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CASE REPORT

Combined Use of Radioactive ^{125}I Seeds and PD-1 Inhibitor Provides Sustained Clinical Benefit in an Elderly Patient with Advanced Non-Small Cell Lung Cancer: A Case Report

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Abstract: Radioactive ^{125}I seed implantation, a minimally invasive and targeted local therapy, is particularly suitable for elderly patients who are ineligible for conventional treatments. Meanwhile, PD-1 inhibitors, as a major focus of current research, have become an essential component of systemic therapy for non-small cell lung cancer. This case report describes a 72-year-old male patient with advanced non-small cell lung cancer(NSCLC) whose disease progressed despite multiple lines of chemotherapy and radiotherapy. Due to the onset of hemoptysis, he underwent combined treatment with radioactive ^{125}I seeds and a PD-1 inhibitor. Postoperatively, his hemoptysis resolved completely, and notably, the patient achieved a progression-free survival of 40 months, demonstrating sustained clinical benefit. These findings suggest that the combination of ^{125}I seed implantation and PD-1 inhibitors may exert a synergistic antitumor effect, offering a promising therapeutic strategy for elderly patients with advanced NSCLC.

Keywords: non-small cell lung cancer, ^{125}I seed implantation, brachytherapy, immunotherapy, synergistic therapy, elderly patients, immunotherapy

Introduction

Non-small cell lung cancer(NSCLC) is the predominant histological subtype of lung cancer, accounting for up to 80% of cases according to epidemiological data.[1] Owing to its atypical and nonspecific early clinical manifestations, the majority of patients are diagnosed at an advanced stage.[2] With the intensification of population aging, the number of elderly lung cancer patients continues to rise. This population commonly presents with multiple chronic diseases and treatment-related complications, coupled with generally poor overall physiological condition and diminished organ functional reserve. These factors collectively lead to significantly reduced tolerance to conventional anticancer therapies such as chemotherapy and radiotherapy, while simultaneously increasing the risk of treatment-related toxicities.[3] Therefore, it is imperative to develop personalized and well-tolerated treatment strategies for elderly cancer patients. CT-guided radioactive ^{125}I seed implantation is an emerging localized therapy that achieves precise intratumoral irradiation through the continuous release of low-dose gamma rays. It offers advantages such as minimal invasiveness, high accuracy, and the delivery of high cumulative radiation doses to the target area, providing a crucial alternative for elderly patients with advanced lung cancer who are unsuitable for conventional radiotherapy or chemotherapy.[4] Previous studies have demonstrated significant efficacy of ^{125}I seed implantation in elderly NSCLC patients, with a mean overall survival of 11.7 ± 7.6 months.[5] Meanwhile, PD-1 inhibitors, which enhance T cell-mediated antitumor immunity by specifically blocking the immunosuppressive PD-1/PD-L1 signaling axis, have been widely incorporated into NSCLC treatment in recent years.[6] Theoretically, combining radioactive ^{125}I seed implantation with PD-1 inhibitors holds the potential to achieve localized high-dose radiation while simultaneously activating a systemic antitumor immune response, resulting

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in a synergistic effect. Here, we report the case of an elderly patient with advanced NSCLC whose disease progressed after prior chemotherapy and radiotherapy. Following a multidisciplinary team evaluation due to comorbid hemoptysis, the patient underwent CT-guided radioactive ^{125}I seed implantation combined with PD-1 inhibitor therapy, ultimately achieving a remarkable progression-free survival(PFS) of 40 months.

Case Presentation

The Initial Symptoms of the Patient

A 72-year-old male smoker (40 pack-year history) presented with morning cough productive of blood-tinged sputum since September 2017. The patient reported an unintentional weight loss of approximately 10 kg within three months since symptom onset. No dizziness, headache, chest tightness, shortness of breath, abdominal pain, diarrhea, or other associated symptoms were documented.

Personal and Family History

The patient had a medical history of hypertension and chronic renal insufficiency. He denied any history of chronic conditions such as diabetes mellitus or coronary heart disease, as well as any infectious diseases including hepatitis or tuberculosis. There was no reported history of or exposure to communicable diseases. Additionally, no family history of malignancy was documented.

