

CASE REPORT

Radiation-induced pseudomembranous tracheobronchitis: A report of two cases

Hye Sook Choi 

Internal Medicine, Kyung Hee University Medical Center, Seoul, Republic of Korea

Correspondence

Hye Sook Choi, Internal Medicine, Kyung Hee University Medical Center, 23 Kyungheedaero, Dongdaemung-gu, Seoul, Republic of Korea.
Email: maxymus72@hanmail.net

Abstract

Radiation therapy can cause radiation pneumonitis, organizing pneumonia, and lung fibrosis. Radiation-induced pseudomembranous bronchitis is a rare condition. Here, we describe a rare case each of pseudomembranous tracheobronchitis and pseudomembrane with total bronchial obstruction which developed after thoracic radiotherapy. A 50-year-old man presented paroxysmal severe cough 1 month after concurrent chemoradiotherapy for small-cell lung cancer. Bronchoscopy revealed a whitish membrane in the trachea and bronchus, which were the fields of radiation. Another 60-year-old man complained of dyspnea 7 months after radiation therapy for metastatic lymph node adenocarcinoma. Bronchoscopy demonstrated a membrane with total obstruction of right lower lobar bronchus, which was the area of radiation. The pathological findings of histological examination in both cases demonstrated radiation-induced pseudomembranous tracheobronchitis. Patients in both cases responded well to steroids and the pseudomembrane disappeared. If patients who have received thoracic radiation therapy complain of persistent cough, bronchoscopy may be helpful.

KEYWORDS

bronchoscopy, lung cancer, pseudomembranous tracheobronchitis, radiation

INTRODUCTION

Radiation therapy is one of the treatment modalities for lung cancer. However, the effects of radiation are not specific to cancer cells but also affect normal cells. Thoracic radiotherapy may induce lung injuries, mainly radiation-induced pneumonitis, radiation-induced lung fibrosis, radiation-induced bronchiolitis obliterans organizing pneumonia,^{1,2} and radiation-induced bronchitis.^{3,4} We report two rare cases of radiation-induced pseudomembranous tracheobronchitis with or without bronchial obstruction in lung cancer patients.

CASE REPORT**Case 1**

A 50-year-old man presented with worsening cough in August 2019. He had a history of pulmonary tuberculosis

30 years ago. He had a smoking history of 45 pack years and had quit smoking 3 years ago. He also had chronic obstructive pulmonary disease (COPD), which was treated with long-acting inhaled bronchodilators. He was diagnosed with small-cell lung cancer of limited stage of the right upper lobe (RUL) and right hilar and mediastinal lymph nodes (LNs) in May 2019. He had been treated with chemotherapy of etoposide and cisplatin every 3 weeks for four cycles. He had also been treated with concurrent radiation therapy of a daily 220-cGy dose, with a total 66-Gy dose from June 5, 2019, to July 17, 2019.

During radiation therapy, his dry cough began and got worse. The cough did not improve even with codeine, sedatives, or narcotic pain relievers. One month after completion of radiation therapy, chest X-ray showed new consolidation on the right upper lung field. We performed a chest computed tomography (CT) scan, and it revealed radiation pneumonitis and a thickened airway wall (Figure 1a). The bronchoscopy showed mucosal edema and diffuse whitish

