


## CASE REPORT

# Fatal rupture of pulmonary artery pseudoaneurysm after thoracic radiation therapy against lung squamous cell carcinoma: A case report and literature review

Yosuke Fukuda<sup>1</sup>  | Tetsuya Homma<sup>1</sup> | Tomoki Uno<sup>1</sup> | Yasunori Murata<sup>1</sup> | Shintaro Suzuki<sup>1</sup> | Eisuke Shiozawa<sup>2</sup> | Masafumi Takimoto<sup>2</sup> | Hironori Sagara<sup>1</sup>

<sup>1</sup>Department of Medicine, Division of Respiratory Medicine and Allergology, Showa University School of Medicine, Tokyo, Japan

<sup>2</sup>Department of Pathology, Showa University School of Medicine, Tokyo, Japan

## Correspondence

Yosuke Fukuda, Department of Medicine, Division of Respiratory Medicine and Allergology, Showa University School of Medicine, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo, Japan.  
Email: yfukuda.showa@gmail.com

## Abstract

Pulmonary artery pseudoaneurysm is a rare but fatal condition. It has been associated with lung cancer, abscesses, and radiation therapy. Identification in patients with hemoptysis is critical, and timely interventional therapy is warranted.

## KEYWORDS

hemoptysis, lung cancer, pulmonary artery pseudoaneurysm, radiation

## 1 | INTRODUCTION

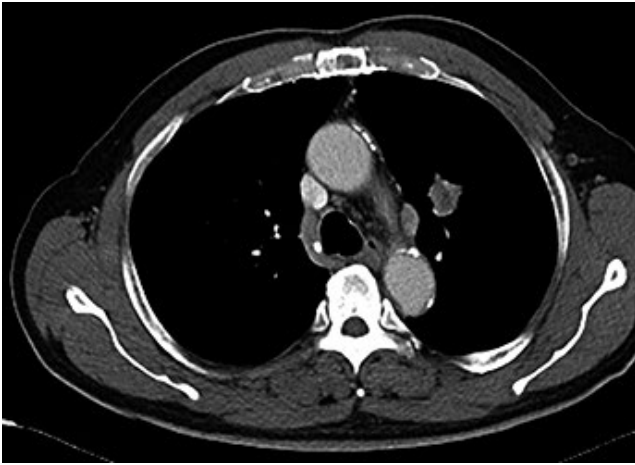
Hemoptysis is often a life-threatening symptom and may cause severe clinical conditions. Causes of hemoptysis are varied and include bronchiectasis, infection (eg, tuberculosis, pneumonia, and fungal infection), trauma, pulmonary vascular disease, iatrogenic injuries, and airway malignancies.<sup>1-4</sup> Among them, pulmonary artery pseudoaneurysm (PAP) is a rare cause of hemoptysis, but careful consideration should always be given as it is potentially fatal, especially in patients with primary or metastatic lung cancer.<sup>5,6</sup> We encountered a 65-year-old male lung cancer patient with hemoptysis due to rupture of PAP induced by thoracic radiation therapy (TRT). An autopsy was performed, and we herein report the detailed clinical, radiological, and pathological findings. Written informed consent was obtained from his relatives.

## 2 | CASE REPORT

A 65-year-old man presented to our hospital with nausea and vomiting. He was diagnosed with lung squamous cell carcinoma (T1aN2M0, stage IIIA) 1 month before, and TRT at 60 Gy total in 30 daily fractions for primary tumor (Figure 1) was started. Performance status at the time of lung cancer diagnosis was one. His past medical history included hypertension, dyslipidemia, type 2 diabetes mellitus, and old myocardial infarction, and medications were imidapril, atorvastatin, alogliptin, and aspirin. On physical examination, decreased breathing sounds were observed in the upper left side of the chest where TRT had been performed. The laboratory results showed white blood cell (WBC) count of 15,100/mm<sup>3</sup> and C-reactive protein (CRP) level of 16.14mg/dl. Chest CT revealed consolidation and cavity in the left upper

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.



**FIGURE 1** Enhanced CT on diagnosis of lung cancer. A 15-mm-sized nodule in the left upper lobe was noted, but there were no findings to suspect a pseudoaneurysm

lobe. He was thus diagnosed as lung abscess and treated with the intravenous antibiotics, meropenem, for three weeks. No significant bacteria were detected in the sputum culture. His clinical and radiographic findings consequently showed improvement. However, he had hemoptysis after the antibiotic treatment, and intravenous contrasted chest CT revealed left PAP (Figure 2). He coughed up a massive amount of blood before his scheduled PAP embolization and could not be resuscitated due to airway occlusion.

