

## CASE REPORT

A case report of refractory pulmonary  
adenocarcinoma

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**Abstract**

As one of the most common types of carcinomas, lung cancer has high incidence and mortality rates. Among the pathological types of lung cancer, pulmonary adenocarcinoma is the most prevalent. Advancements in medical treatments have contributed to improved prognosis in pulmonary adenocarcinomas. However, this case report revealed a rare refractory lung adenocarcinoma, suggesting that further research and robust management strategies are needed to improve clinical outcomes. In this regard,  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography plays a very important role in the comprehensive evaluation of glucose metabolic activity in lung adenocarcinoma and the progression of metastasis in distant organs.

**Keywords:** Pulmonary adenocarcinoma;  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography; Treatment; Prognosis

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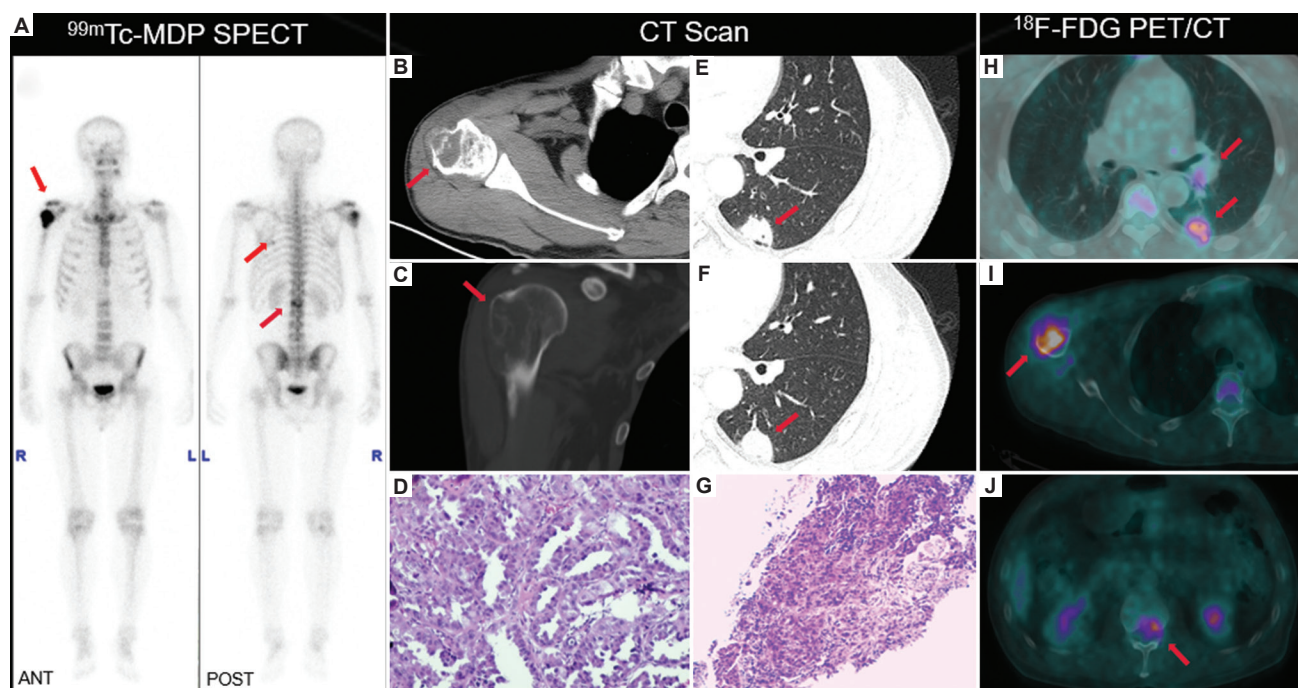
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**1. Background**

Pathological subtypes and clinical staging of lung adenocarcinoma affect patient treatment and prognosis directly. Good outcomes come from a systematic, standardized, and scientific treatment plan based on tumor type and precise clinical staging. This case is a rare refractory papillary adenocarcinoma, presented with a small pulmonary primary lesion but early extensive metastases and poor outcomes after robust systematic treatment medical treatment.

**2. Case presentation**

A 53-year-old man, with pain in the right shoulder joint as well as limited movement for 2 months and a family history of gastrointestinal malignant tumors, was admitted to the hospital for further diagnosis and treatment. The bone scan (Figure 1A) showed increased radioactivity at the proximal end of the right humerus, the left sixth rib, and the first lumbar vertebra that diagnosed metastatic lesions. Computed tomography (CT) scanning of the right shoulder joint (Figure 1B and C) presented destruction of the right humerus with surrounding soft-tissue masses. CT plain examination of the chest (Figure 1E and F) detected a nodule in the lower lobe near the pleura of the left lung and sized 24 mm × 18 mm, which has small bubbles inside. Pathological findings validated the metastatic lesions of the humerus (Figure 1D) were poorly differentiated adenocarcinoma of non-small cell lung cancer (NSCLC) from the lower lobe of the left lung (Figure 1G).  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/CT



