A Case Report: Concurrent Treatment Challenges and Outcomes in Patients with Pulmonary Tuberculosis coexisting Lung Cancer

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A Case Report: Concurrent Treatment Challenges and Outcomes in Patients with Pulmonary Tuberculosis coexisting Lung Cancer

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Background: Although the coexistence of pulmonary tuberculosis and lung carcinoma is rare, it poses challenges to treatment strategies. Understanding the clinical features and treatment outcomes of such patients is clinically significant. Objective: To analyze the clinical characteristics and treatment outcomes of coexisting pulmonary tuberculosis and lung carcinoma, aiming to enhance clinicians' comprehensive understanding of this condition. Methods: A retrospective analysis was conducted on a patient diagnosed with pulmonary tuberculosis coexisting with lung carcinoma at the First People's Hospital of Zigong City. Pathological and microbiological diagnostics were employed, and the diagnostic and treatment experiences were summarized. Results: The patient was an elderly male presenting mainly with cough and hemoptysis. Diagnosis of pulmonary tuberculosis with concomitant squamous cell carcinoma of the lung was confirmed through CT, bronchoalveolar lavage fluid targeted next-generation sequencing (tNGS), and pathological biopsy. After anti-tuberculosis treatment, concurrent sequential radiotherapy, and two cycles of chemotherapy, the disease was assessed as partially relieved. Conclusion: Although the coexistence of pulmonary tuberculosis and lung carcinoma is rare, the comprehensive treatment in this case demonstrated favorable outcomes. Currently, there is no standardized treatment protocol for such patients, emphasizing the need for further research in this specific patient population.

Keywords: pulmonary tuberculosis; non-small-cell lung cancer; radiotherapy; chemotherapy; anti-tuberculosis treatment.

Introduction

According to the 2020 Global Cancer Statistics report, there were 220,677 new cases of lung cancer worldwide, resulting in 1,796,144 deaths. Lung cancer accounts for 11.4% of all new cancer cases globally and 18% of cancer-related deaths. Compared to global averages, China has seen a high incidence and mortality rate of lung cancer, ranking first among all cancer types in terms of incidence and mortality[1,2]. As per the 2020 World Health Organization report, over 10 million new cases of tuberculosis (TB) were reported worldwide, with 1.4 million deaths attributed to the disease, marking it as one of the top global public health concerns. The incidence and mortality rates of pulmonary tuberculosis in China have consistently been at the forefront among Class A and B infectious diseases[3], especially in the Sichuan region where it is prevalent. The

primary treatments for lung cancer include chemotherapy, radiation therapy, and targeted therapies, often combining systemic and localized treatments. In contrast, the main treatment for pulmonary tuberculosis is primarily systemic chemotherapy. Currently, the incidence of pulmonary tuberculosis complicated by lung cancer is on the rise. These two diseases exhibit similarities in clinical and radiographic manifestations, posing challenges in differential diagnosis and treatment. Thus, further research and exploration into the comprehensive treatment of concurrent pulmonary tuberculosis and lung cancer are of utmost importance.

Lung cancer and tuberculosis (TB) are common respiratory diseases, stimulating both the immune and respiratory systems of the patients[4,5]. Lung cancer, a malignant tumor, arises from the abnormal proliferation of cells, while TB is a respiratory infectious disease caused by the Mycobacterium tuberculosis. Many lung cancer patients are diagnosed at intermediate to advanced stages, where chemo-radiotherapy is one of the prevalent therapeutic strategies. Radiotherapy is a localized treatment extensively used for patients at these stages. Pulmonary radiotherapy may lead to hematologic toxicity, pulmonary dysfunction, and liver function abnormalities. Chemotherapeutic agents for lung cancer include taxanes, platinum drugs, vinorelbine, and pemetrexed, while common anti-TB drugs include streptomycin, isoniazid, rifampicin, ethambutol, pyrazinamide, and levofloxacin. These medications carry side effects like hepatorenal toxicity, cardiotoxicity, vascular toxicity, hematologic toxicity, and gastrointestinal toxicity.

Consequently, the diagnosis and treatment of patients co-afflicted with pulmonary tuberculosis and lung cancer present a complex challenge. Determining an accurate diagnosis, minimizing the toxic side effects of treatments, and effectively controlling both lung cancer and tuberculosis merit our in-depth research.