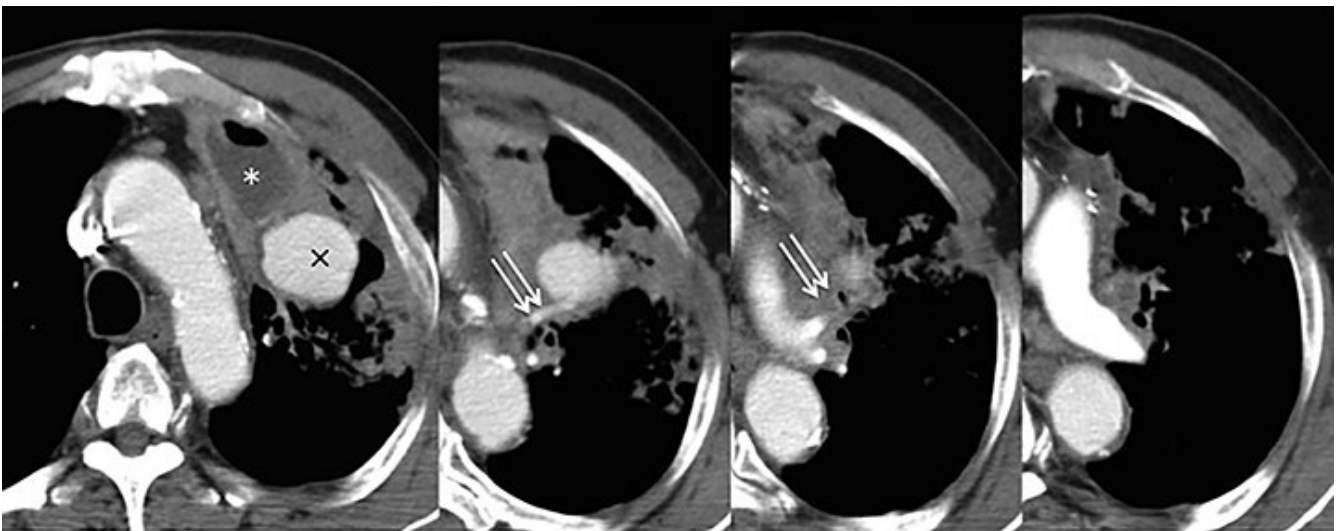
Autopsy was performed on the next day after death. Macroscopic findings showed cavity in the left upper lobe leading to the left pulmonary artery, and whole lung edema was observed (Figure 3A, B). Moreover, blood coagulation was found in the trachea and main bronchus (Figure 3C). Microscopic findings showed that the arterial wall had been damaged with fibrin drainage based on Elastica van Gieson

stain (Figure 4A, B). The lung abscess wall included squamous cell carcinoma cells (Figure 4C).

### 3 | DISCUSSION

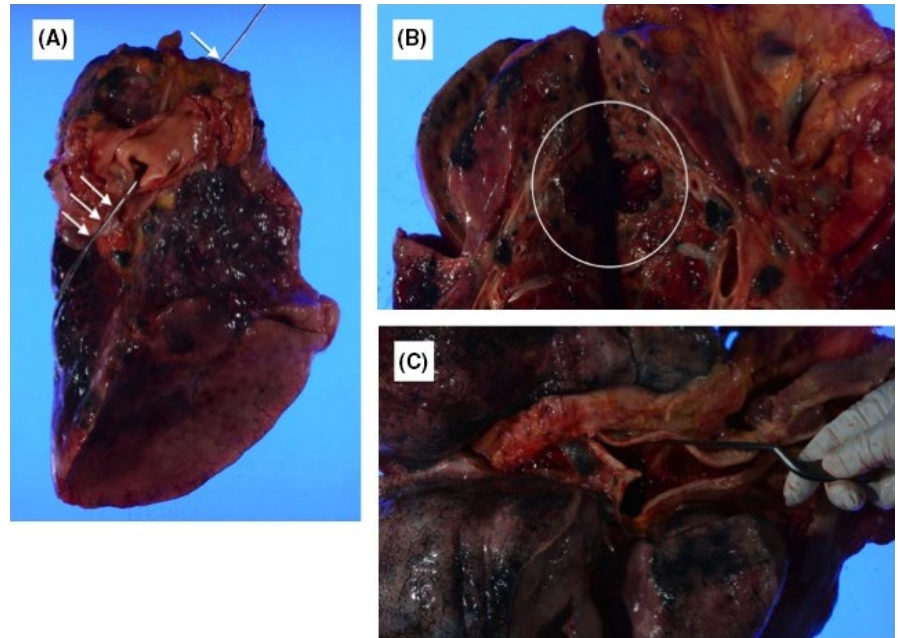
Although the rate of PAP occurrence is rare, bronchiectasis, infection, trauma, iatrogenic, vascular disease, and airway malignancy are its major causes.<sup>1-3</sup> Pseudoaneurysm is defined as focal blood vessel dilation that does not involve all arterial wall layers, while aneurysm is defined as that which involves all three arterial wall layers.<sup>7</sup> The precise mechanism of PAP formation has not yet been elucidated. In our current case, microscopic findings showed arterial wall disruption by inflammation together with invasion of squamous cell carcinoma, which affected the adventitia and the tunica media (Figure 4A). Boerrigter et al recently proposed that the structural changes of elastin and collagen under the influence of an increasing PA pressure may lead to PA dilation and further PAP formation.<sup>8</sup> This disruption and the abnormal formation of the arterial vessel may be further exacerbated by radiation therapy.