Course of Diagnosis and Treatment Following Symptom Onset

Following symptom onset, the patient did not seek any medical evaluation or treatment for three months until his initial presentation at our hospital in December 2017. A contrast-enhanced CT scan of the chest and abdomen revealed a mass in the right lower lobe, highly suspicious for malignancy with associated post-obstructive inflammation, and a nodule in the right adrenal gland, suggestive of metastatic involvement. A subsequent bone scan showed no evidence of abnormal radiotracer uptake. A percutaneous lung biopsy of the right lower lobe lesion was performed. Histopathological examination confirmed the diagnosis of invasive carcinoma, consistent with poorly differentiated squamous cell carcinoma. Due to significant surrounding inflammatory changes, accurate measurement of the primary tumor was not feasible. The patient was clinically staged as cTxN0M1 (Stage IV). Treatment was initiated with six cycles of chemotherapy consisting of docetaxel (120 mg) and nedaplatin (120 mg), along with concomitant antibiotic therapy for the associated pulmonary infection. A follow-up CT scan in April 2018 showed a slight reduction in the size of the right lower lung lesion (0.82 x 1.54 cm), while the right adrenal nodule remained stable In May 2018, a PET-CT scan was performed for further evaluation. It demonstrated increased FDG uptake in the right lower lung lesion (2.33 x 1.86 cm), indicating residual viable tumor. Additional patchy opacities with elevated FDG uptake in the same region were deemed likely inflammatory. The right adrenal nodule also exhibited increased FDG uptake, consistent with a metastatic lesion. To achieve local disease control, the patient opted for and received radiotherapy targeting the primary pulmonary lesion. Subsequent evaluations showed stable disease(SD). However, in December 2020, a surveillance CT scan revealed post-treatment changes in the right lung with an increase in the solid component of the primary lesion, although the adrenal metastasis remained stable This was assessed as progressive disease (PD). After discussion and exclusion of contraindications, second-line chemotherapy with nab-paclitaxel (400 mg) was administered for six cycles. Restaging scans after the third and sixth cycles confirmed SD. In July 2021, the patient experienced recurrent hemoptysis. Despite symptomatic hemostatic treatment, the bleeding persisted which was attributed to disease progression with suspected vascular invasion by the tumor.

Application of Radioactive ^{125}I Seed Implantation Combined with PD-1 Inhibitor Therapy

After multiple prior lines of therapy, the patient's disease continued to progress. His general condition had significantly deteriorated, and he had developed treatment-related complications, including gastrointestinal adverse effects and myelosuppression. Due to a declined performance status, he was deemed unsuitable for further conventional

chemotherapy or radiotherapy. Following multidisciplinary team (MDT) evaluation and detailed discussion with the patient's family, an individualized treatment strategy was formulated, combining radioactive ^{125}I seed implantation with a PD-1 inhibitor. Written informed consent was obtained prior to the procedure. On July 15, 2021, the patient underwent interstitial ^{125}I seed implantation. The seeds (Ningbo Junan Pharmaceutical Technology Co., Ltd.) measured 4.5 mm in length and 0.8 mm in diameter, with an average energy of 27–32 keV, a half-life of 59.6 days, a tissue penetration distance of 1.7 cm, an initial dose rate of 7 cGy/h, and an activity of 2.22×10^7 to 2.59×10^7 Bq per seed. A pre-procedural planning CT scan of the chest was performed, and images were transferred to the treatment planning system (TPS; Zhuhai Hejia Medical Equipment Co., Ltd). The clinical target volume (CTV) was delineated, and three-dimensional reconstruction was conducted. The lesion in the right lower lobe was selected as the target, for which 80 seeds were planned with a prescribed dose of 9000.0 cGy and an activity of 0.6 mCi per seed. With the patient in the prone position, the puncture site was identified and prepared under sterile conditions. Under local anesthesia with 2% lidocaine, the ^{125}I seeds were percutaneously implanted using a brachytherapy applicator. The seeds were deployed at intervals of 5–10 mm while gradually withdrawing the needle from the target lesion. A post-implant CT scan confirmed appropriate seed distribution without evidence of migration. Prophylactic antibiotics and hemostatic agents were administered postoperatively. Figure 1 illustrates the key steps of the seed implantation. The patient received the first dose of immunotherapy (camrelizumab, 200 mg) on day 7 post-seed implantation, which marked the initiation of