Clinical History and Examination

The patient is a 68-year-old elderly male who worked as a sanitation worker. He sought medical attention at Fushun County People's Hospital due to "coughing and hemoptysis for over a month." An enhanced CT scan conducted on March 28th, 2023, revealed: 1. The appearance of a patchy shadow in the lingular segment of the left upper lobe with obstructed bronchus accompanied by obstructive inflammation; the exact cause needs further confirmation through a bronchoscopy examination. 2. Scattered patches, nodules, and linear images in both lungs, adjacent to the pleura with retraction, suggesting a high probability of secondary pulmonary tuberculosis. On March 29th, 2023, the patient underwent a bronchoscopic examination, and a tNGS test was performed on the bronchoalveolar lavage fluid, which revealed a positive result for Mycobacterium tuberculosis and the Enterobacter cloacae complex. A biopsy indicated non-small cell lung cancer, and the immunohistochemistry results were as follows: left upper lobe biopsy tissue showed tumor cells positive for CK, P40, and CK5/6, and negative for Syn and TTF-1. P53 was approximately 40% positive, and Ki-67 was approximately 40% positive. Based on HE staining and immunohistochemistry diagnosis, squamous cell carcinoma was suggested (Figure 1A).

The patient visited our hospital (The First People's Hospital of Zigong) on April 4th, 2023. He denied any history of smoking, alcohol consumption, or exposure to epidemic areas. Our hospital's tests showed: CEA 0.88ng/ml, SCC antigen 0.93ng/ml, and Cyfra 21-1 7.55ng/ml. A whole-body bone scan SPET-CT suggested a dot-like radiopharmaceutical enhancement image in the right paranasal sinus area, suggesting a benign lesion; no definitive signs of bone metastasis were observed (Figure 1B). Pulmonary function tests indicated moderate obstructive pulmonary ventilation dysfunction. A TB infection T-cell culture γ-interferon test was performed, showing the following results: Lymphocyte culture+IFN(N) 4.4 pg/ml, Lymphocyte culture+IFN(T) 144.60 pg/ml, Lymphocyte culture+IFN(P) 921.40 pg/ml, TB-IGRA(T-N) 140.20 pg/ml. The results were deemed positive.

A thoracic CT scan indicated a persistent patchy shadow in the lingular segment of the left upper lobe (Figures 2A, B). Abdominal and cranial enhanced CT scans showed multiple nodules in the right lobe of the liver with progressive enhancement, suggesting hemangiomas that require follow-up observation; multiple cysts were also observed in the liver along with calcifications. The cranial CT did not show any abnormalities, but there was a deviated nasal septum and inflammation in the left ethmoid sinus.

Methods

Based on the above results, the patient's diagnosis is:

1. Left lung squamous cell carcinoma, pT3N0M0, Stage IIB.

2. Secondary pulmonary tuberculosis, smear-negative, culture results pending, molecular biology test positive, undergoing initial treatment.

The patient began anti-tuberculosis treatment on April 8, 2023, following the recommendations from the tuberculosis department's consultation. Anti-tuberculosis regimen is as follows: Rifapentine capsules 0.45g, twice a week; Isoniazid tablets 0.3g, once daily; Ethambutol tablets 0.75g, once daily; Levofloxacin tablets 0.5g, once daily. Close monitoring of liver and kidney functions, as well as blood analyses, are essential during treatment.

Additionally, the patient underwent palliative radiotherapy for lung cancer on April 17, 2023, with the detailed plan as follows: Planning Target Volume (PTV): 6000cGy in 30 fractions, Gross Tumor Volume for lymph nodes (GTVnd): 6000cGy in 30 fractions. The plan was divided into two stages: the first stage was 5000cGy in 25 fractions for both PTV and GTVnd; the second stage was 1000cGy in 5 fractions for both PTV and GTVnd (Figure 2: Radiotherapy plan ABCD). The patient will continue anti-tuberculosis treatment during the radiotherapy period.

On August 1th, 2023, the patient entered the consolidation treatment phase. The anti-tuberculosis treatment plan is: Rifapentine capsules 0.45g, twice a week; Isoniazid tablets 0.3g, once daily; Ethambutol 0.75g, once daily.