Since PAP is a fatal condition, prompt and appropriate diagnosis is essential in the clinical setting. Although pulmonary angiography is the gold standard for PAP diagnosis,<sup>9-11</sup> contrast-enhanced CT enabled PAP diagnosis with less invasiveness.<sup>12</sup> AP is defined as an upper limit of the main pulmonary artery (PA) diameter (29 mm) and an upper limit of the right interlobar artery (17 mm) measured using CT images.<sup>12</sup> The present case fulfilled these criteria (upper limit of the main PA diameter was 31 mm and upper limit of the right interlobar artery was 19 mm). In past reports, maximum intensity projection (MIP) and multiplanar reconstruction images on CT have been useful for PAP diagnosis.<sup>13</sup>

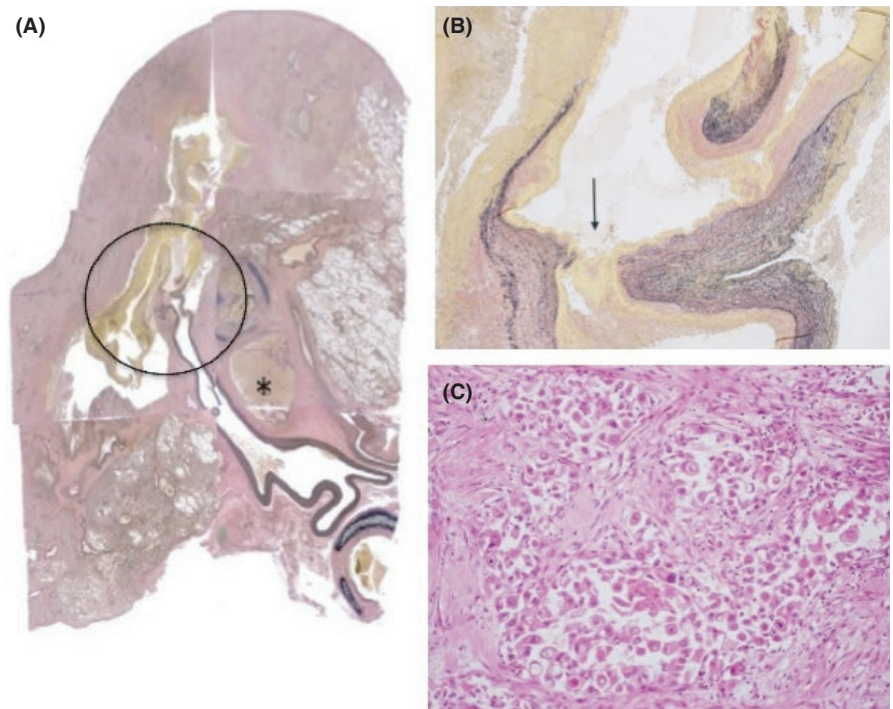


**FIGURE 2** Enhanced CT on admission. Left lung artery pseudoaneurysm (X) was shown on IV contrasted CT. Left lung artery was connected with lung abscess (\*) and pseudoaneurysm (white arrow)

