Letter to the Editor

Fatal acute interstitial pneumonia induced by radiotherapy alone

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Introduction

Radiotherapy (RT) is one of the principal treatment modalities for cancers, especially for medically inoperable lung carcinoma. Radiation-induced lung injury (RILI), which is usually divided into an early inflammatory response known as radiation-induced pneumonitis and a late, chronic complication known as radiation-induced lung fibrosis, remains a clinically significant adverse effect in radiation oncology. Chest computed tomography (CT) characteristics are distinct for these 2 types of injury and can be used to differentiate between them (1). With the advancement of radiation delivery techniques, the incidence of radiation pneumonitis has gradually decreased over recent years (2,3). The advent of immunotherapy has increased the incidence of severe interstitial changes in those patients receiving RT combined with immunotherapy. However, severe interstitial pneumonia (IP) induced by RT is rare. Here, we present a case of a patient with lung carcinoma accompanied by superior vena cava (SVC) syndrome. He experienced fatal acute IP after receiving RT without other treatments such as chemotherapy, targeted therapy, or immunotherapy.

Case presentation

A 77-year-old male patient was referred to the Department of Oncology of the 970 Hospital, with complaints of tightness in the chest and feeling of suffocation for nearly one month. He had no history of smoking or drinking and no history of occupational exposure, but he did have a medical history of coronary heart disease and had previously undergone coronary stent implantation. He took aspirin and atorvastatin regularly. He denied other underlying diseases such as chronic obstructive pulmonary disease (COPD) and autoimmune diseases. CT images showed a mass in the right upper lobe; lymph node enlargement in the mediastinum, pulmonary hilum, and the subpleural region of the left upper lobe; increased and disordered lung texture; locally interlobular septal thickening; very slight reticular shading in the periphery of lung fields with subpleural predominance; unclear boundaries; displacement of the local great vessels, trachea, and esophagus; and narrowing of the tracheal lumen. Finally, he was diagnosed with squamous cell lung carcinoma accompanied by SVC syndrome (stage III). As SVC syndrome is an oncological emergency, RT was applied to the enlarged lymph nodes in the mediastinum (radiation dose: 1,500 cGy/5 f + 4,000 cGy/20 f; V5: 30.9%; V20: 16.8%; and Dmean: 797.6 cGy) to ameliorate the compression on SVC, which was completed in May 2016. No chemotherapy, targeted therapy, or immune checkpoint inhibitor therapy was administered to the patient, and his symptoms were relieved after he received RT.

However, less than one week after the completion of RT, the patient experienced chest distress and feeling of suffocation again. CT images revealed decreased transmittance of both lung fields, patchy or large areas of high-density shadow and ground-glass opacity with predominance in the left lung and the upper lobe of right lung, increased and disordered lung texture, locally interlobular septal thickening, and reticular shading and honeycomb changes in both lungs, indicating the presence of IP. Radiological examinations excluded the possibility

