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CASE REPORT

Potentially fatal complications of systemic air embolism after computed tomography-guided transthoracic needle biopsy in lung cancer harboring epithelial growth factor receptor mutation: A case report

Hyung-Joo Oh[1], Won Gi Jeong[2], Yongwhan Lim[1], Sang-Joon Koh[3], Sung Min Lee[4], Min-Seok Kim[1], Bo-Gun Koh[1], Tae-Ok Kim[1], Yoo-Duk Choi[5], In-Jae Oh[1], Young-Chul Kim[1] & Cheol-Kyu Park[1]

1 Department of Internal Medicine, Chonnam National University Hwasun Hospital, Jeonnam, Republic of Korea
2 Department of Radiology, Chonnam National University Medical School, Gwangju, Republic of Korea
3 Department of Neurology, Chonnam National University Medical School, Gwangju, Republic of Korea
4 Department of Emergency Medicine, Chonnam National University Medical School, Gwangju, Republic of Korea
5 Department of Pathology, Chonnam National University Medical School, Gwangju, Republic of Korea

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Correspondence
Cheol-Kyu Park, Department of Internal Medicine, Chonnam National University Medical School, 322 Seoyang-ro, Hwasun, Jeonnam 58128, Republic of Korea.
Tel: +82 61 379 7615
Fax: +82 61 379 7619
Email: ckpark214@jnu.ac.kr

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Abstract

Air embolism is a rare, fatal complication of computed tomography (CT)-guided transthoracic needle biopsy (TTNB) of the lung. Here, we report a patient who developed an air embolism after CT-guided TTNB, which led to ST-elevation myocardial infarction and acute cerebral ischemia. The patient recovered completely without critical sequelae and was diagnosed with adenocarcinoma harboring activating epidermal growth factor receptor (EGFR) mutation. The patient responded to subsequent treatment with gefitinib.

Key points

Signficant findings of the study:

- Air embolism is a rare, fatal complication of CT-guided transthoracic lung biopsy. Only a few cases have been previously reported where myocardial and cerebral infarction occurred after TTNB, demonstrated not only on CT scan, but also electrocardiogram and electroencephalogram.

What this study adds:

- Detection of driver gene mutation is crucial for planning lung cancer treatment. Despite the need for tissue biopsy, air embolism propagation to vital organs could result in severe end-organ damage and multidisciplinary approaches are needed to improve initial outcomes.

Introduction

Status of tumor driver mutation is a critical factor for deciding the best treatment for patients with advanced non-small cell lung cancer (NSCLC). Because sufficient tumor tissue is required to detect gene mutation, selection of an appropriate method of biopsy is important. Transthoracic needle biopsy (TTNB) is a well-established method for obtaining tissue from peripheral lung nodules for diagnosis and obviates the need for more invasive procedures. Systemic air embolism is a very rare complication after TTNB, but it may result in a fatal outcome. Here, we present a case of systemic air embolism after TTNB, with serious complications of myocardial infarction and cerebral ischemia.

Case report

An 80-year-old female presented with a part-solid nodule measuring 3 cm in the right upper lobe (RUL) of the lung with bilateral multifocal nodular consolidations on chest computed tomography (CT) (Fig 1a). It was anticipated that it would be difficult to obtain enough tissue via conventional bronchoscopy because the nodule was located