**FIGURE 3** Macroscopic findings of PAP. (A) Left lung on macroscopic findings. Metallic sound was inserted through the left pulmonary artery to pseudoaneurysm (white arrow). Congestive edema was appeared on whole lung. (B) Left lung on macroscopic findings. Left pulmonary pseudoaneurysm with cut surface was shown (white circle). (C) Trachea and main bronchus on macroscopic findings. Blood coagulation was found



**FIGURE 4** Microscopic findings of pulmonary pseudoaneurysm. It showed that arterial wall was broken and fibrin was drained as Elastica van Gieson stain section (black circle on Figure 4A, magnification  $\times 40$ , white arrow on Figure 4B, magnification  $\times 100$ ). The wall of lung abscess included squamous cell carcinoma (\*) as hematoxylin and eosin stain section (Figure 4C, magnification  $\times 400$ )



Previous literature has indicated that lung cancer is associated with PAP formation.<sup>14-22</sup> In cases with lung cancer-associated PAP, it is possible that tumor invasion to blood vessels may result in PAP formation.<sup>16</sup> To the best of our knowledge, there have been twelve cases of pseudoaneurysm accompanied with lung cancer, and squamous cell carcinoma was the most frequent in the reported cases (Table 1). Six patients survived without any intervention, while four patients died (two were unknown). It is well known that lung squamous cell carcinoma characteristically presents with hemoptysis.<sup>23</sup> Razazi et al reported that 125 patients had hemoptysis related

to non-small-cell lung carcinoma, and in those patients, the proportion of squamous cell carcinoma was 52%.<sup>23</sup> Moreover, tumor cavitation during cancer treatment has been suggested as a risk factor for hemoptysis.<sup>23</sup> In the present case, we hypothesize that PAP caused by squamous cell lung carcinoma together with a tumor cavity may be a significant risk factor for massive hemoptysis.

Infection such as lung abscess is also known as an important factor for PAP, but the detailed mechanism of PAP formation by lung abscesses is unknown. Several decades ago, syphilis and tuberculosis infection frequently caused PAP, but

**TABLE 1** Cases with pulmonary artery pseudoaneurysm due to cancer

Case No.	Age/Sex	Histology	Initial treatment before PAP occurrence	Clinical Outcome	Ref
1	55M	Sq	none	Survived (coil embolization)	Akpinar E (2006) <sup>14</sup>
2	71F	Sq	none	Survived (coil embolization)	Kim SY (2009) <sup>15</sup>
3	66M	Sq	none	Survived (CT)	Kim SY (2009) <sup>15</sup>
4	54M	Sq	none	Survived (sleeve lobectomy)	Camargo Jde J (2010) <sup>16</sup>
5	55F	Sq	Sleeve lobectomy	Survived (complete pneumonectomy)	Bao M (2013) <sup>17</sup>
6	76F	unknown	Sleeve lobectomy	Survived (sleeve lobectomy)	T Miyazaki (2014) <sup>18</sup>
7	66M	Sq	None	Death (coil embolization)	Kim YI (2014) <sup>19</sup>
8	64M	Sq	CT + TRT	Death (no intervention)	Kim JH (2015) <sup>20</sup>
9	66M	Sq	CT + TRT	Death (coil embolization)	Zhang J (2017) <sup>21</sup>
10	65M	Sq	TRT	unknown	Chen Y (2017) <sup>22</sup>
11	68M	Sq	Sleeve lobectomy	unknown	Chen Y (2017) <sup>22</sup>
12	65M	Sq	TRT	Death (no intervention)	Our Case

Abbreviations: CT, chemotherapy; PAP, pulmonary pseudoaneurysm; Ref, reference; Sq, squamous cell carcinoma; TRT, thoracic radiation therapy.

those causes dramatically decreased nowadays.<sup>9</sup> The cause of PAP formation was primarily thought to be structural destruction of the vessel wall by granulation tissue.<sup>7</sup> Likewise, it is presumed that the spillover of inflammation to the pulmonary arteries due to bacterial infections may be a significant factor. In this case, we diagnosed clinically pulmonary abscesses by blood tests and imaging examinations, although no obvious causative organism could be identified, and autopsy findings were consistent with pulmonary abscesses.