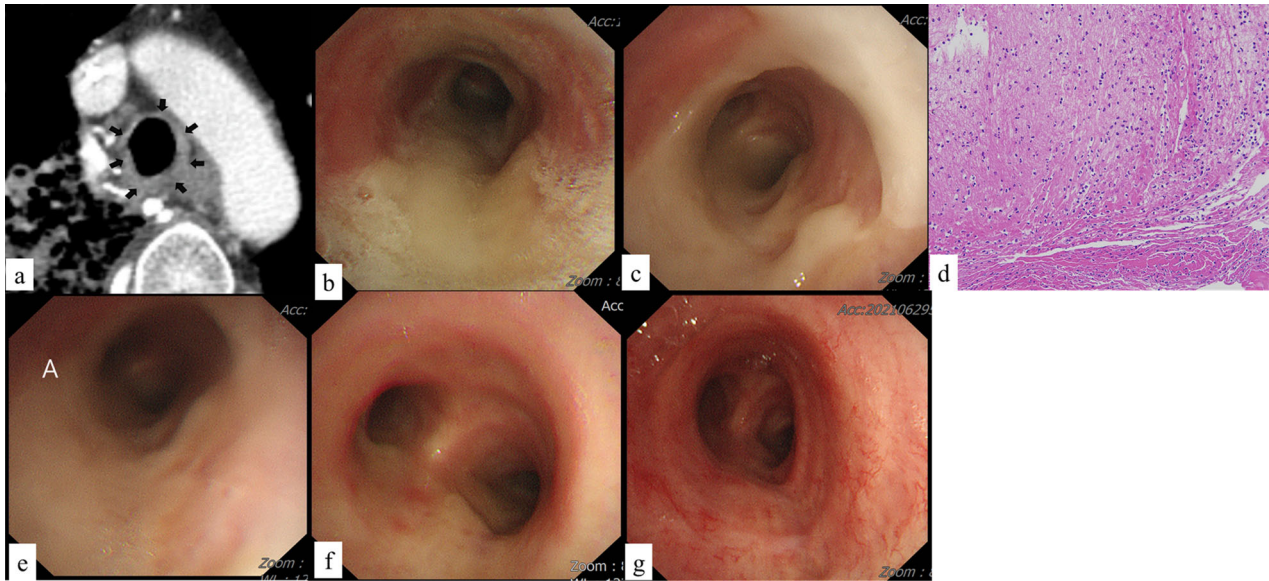


FIGURE 1 (a) Chest computed tomography (CT) showing the thickened trachea wall (black arrows). Bronchoscopy showing (b) yellowish plaque in the posterior wall of the trachea and (c) pseudomembrane progression to the anterior wall of the trachea the next day. (d) Histopathology of pseudomembrane showing inflammatory cells and fibrinous exudate (hematoxylin and eosin stain, $\times 200$). (e) Improved pseudomembrane after 3 days of steroid use and (f) 40 days of steroid use. (g) Bronchoscopy taken 7 months after (c) showing the pseudomembrane had disappeared.

plaques with membrane formation in the trachea and main bronchus (Figure 1b). To exclude a microbiologic cause, we tried to do a biopsy of the membrane of trachea using forceps. Two days later, follow-up bronchoscopy showed a more aggravated whitish patch with membrane formation to the anterior wall of the trachea (Figure 1c). Pathologic findings of membrane showed necrotic fibrin and inflammatory cells (Figure 1d). According to these findings, we diagnosed pseudomembranous tracheitis and bronchitis. We started prednisolone 50 mg/day. After 3 days of steroid administration, the whitish patch had improved on the follow-up bronchoscopy (Figure 1e). After 40 days of steroid administration, the whitish patch disappeared (Figure 1f) and the steroid was tapered after 3 months of use. After 7 months, there was no pseudomembrane in the bronchoscopy findings (Figure 1g).

Case 2

A 60-year-old man presented with worsening cough in February 2022. He had a smoking history of 15 pack years and had quit smoking 6 years ago. He had COPD treated with inhaled long-acting bronchodilators. He was diagnosed with adenocarcinoma of the RUL of stage IB and had undergone RUL posterior segmentectomy on February 2019. In April 2021, metastatic left interlobar LN developed, and a fractional stereotactic radiosurgery of 17 Gy daily, three times with a total dose of 51 Gy for metastatic left interlobar LN was performed. Chemotherapy was done 4 cycles, every 3 weeks of pemetrexed and cisplatin chemotherapy were administered, and then a monotherapy of pemetrexed was

maintained every 3 weeks. Radiation pneumonitis developed in September 2021 and was treated with oral prednisolone 30 mg/day from September 2021, which was tapered in January 2022.