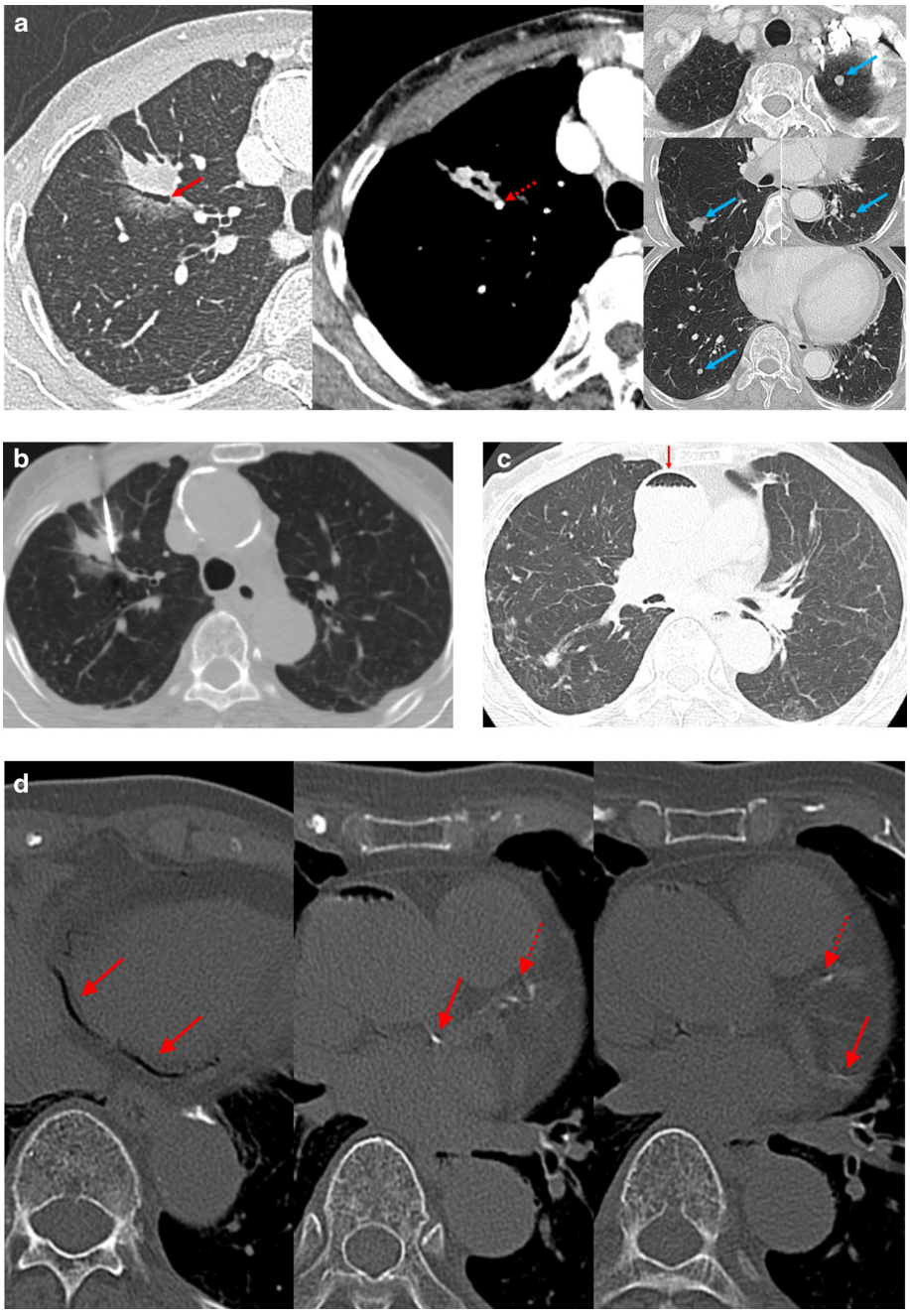

Figure 1 Transthoracic needle biopsy of a pulmonary nodule. (**a**) A part-solid nodule was located in the right upper lobe and multiple metastatic nodules in bilateral lungs. An open-bronchus sign (left, red arrow), an adjacent branch of pulmonary vein (mid, dashed red arrow), and multiple separate nodules in bilateral lungs (right, blue arrows) were seen on axial high-resolution and contrast-enhanced CT, respectively. (**b**) Transthoracic biopsy using an 18-G needle. (**c**) Air-fluid level in the ascending aorta noted on post-biopsy CT. (**d**) Air embolism in the right coronary artery (left, arrows), left main (mid-, arrow) and left anterior descending artery (mid- and right, dashed arrows), and left circumflex artery (right, arrow) noted on post-biopsy CT.

close to the chest wall with a solid portion of less than 2 cm. With a clinical suspicion of stage IVA (T4N0M1a) lung cancer, the patient underwent CT-guided TTNB for the RUL nodule. The patient was placed in a supine position and an 18-G needle was inserted at a right angle to the CT plane (Fig 1b). When the biopsy needle was inserted into the thorax, the patient coughed several times. A few seconds after extraction of the needle, the patient became unconscious and cyanotic. Immediate post-biopsy CT revealed a large air bubble in the ascending aorta (Fig 1c) and filling defects with air emboli in all three coronary arteries (Fig 1d). Resuscitation with intravenous fluids and ventilation with tracheal intubation and 100% oxygen were initiated as unconsciousness, hypotension, and respiratory failure persisted.