The patient underwent four cycles of chemotherapy with the TC regimen on August 5th and August 26th and October 17th and November 7th, 2023, respectively. The specific drug dosages were: Paclitaxel 135mg/m2 + Carboplatin (ACU: 5, once every 21 days).

Conclusion and Results

One month after completing radiotherapy, the patient had a CT re-examination on July 3, 2023, which showed a significant reduction in the lung cancer lesion (see Figure 3,a2, b2,c2,d2) compared to before the radiotherapy (see Figure 3,a1, b1,c1,d1). No significant abnormalities were found in liver and kidney functions or blood analysis. Through the bronchoalveolar lavage fluid test combined with non-tuberculosis mycobacteria detection, the DNA of non-tuberculosis mycobacteria was found to be positive, but no tuberculosis mycobacteria were detected. Based on the consultation instructions from the tuberculosis department's doctor, the patient's anti-tuberculosis treatment was effective.

After two cycles, a therapeutic evaluation was conducted, revealing a slight reduction in the lung cancer lesion(see Figures 3 ,a3,b3,c3,d3) compared to before the chemotherapy(see Figure 3,a2, b2,c2,d2).

On December 16th, 2023, The patient completed anti-tuberculosis treatment. The treatment for pulmonary tuberculosis was effective, and no significant abnormalities were found in liver and kidney functions or blood analysis.

On December 26th, 2023, The patients was reexamined for the first time after all treatments finished. CT showed that the lung lesions were significantly smaller than before treatment (Fig 4 A,B), and the DNA of non-tuberculosis mycobacteria and tuberculosis mycobacteria weren't detected.

In short, after treatments, the patient's tumor was obviously reduced and stabilized, tuberculosis was cured. Both anti-tuberculosis treatment and Anti-tumor treatment is effective.

Discussion

Tuberculosis (TB) is an infectious disease caused by the Mycobacterium tuberculosis complex, characterized by granulomas with caseous necrosis. In contrast, lung cancer is a malignant tumor resulting from genetic mutations due to various factors leading to abnormal cell proliferation. According to studies conducted in China, the incidence of TB can increase the risk of developing lung cancer[6]. It has been found that

in pulmonary TB lesions of mice, most squamous cells exhibit abnormally high proliferative activity[7]. Cytokines produced from TB infection, such as TGF-β and IL-10, have immunosuppressive properties, which can enhance the incidence of tumors[8]. During the progression of lung cancer, cytokines like IL-4, IL-10, and TGF-β1 are produced. These factors assist in TB evasion from immune detection[9]. Moreover, some studies suggest that TB dissemination may occur during clinical lung cancer immunotherapy, but the precise mechanisms still require further investigation[10]. Compared to patients with only lung cancer or TB, those afflicted by both conditions have a shorter average survival period, with even shorter life expectancy for those with active TB[11].

The clinical symptoms of both lung cancer and TB have many similarities. In this case, the patient primarily presented with symptoms of coughing and hemoptysis, which are nonspecific. The gold standard for diagnosing TB is a positive sputum culture for Mycobacterium tuberculosis, although the positivity rate is relatively low[12]. At this juncture, radiographic examinations are crucial for both diagnosis and differential diagnosis. CT scans have a high accuracy rate, over 90%, in diagnosing concurrent TB and lung cancer, with common signs including pleural adhesions, pleural retraction, bronchial narrowing, and bronchial obstruction[13]. However, CT scans have a lower specificity for fibrotic changes due to benign lesions, leading to frequent false-positive results[14]. There have been numerous recent reports on the diagnostic use of MRI for thoracic diseases, where MRI can predict changes in TB lesions based on T2 signal intensity[15]. In recent years, 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) imaging has been widely confirmed for the specific diagnosis of malignant tumors[16]. However, due to its high cost and radiation, it is not suitable for screening lung cancer combined with TB. Ultimately, diagnoses of both lung cancer and TB should be confirmed through etiology and histopathology.