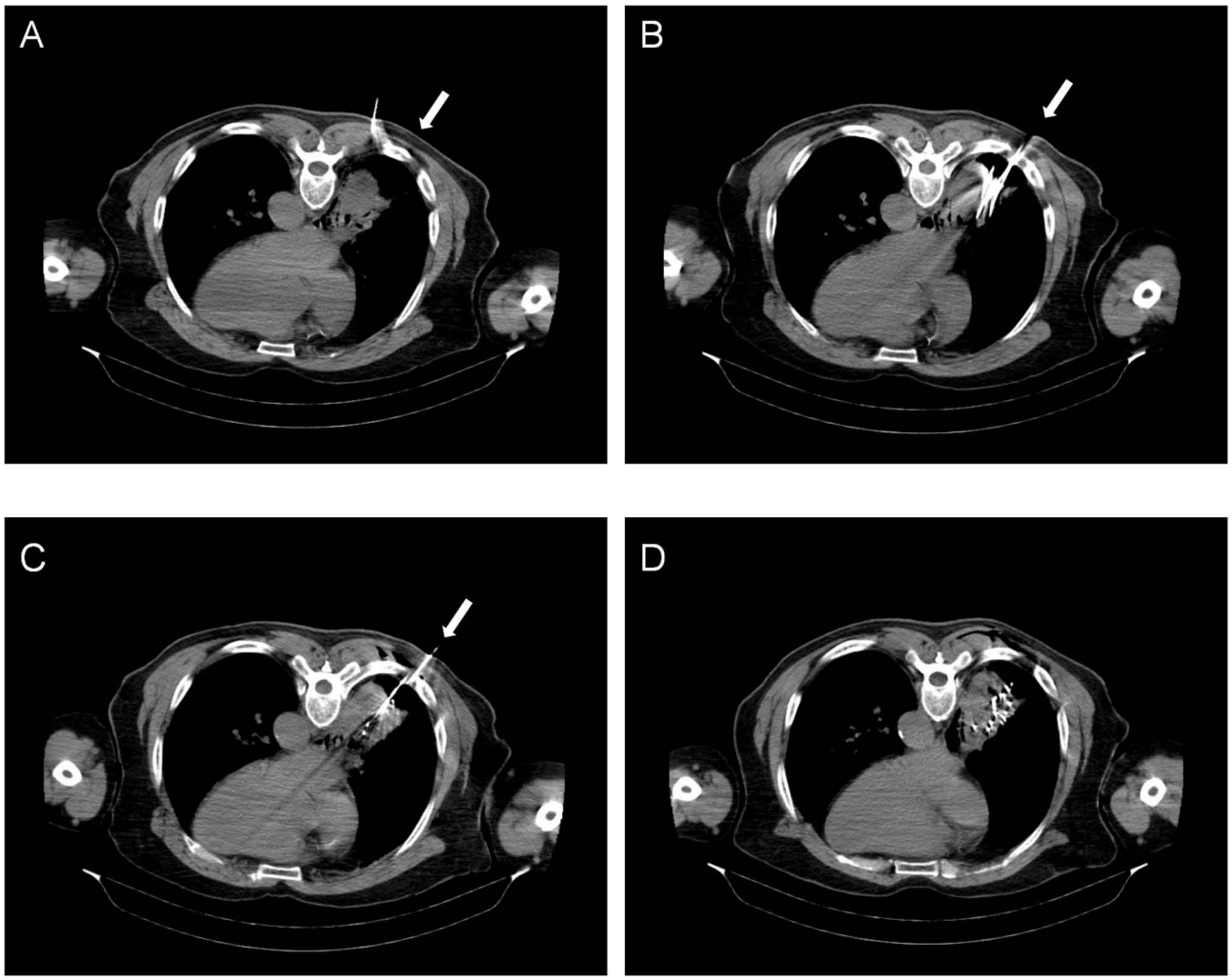

Figure 1 (**A–C**) The procedure of particle implantation performed with the patient in a prone position under CT guidance. The arrows indicate the needle insertion trajectory. (**D**) Post-procedural imaging confirming the homogeneous distribution of implanted particles within the target lesion.

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maintenance therapy administered every three weeks. During the treatment period, chest CT scans were performed for follow-up assessment every three cycles. A follow-up CT at 40 months post-procedure revealed significant lesion enlargement and the emergence of multiple lymph node metastases. Consequently, the patient's PFS was recorded as 40 months.