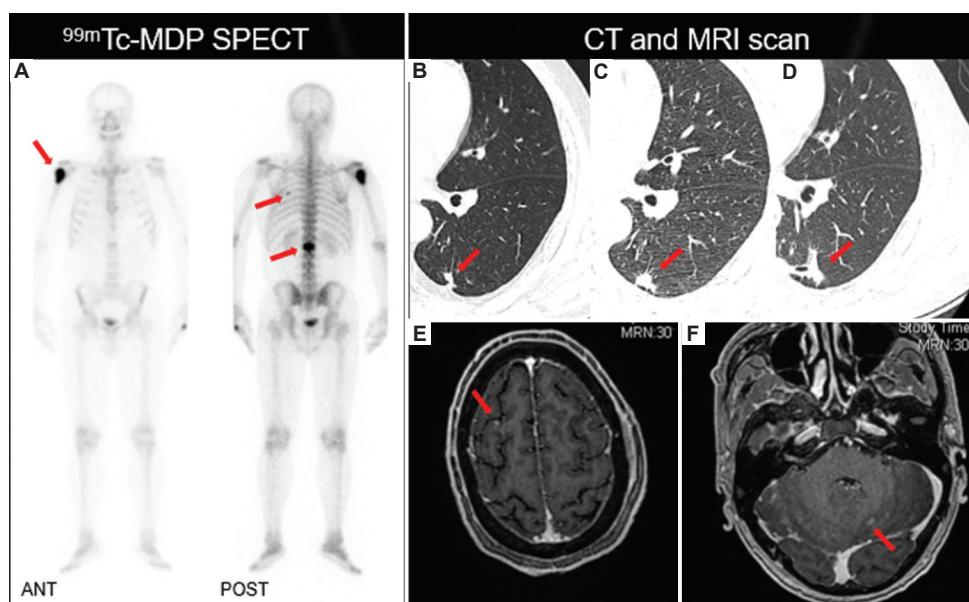
**Figure 1.** (A) Whole-body bone scan: The right humerus, the sixth rib on the left, and the first lumbar vertebra with increased radioactivity. (B and C) computed tomography (CT) scan of the shoulder joint: Destruction of right humerus with surrounding soft-tissue masses. (D) Pathology of the lesion of the right humerus, hematoxylin and eosin (H&E)  $\times 100$ : Microscopically, heterotypic cells are papillary and nest-like with infiltrating growth. (E and F) CT examination: A nodule near the pleura with small hollow bubbles inside, sized 24 mm  $\times$  18 mm, in the lower lobe of the left lung. (G) Pathology of the nodule in the lower lobe of the left lung, H&E  $\times 100$ : Microscopically, heterotypic cells are arranged in a nest-like pattern, infiltrating growth, large and deeply stained nuclei, and mitotic figures are visible. (H-J) Axial fused  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography/computed tomography ( $^{18}\text{F}$ -FDG PET/CT) images: The examination showed a diffuse strong FDG uptake in the nodule of the left lung (maximum standardized uptake value [SUVmax], 5.81), the proximal end of the right humerus and the first lumbar vertebra (SUVmax, 7.98).

( $^{18}\text{F}$ -FDG PET/CT) imaging (Figure 1H-J) was performed and detected additional metastatic mediastinal lymph nodes and bone metastasis lesions on the right ilium besides pulmonary nodule and bone metastasis lesions on the right humerus rib and lumbar. The staging result of  $^{18}\text{F}$ -FDG PET/CT showed that the case was in stage IVB and indicated a bad outcome for this patient, although a CT scan only showed a small primary lesion in the left lung.

The patient with NSCLC received salvage systemic therapy. The first stage of treatment was ametinib (110 mg qd, for 19 months) as a targeted drug owing to EGFR gene mutation, along with chemotherapy of pemetrexed (0.85 g, day 1) and cisplatin (40 mg, day 1–3) regimen (AP). After six cycles of chemotherapy, images of the CT scan (Figure 2B) showed a smaller lesion in the lower lobe of the left lung compared to pre-treatment images. However, 3 months later, the lesion in the left lung enlarged obviously (Figure 2C), and clinical treatment then changed accordingly with bevacizumab (600 mg). Unfortunately, 2 months later, the chest CT showed that the lesion was continuously increasing and not responding to bevacizumab. Therefore, clinical treatment with radiation (DT 60 Gy/30 Fx) was given to the left lung and

bone metastatic lesions; subsequent whole-body bone scan (Figure 2A) found that there were no significant changes in metastatic bone lesions, and chest CT scan showed slightly shrank of lesion size in the left lung within 3 months and then enlarged again (Figure 2D). After 6 months of traditional Chinese medicine treatment, the patient developed persistent headaches accompanied by nausea and vomiting. Chest CT scan detected multiple pleural thickening, and brain magnetic resonance imaging (Figure 2E and F) detected multiple intracranial metastases with leptomeningeal metastasis included in the study. Whole-brain radiation (DT 30 Gy/10 Fx) and immunotherapy with separizumab (240 mg) were going to be carried out on this patient but discontinued due to the patient's uncontrolled headache, nausea, vomiting, dizziness, and restlessness. The patient died within 2 months after brain metastasis.