After stopping prednisolone, a dry cough developed. We performed chest CT scan for surveillance of lung cancer. The chest CT scan and chest X-ray (Figure 2a) revealed fibrotic changes of previously treated radiation pneumonitis on the right middle lobe and right lower lobe (RLL) without new lesions. Despite the administration of antitussive drugs, the cough worsened. Three days later, dyspnea developed and the follow-up chest X-ray (Figure 2b) showed new atelectasis in the right lower lung field compared to previous chest X-ray (Figure 2a). We performed bronchoscopy and it showed whitish membrane (Figure 2c) with total obstruction of the RLL lobar bronchus (Figure 2d). We removed the whitish membrane of the RLL bronchus and the obstructed RLL bronchus reopened (Figure 2e). Pathologic findings of the whitish membrane revealed fibrin clot and inflammatory exudate without evidence of malignancy or infection (Figure 2f). On the basis of all these findings, we finally made a diagnosis of pseudomembranous bronchitis with bronchial obstruction after radiation therapy. We restarted prednisolone therapy 30 mg/day for pseudomembranous bronchitis. The pseudomembrane disappeared and the bronchial obstruction also improved on follow-up bronchoscopy.

DISCUSSION

Risk factors for radiation lung injuries are age older than 65, female, nonsmoker, poor performance status, higher

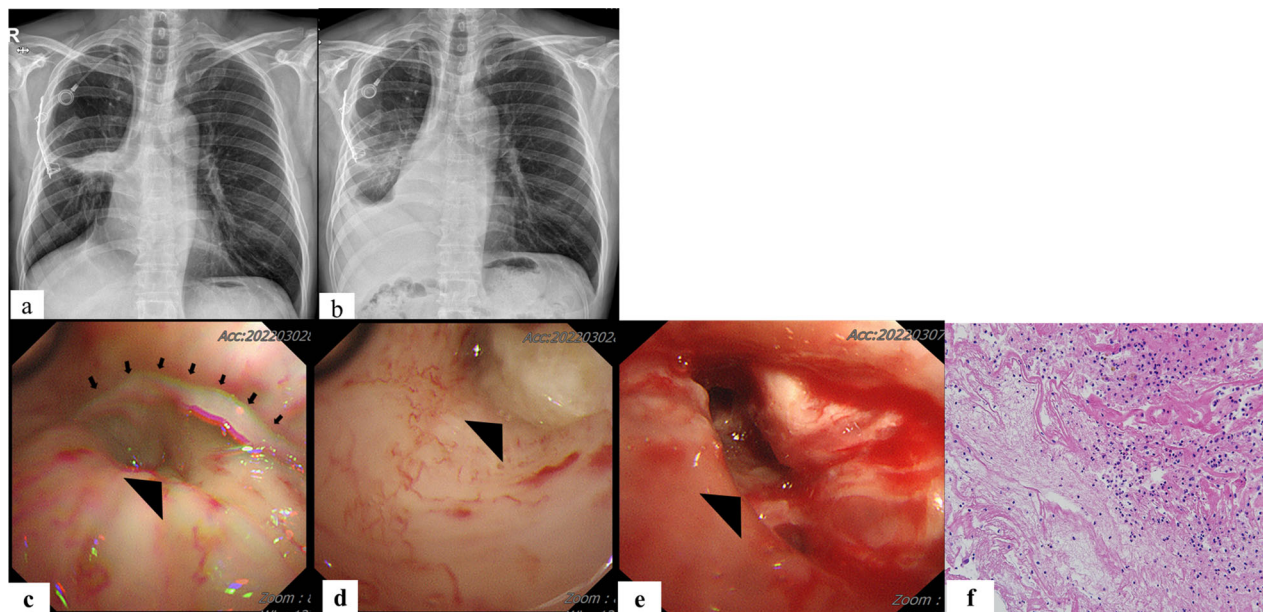


FIGURE 2 Chest X-ray showing (a) fibrotic change after radiation therapy in the right middle lung field. Three days after (a), (b) chest X-ray showing atelectasis and bronchoscopy showing (c) pseudomembrane (black arrows) at the entrance to the right lower lobar bronchus (black triangle) and (d) obstruction of the right lower lobar bronchus with pseudomembrane (black triangle). (e) Reopening of the right lower lobar bronchus (black triangle) after removal of the pseudomembrane using forceps. (f) Histopathology of the pseudomembrane showing inflammatory exudate (hematoxylin and eosin stain, $\times 200$).