There have been some clinical reports on lung cancer concurrent with pulmonary tuberculosis [17,18], but the number remains limited. The majority of patients face the choice between anti-tuberculosis treatment and anti-tumor therapy. Over 80% of lung cancer patients are diagnosed in the intermediate or advanced stages, with the main treatment approaches being concurrent or sequential radiotherapy, chemotherapy, and targeted therapy. Literature has reported poor prognoses for patients with lung cancer and concurrent tuberculosis post-surgical treatment. Smoking history, irritative cough, TNM staging, and the presence of prior tuberculosis lesions have all been identified as risk factors for non-small cell lung cancer patients with active tuberculosis [19]. There is also literature documenting cases of lung adenocarcinoma patients with EGFR mutations treated with afatinib in combination with anti-tuberculosis therapy. Studies indicate that the combination of erlotinib and anti-tuberculosis treatment can effectively control both tuberculosis and the tumor [18].

This paper reports a case of a patient with squamous cell carcinoma of the lung concurrent with pulmonary tuberculosis, who declined genetic mutation testing. Radiotherapy is a commonly used local treatment for malignant tumors. Compared to chemotherapy, its toxic effects on the patient's liver, kidney functions, blood, gastrointestinal tract, and respiratory system are relatively less. Therefore, we opted for concurrent radiotherapy for lung cancer during the intensive phase of tuberculosis treatment. During the intensive phase of tuberculosis, a combination of four drugs is typically used. Isoniazid is primarily metabolized through the acetylation reaction mediated by NAT2, while rifampin is predominantly deacetylated to form acetylated rifampin. The combined use of these two drugs increases hepatotoxicity[20]. In this report, the patient chose rifapentine capsules, which ensures effective treatment concentrations while reducing side effects[21]. Ethambutol is mainly metabolized in the liver and excreted through the kidneys. Compared to isoniazid and rifampicin, its hepatotoxicity is minimal[22]. Aminoglycosides, such as streptomycin, kanamycin, and amikacin, are primarily metabolized in the kidneys. Among them, streptomycin has a high ototoxicity, but its nephrotoxicity is lower than other aminoglycosides. These drugs exhibit concentration-dependent bactericidal effects; hence, reducing drug dosage is not recommended to prevent an increased risk of drug resistance[23]. Quinolones, like ofloxacin and moxifloxacin, are metabolized in the body through both liver and renal pathways, with approximately 52% through the liver and 45% through the kidneys[23]. During the patient's anti-tuberculosis treatment and radiotherapy, we continuously monitored their complete blood count, liver and kidney functions, and electrolytes, and no abnormalities were observed.

The patient entered the consolidation phase of combined therapy, during which two or three drugs are typically administered in tandem. The treatment regimen was adjusted to rifapentine capsules, isoniazid tablets, and ethambutol. At this stage, the anti-tuberculosis treatment's impact on liver and kidney functions is relatively minor. Considering the patient's upcoming chemotherapy phase, after consultation with the pharmacy department, we opted for a treatment scheme with paclitaxel and carboplatin. Paclitaxel acts by stabilizing microtubules, thus inhibiting tumor cell division. It is primarily metabolized in the liver via CYP2C8 and CYP3A4, different from the metabolism pathway of tuberculosis drugs. However, liver functions still need to be stringently monitored during treatment. Platinum-based drugs play a crucial role in lung cancer chemotherapy. Compared to cisplatin, carboplatin has higher solubility, reduced toxicity, no nephrotoxicity, and reduced ototoxicity[24]. Considering the patient's financial situation, we selected this regimen. Throughout the treatment, we closely monitored the patient's liver and kidney functions and blood routine. The patient demonstrated good tolerance and did not experience any adverse reactions.

In conclusion, the patient underwent combined treatment for tuberculosis and lung cancer. Upon evaluation, therapeutic results were observed for both diseases, with significant lesion reduction. However, when treating patients with concurrent lung cancer and pulmonary tuberculosis, the selection of an appropriate treatment plan should consider the patient's specific circumstances. How to effectively treat both diseases simultaneously to enhance patient survival remains an area we need to further explore.

Informed consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Author's contribution

Na Wang is responsible for the formulation of the treatment plan for patients with lung cancer and article writing, Yajiao Wang is responsible for the formulation of tuberculosis plans, Ke Liu is responsible for the formulation of patients' radiotherapy plan, the quality control of radiotherapy and the collection of patients' pictures. Shu Cao is responsible for the review of patients' treatment plans and the editing and review of articles.