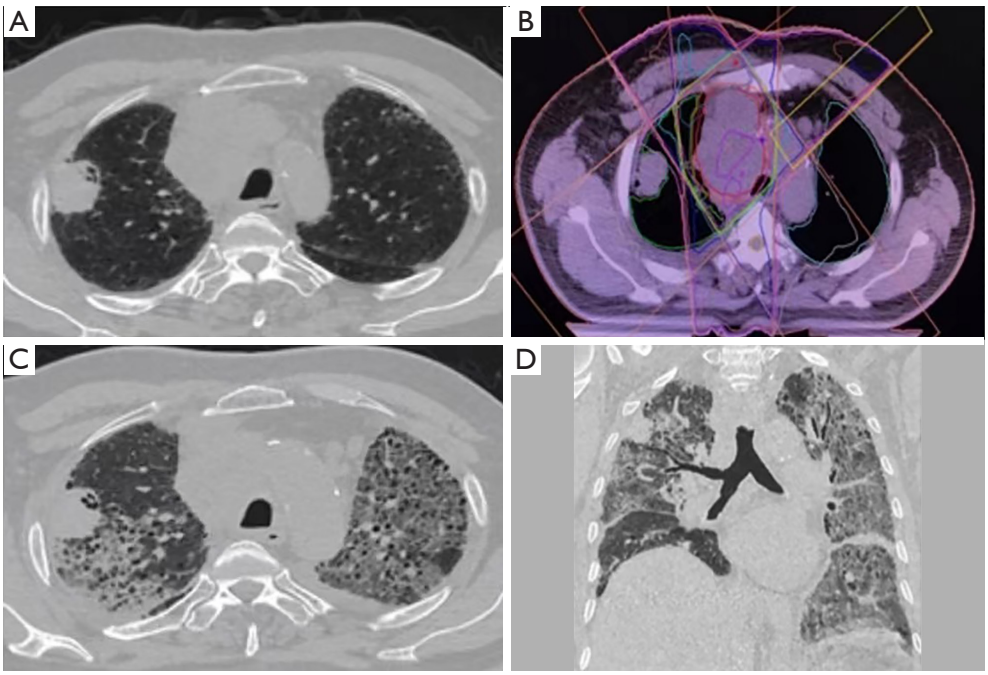

Figure 1 Chest CT before and after radiotherapy. (A) Pretreatment chest CT with a lung window showed a mass in the right upper lobe; lymph node enlargement in the mediastinum, pulmonary hilum, and the subpleural region of the left upper lobe; and minimal reticular opacities with subpleural predominance. (B) Radiotherapy was applied to the mediastinum using a 3D-shaped technique. (C,D) A CT scan after completion of radiotherapy in the axial plane (C) and coronal reconstruction (D) showed a honeycomb lung aspect, which was more evident in the left lung. CT, computed tomography; 3D, three dimensional.

of carcinomatous lymphangitis, and further laboratory examinations excluded the possibility of *Pneumocystis jirovecii* pneumonia, cytomegalovirus infection, and other viral infections. In addition, fluconazole was administered to prevent fungal infections. Due to the possibility of acute exacerbation of subtle IP, the patient was treated with methylprednisolone in timely fashion. However, he failed to improve after receiving symptomatic treatments consisting of corticosteroids, broad-spectrum antibiotics, and oxygen inhalation (*Figure 1*). He experienced progressive aggravation of dyspnea and died about 1 month after the completion of RT.

All procedures performed in this study were in accordance with the ethical standards of the relevant institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

RILI is a key potential adverse event of thoracic RT, the incidence of which has reached up to 30% in some settings (4). Treatment-related factors (such as radiation dose, fractionation, lung dose, and combined treatment), tumor-related factors (such as tumor location and tumor volume), and patient-related factors (such as age, comorbidities, smoking habit, and genetic phenotypes) all affect the incidence of RILI. Significantly, patients who receive RT combined with other treatments, especially immunotherapy, may be at higher risk for RILI (1). However, severe interstitial changes in both lungs induced by RT is rare. Here, we report on a patient with squamous cell lung carcinoma accompanied by SVC syndrome who experienced fatal acute interstitial changes in both lungs after he received RT without other combined treatments.

RT is the primary treatment for patients with locally advanced non-small cell lung cancer (NSCLC), especially accompanied with SVC syndrome (5). Among patients with advanced NSCLC, 5–10% have IP at definite diagnosis (6).

Thoracic RT induces acute aggravation of pre-existing IP in 20–30% of patients with lung cancer and concurrent IP. In addition, the mortality rate is extremely high if acute exacerbation of pre-existing IP occurs (7). Consequently, the risk of death during thoracic RT is reported to be 165.7 times higher in patients with lung cancer accompanied by comorbid IP than in those without IP (8). Even if pre-existing IP is slight and no shadows are observed in the irradiated area, RT can still cause lethal acute aggravation. Regardless of how evident the therapeutic effect of RT for lung cancer is, once an acute aggravation of pre-existing IP occurs, there is a high probability that it will be lethal to the patient. Risk factors for acute exacerbation of IP induced by RT include the proportion of normal lungs irradiated and the mean lung dose that the normal lungs have received (9,10). Timely application of glucocorticoids and immunosuppressants may benefit some patients.