radiation dose, sequential chemoradiation therapy, and COPD.⁵ Case 1 and 2 patients both had COPD but were younger than 65 years. Radiation-induced lung injuries mainly include radiation pneumonitis, lung fibrosis, and organizing pneumonia.^{6,7} Radiation bronchitis with stenosis or granulation was reported in lung cancer patients, but they had received brachytherapy^{3,4} or combined external-beam and high dose-rate iridium brachytherapy.⁸ Radiation bronchitis was reported in esophageal cancer patients who had a total 68.4 Gy dose.⁹

Pseudomembranous tracheobronchitis is a rare condition that shows a pseudomembrane in the airway. The exact pathogenesis and pathology of the pseudomembrane formation in the airway has not been clarified. Presumed mechanisms are radiation-induced injury of epithelial and endothelial cells, and exudation.⁷ Pseudomembranous tracheobronchitis due to unknown cause with severe bronchial obstruction,¹⁰ *Aspergillus*,^{11–14} or *Mycoplasma pneumoniae*¹⁵ have been reported. However, there are no reports about radiation-induced pseudomembranous tracheobronchitis or pseudomembrane with bronchial obstruction in lung cancer patients. The case 1 patient developed radiation pneumonitis and pseudomembranous tracheobronchitis 1 month after radiation therapy. The pseudomembrane was observed in the trachea and the bronchus exposed to radiation and became thicker. Although the optimal corticosteroid types, dosage, and duration have not been evaluated prospectively,⁵ radiation lung injuries usually improve and recover quickly with corticosteroid treatment.⁵ We started prednisolone 1 mg/kg because the pseudomembrane was

severe and the patient could not sleep due to severe frequent paroxysmal cough. The case 2 patient was initially diagnosed with radiation pneumonitis after stereotactic radiotherapy and was treated with prednisolone 0.5 mg/kg for 3 months. One month after stopping prednisolone, the patient developed sudden bronchial obstruction due to pseudomembrane. To the best of our knowledge, this is the first report of airway obstruction caused by pseudomembranous bronchitis after radiation therapy in a lung cancer patient. In this report, the patients were former smokers and had COPD. On the contrary, Pezzuto et al. reported that smoking cessation notably improved pulmonary functional parameters.¹⁶ Condoluci et al. reported that non-smokers showed better outcomes of radiation therapy compared to smokers.¹⁷ Cihanbeylerden et al. reported no relationship between pulmonary function and survival in patients with operable lung cancer.¹⁸ The risk factors for pseudomembranous tracheobronchitis after radiation therapy are not yet known. We suggest that smoking or COPD might be related to the development of pseudomembrane in the airway after radiation therapy. Usually, lung injury by stereotactic radiotherapy is lower than for conventional radiation therapy. In the case 2 patient, what might have caused the pseudomembrane in the targeted area with obstruction? It might be the host factor such as smoking history or immune mechanism. However, there is no clarified evidence. Targeted stereotactic radiotherapy can also form a pseudomembrane, especially if the target was close to the bronchus. We need to consider pseudomembrane formation when a patient complains of respiratory

symptoms. Just as we did to find the exact cause and mechanism, we did not know how to prevent it. Further studies will be needed.

Pseudomembranous tracheobronchitis usually does not manifest on chest X-ray, except in cases with obstruction or pneumonitis. When a patient presents with cough after radiation therapy, a first chest X-ray will be needed to exclude radiation pneumonitis. In such cases, we tried to use antitussive drugs because the chest X-ray did not show new lesions. If cough persists after radiation therapy in lung cancer patients or the chest CT scan does not reveal progression of lung cancer or radiation pneumonitis, we should perform bronchoscopy though chest X-ray.

In conclusion, we reported two rare cases of radiation-induced pseudomembranous tracheobronchitis and bronchial obstruction due to pseudomembrane in lung cancer patients, and they responded well to steroids. If thoracic radiation-treated patients have persistent cough, bronchoscopy may be helpful.

AUTHOR CONTRIBUTIONS

Hye Sook Choi: conceptualization, data curation, investigation, supervision, visualization, writing-original draft preparation, and writing – review and editing.

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CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest.