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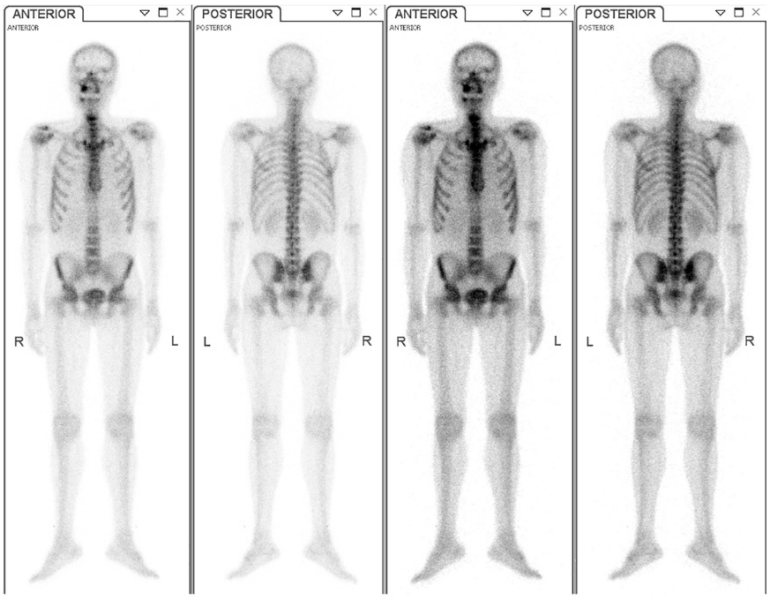
Figures:

Fig.1

A



B

Figure 1, A shows the pathological diagnosis results of the patient; B is the result of the patient's bone scan.