Conclusions

Although no ideal, reliable biomarkers or risk models of RILI are currently available in clinical practice, more promising research results are emerging. Risk factors related to patients, treatments, and tumor can all influence the severity and extent of RILI. Underlying conditions such as interstitial lung disease are closely associated with increased risk of RILI. For those with pre-existing interstitial pneumonia, RT should be avoided as much as possible. Dose distribution parameters remain one of the most important risk factors of lung injuries. If RT is necessary, precise planning is critical (V5 and Dmean should be maintained as low as possible) for decreasing the volume of irradiation to normal lungs. It is essential to prevent the occurrence and acute exacerbation of severe interstitial changes induced by RT.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-823/coif). All authors report that this research was funded by the Shandong Medical Association clinical research fund (grant No. YXH2022ZX02042). The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the relevant ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

References

1. Yan Y, Fu J, Kowalchuk RO, Wright CM, Zhang R, Li X, Xu Y. Exploration of radiation-induced lung injury, from mechanism to treatment: a narrative review. Transl Lung Cancer Res 2022;11:307-22.
2. Käsmann L, Dietrich A, Staab-Weijnitz CA, Manapov F, Behr J, Rimner A, Jeremic B, Senan S, De Ruysscher D, Lauber K, Belka C. Radiation-induced lung toxicity - cellular and molecular mechanisms of pathogenesis, management, and literature review. Radiat Oncol 2020;15:214.
3. Konkol M, Śniatała P, Milecki P. Radiation-induced lung injury - what do we know in the era of modern radiotherapy? Rep Pract Oncol Radiother 2022;27:552-65.
4. Keffer S, Guy CL, Weiss E. Fatal Radiation Pneumonitis: Literature Review and Case Series. Adv Radiat Oncol 2020;5:238-49.
5. Narang M, Mohindra P, Mishra M, Regine W, Kwok Y. Radiation Oncology Emergencies. Hematol Oncol Clin North Am 2020;34:279-92.

6. Raghu G, Nyberg F, Morgan G. The epidemiology of interstitial lung disease and its association with lung cancer. Br J Cancer 2004;91 Suppl 2:S3-10.
7. Ikeda S, Kato T, Kenmotsu H, Sekine A, Baba T, Ogura T. Current Treatment Strategies for Non-Small-Cell Lung Cancer with Comorbid Interstitial Pneumonia. Cancers (Basel) 2021;13:3979.
8. Ohe Y, Yamamoto S, Suzuki K, Hojo F, Kakinuma R, Matsumoto T, Ohmatsu H, Nishiwaki Y. Risk factors of treatment-related death in chemotherapy and thoracic radiotherapy for lung cancer. Eur J Cancer 2001;37:54-63.
9. Hagiwara Y, Nakayama Y, Kudo S, Hayakawa T, Nakamura N, Kitamoto Y, Takahashi S, Tsujino K, Kubo N, Tamaki Y, Nagata Y; Japan Radiation Oncology Study Group (JROSG) Working Subgroup for Lung and Mediastinal Tumors. Nationwide survey of radiation therapy in Japan for lung cancer complicated with interstitial lung disease. J Radiat Res 2020;61:563-74.
10. Chen H, Senan S, Nossent EJ, Boldt RG, Warner A, Palma DA, Louie AV. Treatment-Related Toxicity in Patients With Early-Stage Non-Small Cell Lung Cancer and Coexisting Interstitial Lung Disease: A Systematic Review. Int J Radiat Oncol Biol Phys 2017;98:622-31.

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