Additionally, radiation therapy is known to cause vascular diseases including PAP.<sup>24</sup> Schultz et al reported that radiation therapy causes acute upregulation of pro-inflammatory cytokines and adhesion molecules in the endothelium that recruits inflammatory cells to the sites of vascular injury.<sup>25</sup> Martin et al subsequently proposed a mechanism of radiation-induced vascular disease whereby resultant oxidative stress causes nuclear factor-kappa B (NF- $\kappa$ B) activation that in turn causes inflammatory cytokine upregulation.<sup>26</sup> Moreover, preexisting cardiac disease has been significantly associated with development of cardiac events in patients with lung cancer who have received radiation therapy. In the Netherlands, 23% of patients with lung cancer had developed cardiovascular disease.<sup>27</sup> In Table 1, four patients had received radiation therapy for lung cancer treatment before PAP diagnosis (two had received combined chemotherapy with radiation therapy, and two including our case had received radiation therapy alone). As with these cases, there was a possibility that PAP development was accelerated by radiation therapy in our case.

Endovascular and percutaneous interventional procedures are often used for PAP treatment. Percutaneous intervention is a

less invasive option than surgical treatment. While the primary intervention is the embolization of systemic arteries, other therapeutic options may be considered depending on the size and location of the PAP.<sup>12</sup> Unfortunately, the current case had died from massive hemoptysis before receiving intervention therapy.

## 4 | CONCLUSIONS

In summary, we encountered a lethal clinical course of pulmonary artery pseudoaneurysm after thoracic radiation therapy against lung squamous cell carcinoma. In this case, there was no evidence of PAP prior to radiation therapy. Therefore, it was possible that a combination of factors, such as infection and squamous cell carcinoma, were involved in addition to radiation therapy. Although rare, lung cancer can be associated with a pseudoaneurysm of the pulmonary artery, which can be exacerbated and fatal, especially after radiation therapy, so prompt intervention should be done if diagnosed.

## ETHICS STATEMENT

The study complied with the principles of the Declaration of Helsinki. The Showa University Ethics Committee approved this study (approval number: 2659).

## ACKNOWLEDGEMENTS

The authors gratefully acknowledge the support of the medical staff of Department of Pathology at Showa University Hospital for great assistance and contributions to our study. Published with written consent of the patient.

## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTIONS

Yosuke Fukuda: Conceptualization and writing (original draft); Tetsuya Homma: Supervision and writing (review and editing); Tomoki Uno, Yasunori Murata, and Shintaro Suzuki: Investigation; Eisuke Shiozawa and Masafumi Takimoto: Supervision. Hironori Sagara: Writing (review and editing).

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, YF. The data are not publicly available due to restrictions that their containing information could compromise the privacy of research participants.