Initial electrocardiography (ECG) showed ST-segment elevation in leads II, III, and aVF (Fig. 2a). Transthoracic echocardiography revealed regional wall motion

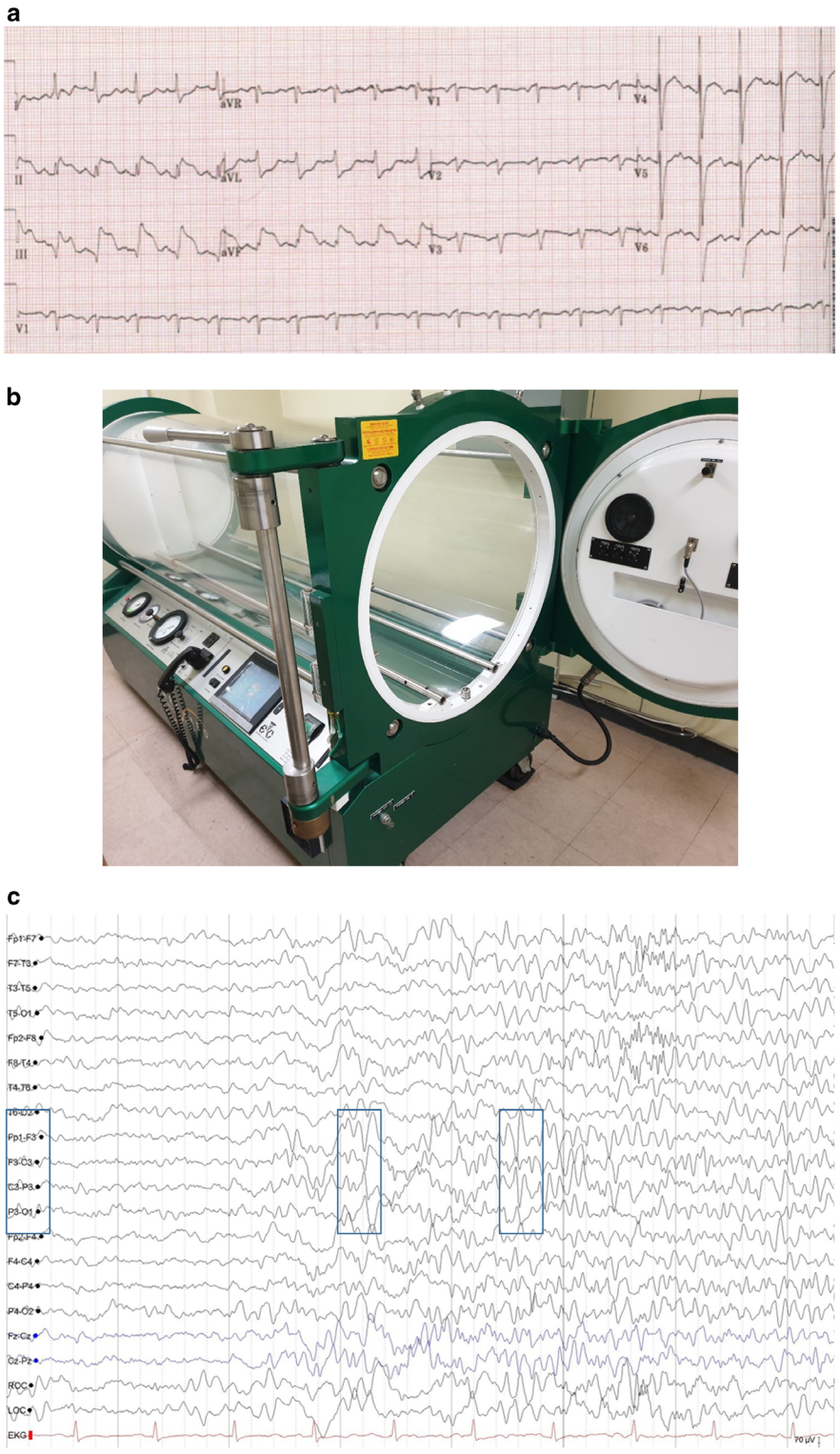

Figure 2 Systemic complications and management of air embolism. (**a**) ST-segment elevation in lead II, III, and aVF on post-biopsy electrocardiography. (**b**) Hyperbaric chamber for oxygen therapy (BARA-MED Monoplace Hyperbaric Chamber, ETC Biomedical System, Southampton, PA, US). (**c**) An episode of ictal activity in the left frontal cortex on electroencephalography.