Fig. 2

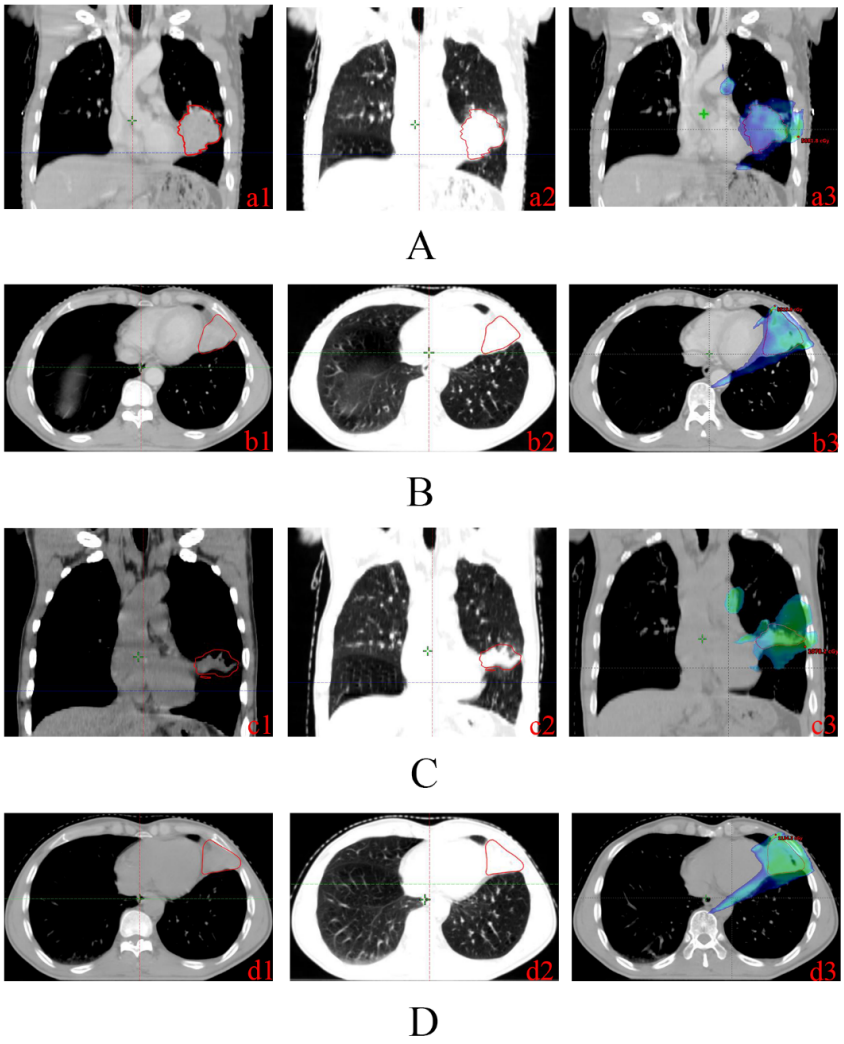


Fig. 2, patient radiotherapy plan, A and B are one-course radiotherapy plans, PTV: 5000 cGy/25f, GTVnd: 5000 cGy /25f; C and D are two- course radiotherapy plan: PTV:1000 cGy/5f, and GTVnd: 1000 cGy/5f. The focus of lung cancer was smaller than before during two-course radiotherapy.

Fig. 3

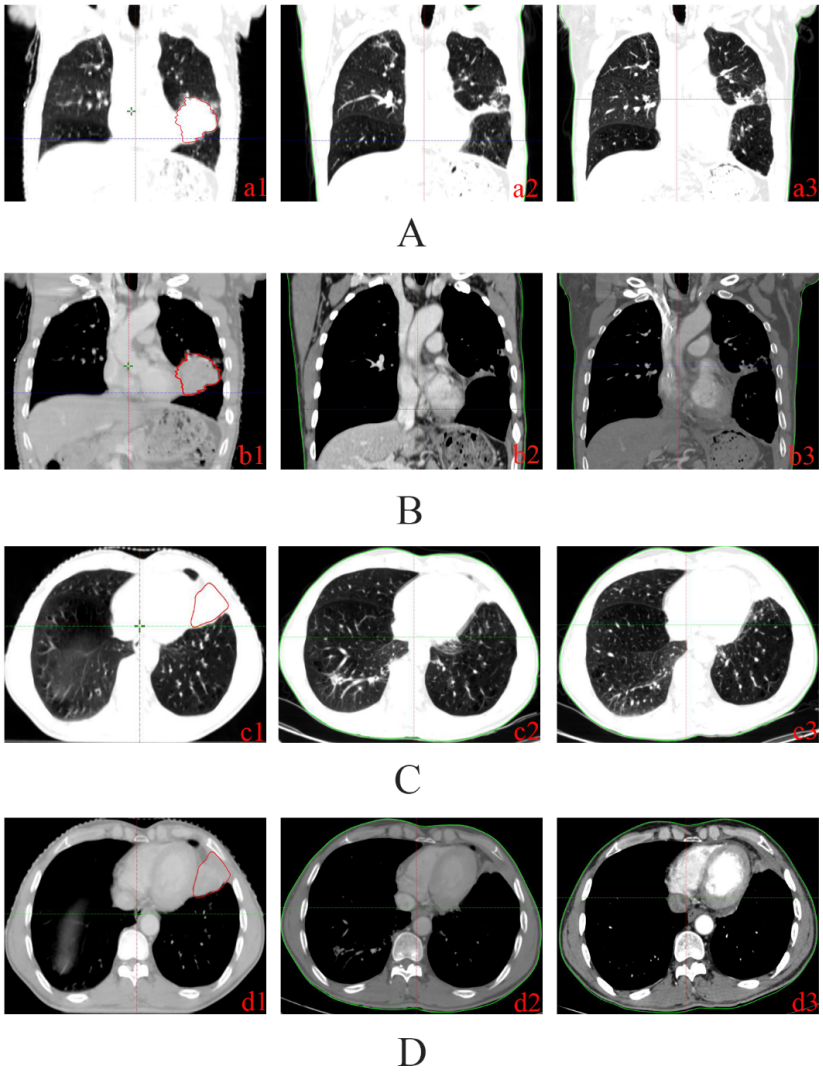


Fig. 3. The results of patients before and after treatment are compared, and the treatment is effective. Figure A shows the coronary position, and the lung window: a1 before treatment, a2 after one month of radiotherapy, and a3 after two cycles of chemotherapy. Figure B shows the coronal position, mediastinal window: b1 before treatment, b2 after one month of radiotherapy, b3 after two cycles of chemotherapy. Figure C shows the horizontal position, and the lung window: c1 before treatment, c2 after one month of radiotherapy, and c3 after two cycles of chemotherapy. Figure D shows the horizontal position, and the mediastinal window: d1 before treatment, d2 after one month of radiotherapy, and d3 after two cycles of chemotherapy.