## ORCID

Yosuke Fukuda  <https://orcid.org/0000-0002-7087-1595>

## REFERENCES

- Corder R. Hemoptysis. *Emerg Med Clin North Am.* 2003;21:421-435.
- Nguyen DV, Murin S. Bronchial artery pseudoaneurysm with major hemorrhage after bronchial thermoplasty. *Chest.* 2016;149:e95-97.
- Oguma T, Morise M, Harada K, et al. Pulmonary artery aneurysm/pseudoaneurysm, a delayed complication of lung abscess: A case report. *Tokai J Exp Clin Med.* 2015;40:86-89.
- Lafita V, Borge MA, Demos TC. Pulmonary artery pseudoaneurysm: etiology, presentation, diagnosis, and treatment. *Semin Intervent Radiol.* 2007;24:119-123.
- Tantrige P, Johnston E, Garzillo G, Huang DY. Pulmonary artery pseudoaneurysm embolisation to treat massive haemoptysis due to metastatic oropharyngeal squamous cell carcinoma. *BMJ Case Rep.* 2019;12:e230283.
- Kang T, Kang MJ. Pulmonary artery pseudoaneurysm showing rapid growth in a patient with lung cancer. *Radiol Case Rep.* 2020;15:2144-2148.
- Kreibich M, Siepe M, Kroll J, Höhn R, Grohmann J, Beyersdorf F. Aneurysm of the pulmonary artery. *Circulation.* 2015;131:310-316.
- Boerrigter B, Mauritz GJ, Marcus JT, et al. Progressive dilation of the main pulmonary artery is a characteristic of pulmonary arterial hypertension and is not related to changes in pressure. *Chest.* 2010;138:1395-1401.
- Theodoropoulos P, Ziganshin BA, Tranquilli M, Elefteriades JA. Pulmonary artery aneurysm: four case reports and literature review. *Int J Angiol.* 2013;22:143-148.
- Shin TB, Yoon SK, Lee KN, et al. The role of pulmonary CT angiography and selective pulmonary angiography in endovascular management of pulmonary artery pseudoaneurysms associated with infectious lung diseases. *J Vasc Interv Radiol.* 2007;18:882-887.
- Khalil A, Parrot A, Nedelcu C, Fartoukh M, Marsault C, Carrette MF. Severe hemoptysis of pulmonary arterial origin: signs and role of multidetector row CT angiography. *Chest.* 2008;133:212-219.
- Nguyen ET, Cl S, Seely JM, Chong S, Lee KS, Muller NL. Pulmonary artery aneurysms and pseudoaneurysms in adults: findings at CT and radiography and pseudoaneurysm. *Am J Roentgenol.* 2007;188:126-134.
- Haranaga S, Teruya H, Nakamura H, Higa F, Tateyama M, Fujita J. Pulmonary artery pseudoaneurysm secondary to lung abscess. *Intern Med.* 2009;48:2159-2160.
- Akpinar E, Turkbey B, Canyigit M, et al. Bleeding pulmonary artery pseudoaneurysm secondary to squamous cell lung cancer: computer tomography findings and endovascular management. *Acta Radiol.* 2006;47:944-946.
- Kim SY, Kim HR, Song JS, et al. Pseudoaneurysm due to squamous cell carcinoma of the lung: two cases of spontaneous resolution after chemotherapy. *Cancer Res Treat.* 2009;41:237-240.
- Camargo Jde J, Camargo SM, Machuca TN, Bello RM. Large pulmonary artery pseudoaneurysm due to lung carcinoma: pulmonary artery aneurysm. *J Thorac Imaging.* 2010;25:4-5.
- Bao M, Zhou Y, Jiang G, Chen C. Pulmonary artery pseudoaneurysm after a left upper sleeve lobectomy. *World J Surg Oncol.* 2013;11:272.
- Miyazaki T, Yamasaki N, Tsuchiya T, et al. Surgical resection of a pulmonary artery pseudoaneurysm after middle lobectomy: Report of a case. *Acta Med Nagasaki.* 2014;60:25-27.
- Kim YI, Kang HC, Lee HS, et al. Invasive pulmonary mucormycosis with concomitant lung cancer presented with massive hemoptysis by huge pseudoaneurysm of pulmonary artery. *Ann thorac Surg.* 2014;98:1832-1835.
- Kim JH, Han SH. A pulmonary artery pseudoaneurysm caused by concurrent chemoradiation therapy for lung cancer. *Pak J Med Sci.* 2015;31:220-222.
- Zhang J, Jiang S. Massive hemoptysis from a central pulmonary arterial pseudoaneurysm secondary to advanced cancer: successful treatment by Guglielmi detachable coil embolization. *Clin Respir J.* 2017;11:258-262.
- Chen Y, Gilman MD, Humphrey KL, et al. Pulmonary Artery Pseudoaneurysm: Clinical Features and Ct Findings. *AJR Am J Roentgenol.* 2017;208:84-91.
- Razazi K, Parrot A, Khalil A, et al. Severe haemoptysis in patients with nonsmall cell lung carcinoma. *Eur Respir J.* 2015;45:756-764.
- Weintraub NL, Jones WK, Manka D. Understanding radiation-induced vascular disease. *J Am Coll Cardiol.* 2010;55:1237-1239.
- Schultz-Hector S, Trott KR. Radiation-induced cardiovascular diseases: is the epidemiologic evidence compatible with the radiobiology data? *Int Radiat Oncol Biol Phys.* 2007;67:10-18.
- Halle M, Gabrielsen A, Paulsson-Berne G, et al. Sustained inflammation due to nuclear factor-kappa B activation in irradiated human arteries. *J Am Coll Cardiol.* 2010;55:1227-1236.
- Janssen-Heijnen ML, Schipper RM, Razenberg PP, Crommelin MA, Coebergh JW. Prevalence of co-morbidity in lung cancer patients and its relationship with treatment: a population-based study. *Lung Cancer.* 1998;21:105-113.

**How to cite this article:** Fukuda Y, Homma T, Uno T, et al. Fatal rupture of pulmonary artery pseudoaneurysm after thoracic radiation therapy against lung squamous cell carcinoma: A case report and literature review. *Clin Case Rep.* 2021;9:737–741. <https://doi.org/10.1002/ccr3.3647>