Discussion

The phenomenon of "immunosenescence" is widespread among elderly patients with advanced NSCLC. Manifested as a progressive deterioration of immune function with age, it results in a markedly diminished capacity to mount effective immune responses against both exogenous and autoantigens.[7] Consequently, the restoration of potent anti-tumor immunity in these patients represents a pivotal determinant of treatment efficacy. The mechanism of ^{125}I seed implantation involves continuous low-dose gamma radiation, which causes direct DNA damage via single- and double-strand breaks. This inherent radiosensitivity profile—where cells in M and G2 phases are vulnerable, but quiescent cells are resistant—limits the efficacy of conventional radiotherapy. The protracted half-life of ^{125}I seeds enables sustained tumoricidal activity, addressing this fundamental shortcoming of standard radiation approaches.[8] Furthermore, radioactive ^{125}I seeds can effectively inhibit tumor proliferation and concurrently induce immunogenic cell death, thereby eliciting a robust immune response. This process not only activates local immunity but may also initiate a systemic immune reaction through the "abscopal effect", ultimately generating more durable anti-tumor immunity.[9] The PD-1/PD-L1 complex within the tumor microenvironment plays a critical role in tumor immune escape, and its expression level is positively correlated with tumor progression.[10] Tumor cells can evade immune surveillance and interfere with ligand-receptor interactions, thereby escaping elimination by the host immune system. In contrast, PD-1 inhibitors function by specifically blocking the inhibitory signaling pathway between PD-1 and its ligand PD-L1, thereby reversing the suppression of T-cell function. This directly promotes the proliferation and activation of tumor-infiltrating lymphocytes and, more importantly, reverses the immunosuppressive state in the tumor microenvironment.[11] The immune activation induced by ^{125}I seeds and the reversal of immunosuppression by PD-1 inhibitors act synergistically to enhance anti-tumor immunity, resulting in a sustained and systemic therapeutic effect. Although immune checkpoint inhibitors demonstrate significant clinical efficacy in advanced NSCLC, the emergence of primary and acquired resistance over time remains a major clinical challenge. An in vitro study[12] which investigated the combined effect of pembrolizumab (a PD-1 inhibitor) and ^{125}I seeds on NSCLC cell proliferation, invasion, and apoptosis, revealed that the combination therapy enhanced tumor cell resistance to PD-1/PD-L1 targeted treatment by modulating ADAM17 expression. In this case, an elderly patient with advanced NSCLC presenting with hemoptysis was managed with combination therapy involving ^{125}I seed implantation and a PD-1 inhibitor. This approach not only markedly alleviated clinical symptoms but also resulted in an unexpected PFS of 40 months. In contrast, a clinical trial evaluating the efficacy of PD-1/PD-L1 inhibitors in elderly patients with advanced NSCLC reported a median PFS of only 7 months among 58 participants.[13] Another study investigating ^{125}I seed implantation for patients with recurrent NSCLC after chemoradiotherapy demonstrated a median PFS of 14.5 months in a cohort of 30 patients, although not exclusively elderly.[14] The notable clinical benefit observed in this case suggests a synergistic interaction between radioactive ^{125}I seed therapy and immunotherapy. This dual-mechanism approach not only achieves precise local tumor control but also potentiates a systemic anti-tumor immune response, thereby significantly improving survival and prognosis—a finding that merits further validation in larger-scale studies.

Prior to radioactive ^{125}I seed implantation, a CT scan is routinely performed to clearly delineate the tumor location, boundaries, and its anatomical relationship to adjacent critical vessels and organs. Subsequently, TPS is used to determine the required number of seeds and the radiation dosage based on tumor morphology and size. The radiation dose from ^{125}I seeds decays rapidly with increasing distance, which underpins the technique's minimally invasive and precisely targeted advantage. The TPS plan ensures that 95% of the tumor volume receives 100% of the prescription dose while sparing the surrounding normal tissues.[15] In clinical practice, pneumothorax represents the most common complication associated with ^{125}I seed implantation. Elderly patients, who often present with underlying conditions such as bullae, emphysema, or chronic obstructive pulmonary disease, are at increased risk of pneumothorax during needle insertion, significantly elevating procedural risks.[16] Consequently, current research focuses on optimizing

implantation pathways, needle depth, and radiation dosage under advanced image guidance to enhance treatment efficacy while reducing complication rates and improving tolerance in elderly populations. In the present case, no procedure-related complications—such as pneumothorax or hemorrhage—were observed. Furthermore, the complete resolution of hemoptysis postoperatively underscores the efficacy of ^{125}I seed implantation in controlling local symptoms.

Conclusion

In summary, the combination of radioactive ^{125}I seed implantation and PD-1 inhibitor therapy demonstrates significant clinical benefits in elderly patients with advanced NSCLC. This combined approach not only achieves excellent local symptom control but also exhibits a favorable safety profile with no documented treatment-related adverse events. These findings suggest that this strategy holds considerable promise for clinical application and may represent a valuable therapeutic option for elderly patients in this setting. One limitation of this study is the lack of biomarker data, including PD-L1 expression and tumor mutational burden, as well as immunohistochemical analyses. This gap makes it challenging to elucidate the mechanistic basis underlying the synergistic effect observed between ^{125}I seed implantation and PD-1 inhibitor therapy. Furthermore, it restricts a deeper understanding of how the combined modality influences the tumor immune microenvironment and accounts for interpatient variability. Therefore, future work should involve larger-scale, prospective, and ideally randomized controlled trials to further explore the mechanisms and validate the clinical benefits of this approach.

Abbreviations

NSCLC, non-small cell lung cancer; PFS, prolonged progression-free survival; SD, stable disease. PD, progressive disease; MDT, multidisciplinary team; TPS,treatment planning system; CTV, clinical target volume.

Consent for Publication

The authors obtained informed consent from the patient for publication of the case details and any accompanying images. This study was approved by the Ethics Committee of The Affiliated Huaian No.1 People's Hospital of Nanjing Medical University (Ethical Approval No.: KY-2025-262-01).

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Author Contributions

All authors have made significant contributions to the work reported in this study, including contributions to the conception of the study, study implementation, provision of professional knowledge interpretation and images; participation in the drafting, revision, or critical review of the manuscript; final approval of the version to be published; agreement on the journal to which the manuscript has been submitted; and agreement to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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