The first symptom of this patient with a relatively small lesion of adenocarcinoma in the left lung was right shoulder pain for more than 2 months. A bone scan and  $^{18}\text{F}$ -FDG PET/CT were performed on the patient to stage and comprehensively assess the systemic progression of the left lung lesion before therapy, which indicated a poor



**Figure 2.** (A) The lesion in the lower lobe of the left lung after radiotherapy: The whole-body bone scan showed the right humerus, the sixth rib on the left, and the first lumbar vertebra with increased radioactivity. (B) After six cycles of chemotherapy: Computed tomography (CT) examination showed the nodule sized 10 mm × 5 mm in the lower lobe of the left lung. (C) Three months after six cycles of chemotherapy: CT scan showed the nodule sized 11 mm × 10 mm in the lower lobe of the left lung. (D) Three months after radiotherapy: CT images showed the nodule sized 16 mm × 12 mm nodules with increased solid parts in the lower lobe of the left lung. (E and F) After treatment with traditional Chinese medicine: The magnetic resonance imaging scan showed a high signal shadow with local enhancement on enhanced scanning in the left cerebellar hemisphere.

prognosis. Within 20 months after the diagnosis of the disease, the patient received targeted therapy (ametinib and bevacizumab), chemical therapy (pemetrexed with cisplatin), radiation therapy, and immunotherapy (separizumab). However, clinical outcomes were severely poor for this relatively rare refractory pulmonary adenocarcinoma, even after robust medical therapy, and the patient died in 2 years.

### 3. Discussion

Papillary carcinoma is known for its aggressive growth pattern and clinical behavior, which necessitates extensive research and individualized treatment approaches<sup>[1]</sup>. Strengthening the understanding of different pathological subtypes of pulmonary adenocarcinomas, such as invasive mucinous adenocarcinoma, colloid, fetal, and enteric adenocarcinoma, is essential for prognostic improvement<sup>[2]</sup>. Chemotherapy is a first-line treatment method for advanced lung adenocarcinoma, mainly including platinum-based dual drug combination chemotherapy (such as pemetrexed and cisplatin) and non-platinum based dual drug combination chemotherapy (such as capecitabine and cisplatin)<sup>[3]</sup>. Targeted therapy could prolong the survival period and improve the life quality of patients, following the significant progression in recent research works<sup>[4]</sup>. Many researchers indicated that patients with EGFR and EML4-ALK gene mutations and

positive expression of programmed death ligand 1 would benefit from treatment of targeted and immunosuppressive therapy such as icotinib and separizumab<sup>[3,5-7]</sup>. However, there have been scarce research and reports of refractory pulmonary adenocarcinoma which responded poorly to medical therapy. At present, the research on drug resistance in lung adenocarcinoma mainly focuses on targeted therapy and immunotherapy, but the auxiliary therapeutic effect of traditional Chinese medicine cannot be ignored. The overall survival period of patients who received pemetrexed maintenance therapy was longer than those who did not receive the therapy<sup>[5,8,9]</sup>. Chinese Medical Association guidelines for clinical diagnosis and treatment of lung cancer (2022 edition) recommend that patients with good performance status (PS) score and good chemotherapy tolerance may accept maintenance therapy when patients undergo 4–6 cycles of chemotherapy to improve their disease control, including complete remission, partial remission, and stability<sup>[10]</sup>. In this patient, with a PS score of 1, the lung lesion was significantly reduced after six cycles of chemotherapy, but maintenance treatment was not continued, which may be related to the progress of the patient's condition.

### 4. Conclusion

This case suggests that it is necessary to perform <sup>18</sup>F-FDG PET/CT before tumor therapy. The treatment of refractory

pulmonary adenocarcinoma remains a constant research challenge worldwide. It is necessary to assess patients comprehensively and apply clinical treatment guidelines flexibly. In addition, further understanding and research are still needed to improve the prognosis of these patients.

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## Conflict of interest

There is no conflicts of interest in this study.

## Author contributions

Conceptualization: Haiyan Li, Xia Lu

Investigation: All authors

Writing – original draft: Haiyan Li

Writing – review & editing: Haiyan Li, Xia Lu

## Ethics approval and consent to participate

Not applicable.

## Consent for publication

We obtained informed consent from study subjects for publishing their data.

## Availability of data

The original data of the study are included in the article, further inquiries can be directed to the corresponding author.

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