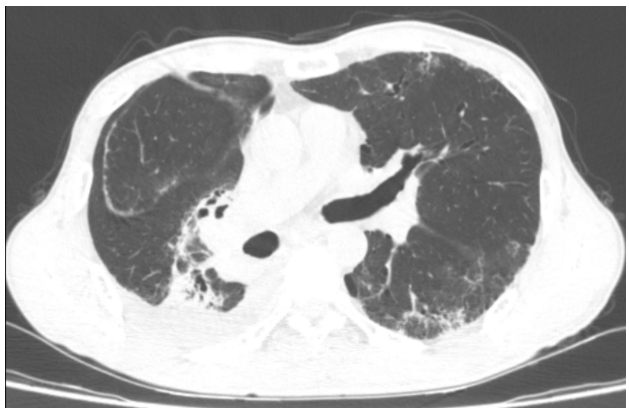

Figure 4. CT chest images after 1 month of treatment with corticosteroids and prophylactic antibiotics

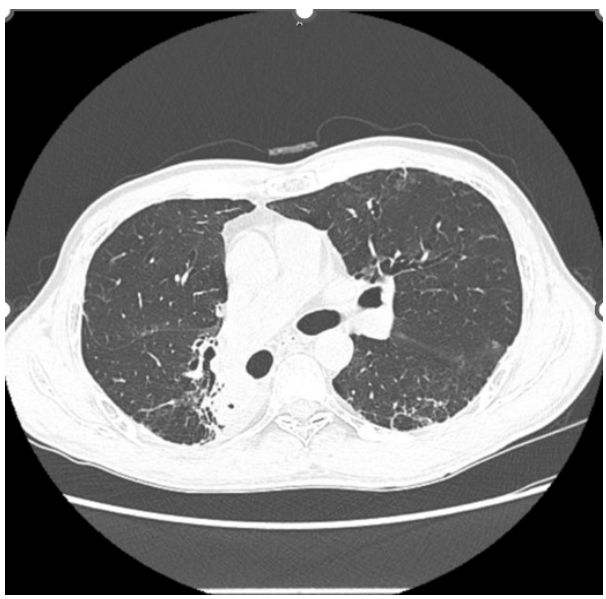

Figure 5. CT chest image after continuing with 8 cycles of Durvalumab

III. DISCUSSION

Immune-related pneumonitis (IRP) is a rare but serious complication in patients with non-small cell lung cancer (NSCLC) treated with PD-1/PD-L1 inhibitors.[8] In the PACIFIC trial, the incidence of IRP was 4.4% in the durvalumab group compared to 3.8% in the placebo group.[4] Clinical reports indicate that IRP can be fatal if not promptly diagnosed and treated.[5] IRP often presents with nonspecific symptoms, making it easily confused with radiation pneumonitis (RP) or pulmonary infections. It can occur at any time during immunotherapy and typically manifests with symptoms such as cough, dyspnea, and low-grade fever. Radiation pneumonitis (RP) is a more common complication, occurring in approximately 15 - 20% of patients following thoracic radiotherapy.[9,10] RP usually arises between 4 and 12 weeks after completing

radiotherapy, with pulmonary lesions typically confined to the irradiated fields. This contrasts with IRP, where lesions are often more widespread and not limited to the radiation fields. Imaging of RP may show ground-glass opacities or fibrosis confined to the irradiated lung, whereas IRP often presents with interstitial patterns diffusely affecting both lungs.[11,12]

In this case, the patient's respiratory symptoms emerged 3 weeks after the first cycle durvalumab initiation, with chest CT revealing diffuse bilateral pulmonary inflammation. This presentation aligns with IRP, whereas RP is usually confined to the irradiated area. Excluding infections and other causes is crucial. The diagnosis of IRP was made based on criteria from the American Society of Clinical Oncology (ASCO) and the Society for Immunotherapy of Cancer (SITC).[13]

Treatment of IRP involves discontinuation of immunotherapy and administration of high-dose corticosteroids. Corticosteroids are considered the standard therapy, helping to reduce inflammation and alleviate symptoms.[13,14] In this case, the patient was also treated with empirical prophylactic antibiotics to prevent and manage potential infections.[7] He responded well to treatment, with symptom improvement after 48 hours and significant reduction of pulmonary lesions after one week.

Rechallenging with durvalumab after IRP is a complex decision, requiring careful consideration of the risk of recurrence versus therapeutic benefits. Current guidelines suggest that resuming immunotherapy may be considered in patients with mild to moderate IRP who have fully recovered and are under close monitoring.[13] In this case, after the patient fully recovered, we decided to resume durvalumab at a reduced dose with vigilant monitoring. The patient did not experience recurrence of IRP during subsequent treatment. This result is consistent with some studies that have reported that rechallenging with immunotherapy after IRP can be safe in certain patients, although the risk of recurrent complications remains. Close monitoring and educating the patient about warning signs are essential.[15,16]

IV. CONCLUSION

This clinical case presents an instance of pneumonitis following concurrent chemoradiotherapy and immunosuppressive treatment, highlighting the challenges in diagnosing and managing complications, particularly post-treatment pneumonitis. It highlights that with appropriate treatment and monitoring, patients may successfully resume immunotherapy, potentially improving their overall outcomes and quality of life.

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