ORCID

Hye Sook Choi  <https://orcid.org/0000-0001-8387-4907>

REFERENCES

- Ducray J, Vignot S, Lacout A, Pougnet I, Marcy PY, Chapellier C, et al. Radiation-induced bronchiolitis obliterans with organizing pneumonia. *Cancer Radiother.* 2017;21(2):148–54.
- Aguiar Bujanda D, Hernández SM. Radiation-induced bronchiolitis obliterans organizing pneumonia. *Clin Adv Hematol Oncol.* 2012;10(10):691–3.
- Lee SJ, Lee JY, Jung SH, Lee SN, Lee JH, Kim CW, et al. A case of radiation bronchitis induced massive hemoptysis after high-dose-rate endobronchial brachytherapy. *Tuberc Respir Dis (Seoul).* 2012;73(6):325–30.
- Speiser BL, Spratling L. Radiation bronchitis and stenosis secondary to high dose rate endobronchial irradiation. *Int J Radiat Oncol Biol Phys.* 1993;25(4):589–97.
- Giuranno L, Ient J, De Ruysscher D, Vooijs MA. Radiation-induced lung injury (RILI). *Front Oncol.* 2019;9:877.
- Vallard A, Rancoule C, Le Floch H, et al. Medical prevention and treatment of radiation-induced pulmonary complications. *Cancer Radiother.* 2017;21(5):411–23.
- Tzilas V, Poletti V, Bouros D. Reversed halo sign in radiation induced organizing pneumonia: natural course of the underlying pathophysiology. *Pulmonology.* 2021;27(5):460–4.
- Awan AN, Ashraf R, Meyerson MB, Dunn TL. Radiation-induced bronchial stenosis: a new cause of platypnea-orthodeoxia. *South Med J.* 1999;92(7):720–4.
- Zhao KL, Shi XH, Jiang GL, Wang Y. Late-course accelerated hyperfractionated radiotherapy for localized esophageal carcinoma. *Int J Radiat Oncol Biol Phys.* 2004;60(1):123–9.
- Kawakami N, Ito M, Takahashi K, Moriya T, Saito H, Wakai Y, et al. Pseudomembranous tracheobronchitis with severe tracheal stenosis and masked bronchial obstruction. *J Emerg Med.* 2021;60(3):e39–44.
- Mahishmita P, Dipti G. Pseudomembranous aspergillus tracheobronchitis with secondary *Acinetobacter baumannii* pneumonia. *Indian J Med Res.* 2020;152(Supplement):S136–s137.
- Sakaguchi K, Koga Y, Yagi T, Nakahara T, Todani M, Fujita M, et al. Severe fever with thrombocytopenia syndrome complicated with pseudomembranous aspergillus tracheobronchitis in a patient without apparent risk factors for invasive Aspergillosis. *Intern Med.* 2019;58(24):3589–92.
- Romero-Palacios A, Mera Gallardo O, Jiménez Aguilar P, Borrallo Torrejón JJ, Maza Ortega C, Rodríguez-Iglesias MA. Obstructive tracheobronchitis due to aspergillus fumigatus in an immunocompetent patient. *Rev Iberoam Micol.* 2019;36(1):34–6.
- Pal RS, Spalgais S, Murar AK, Ojha UC. Invasive aspergillus pseudomembranous and obstructive tracheo-bronchitis in an immunocompetent patient. *J Assoc Physicians India.* 2017;65(11):92–3.
- Lee YH, Seo H, Cha SI, Kim CH, Lee J. A case of pseudomembranous tracheitis caused by *Mycoplasma pneumoniae* in an immunocompetent patient. *Ann Transl Med.* 2019;7(9):205–5.
- Pezzuto A, Carico E. Effectiveness of smoking cessation in smokers with COPD and nocturnal oxygen desaturation: functional analysis. *Clin Respir J.* 2020;14(1):29–34.
- Condoluci A, Mazzara C, Zoccoli A, Pezzuto A, Tonini G. Impact of smoking on lung cancer treatment effectiveness: a review. *Future Oncol.* 2016;12(18):2149–61.
- Cihanbeylerden M, Yumrukuz M, Kurt B, Tuccar C, Safak C. Effect of pulmonary functions on survival in patients with operable non-small cell lung cancer. *J Coll Physicians Surg Pak.* 2022;32(5):606–12.

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