Fig.4

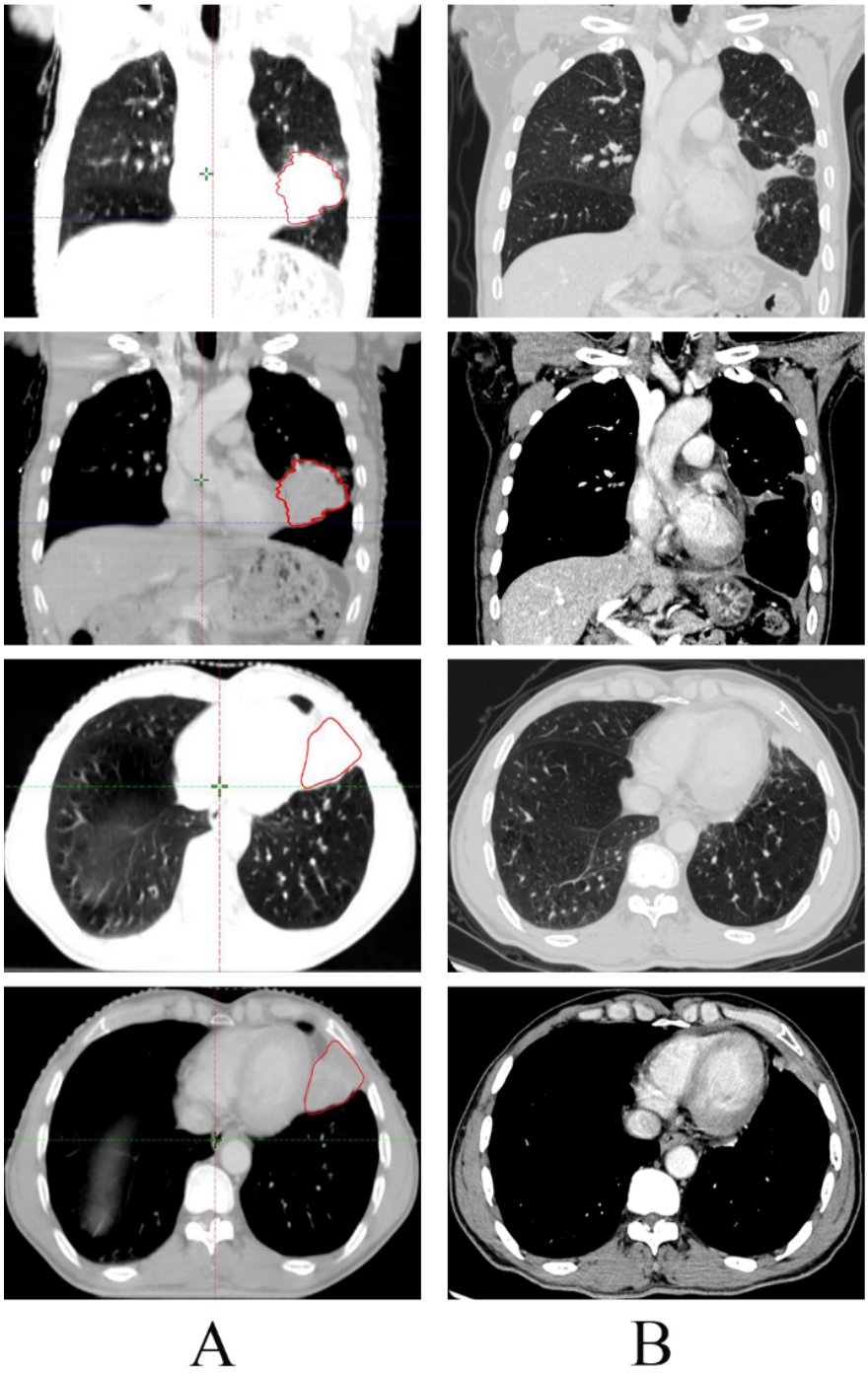


Fig. 4 The results of the patient before and after all treatments are compared, and the treatment is effective. A shows the coronary position and the horizontal position In the pulmonary window and mediastinal window respectively before treatments (April 17th, 2023). B shows the coronary position and the horizontal position In the pulmonary window and mediastinal window respectively after all treatments (December 26th, 2023).

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