abnormalities in multiple segments and moderate systolic dysfunction (left ventricular ejection fraction: 35%). Troponin-I level was elevated (3.82 ng/mL, normal: <0.05 ng/mL), suggesting the patient had suffered an acute myocardial infarction. After initiating mechanical ventilation, the patient experienced an episode of generalized tonic-clonic seizure and neurological examination after administration of anticonvulsants revealed right hemiplegia, suggesting acute cerebral ischemia. However, brain CT angiogram taken three hours after the embolic event showed patent large vessels without evidence of thrombotic or air embolic infarction. Because the patient did not have any other risk factors for stroke apart from age, it was strongly suspected that the ischemic event had been caused by an air embolism. To prevent further deterioration of neurological signs, hyperbaric oxygen therapy (HBOT) was initiated (Fig 2b) and maintained for two hours (2.8 atm; atmospheres absolute) over two consecutive days. The patient regained consciousness and completely recovered from right hemiplegia. However, electroencephalography (EEG) showed frequent episodes of ictal activity in several of the left frontal cortex leads (Fig 2c), suggesting non-convulsive status epilepticus caused by injury to the left cerebral hemisphere.

The biopsy revealed lung adenocarcinoma (Fig 3a), harboring activating epidermal growth factor receptor (*EGFR*) mutation (exon 19 deletion), which was confirmed by peptide nucleic acid-mediated polymerase chain reaction clamping method (Mutyper; Panagene Inc., Daejeon, Korea). However, antecedent plasma EGFR test showed a negative result. Gefitinib was initiated, and follow-up CT performed after eight weeks revealed that the RUL nodule and solid component proportion had reduced (Figs 3b and 4).

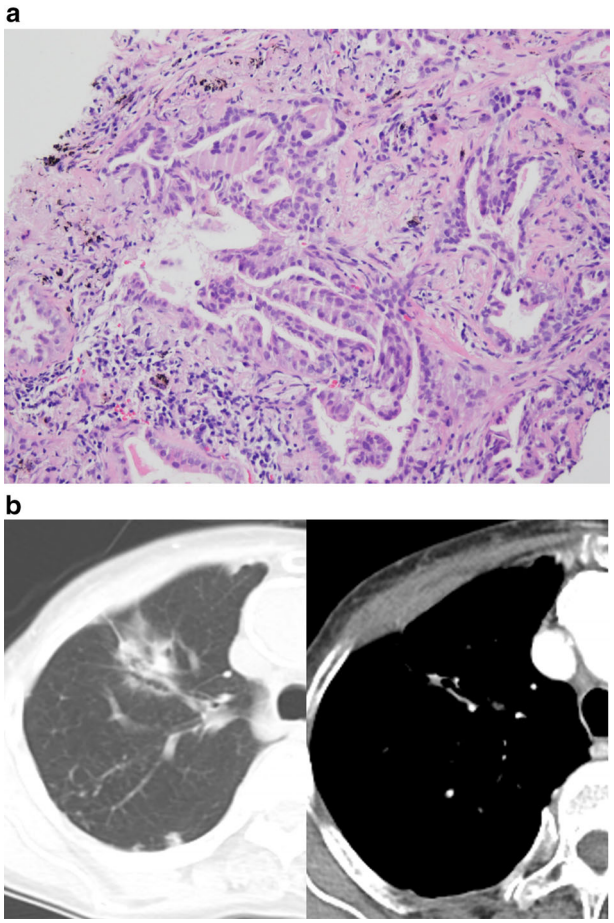

Figure 3 Diagnosis and treatment of *EGFR*-mutated non-small cell lung cancer (NSCLC). (**a**) Microscopic evaluation following hematoxylin-eosin staining of the tumor tissue showed crowded atypical glands with focal papillary pattern, suggestive of adenocarcinoma (x200). (**b**) Follow-up CT scan showed a nodule in the right upper lobe after EGFR-TKI treatment. EGFR, epidermal growth factor receptor; TKI, tyrosine kinase inhibitor.

Discussion

CT-guided TTNB is a common modality used to confirm the diagnosis of peripheral pulmonary nodules.[1] Air embolism is a rare complication of TTNB, with a previously reported incidence of approximately 0.06% in a large registry.[2] The pathogenesis of air embolism is complex and has not yet been clearly identified. The commonly accepted pathogenic mechanisms are situations where air can enter the pulmonary vein through a bronchovenous fistula created by the needle because of a pressure gradient.[3] In our patient, a branch of prominent pulmonary vein was seen near the target lesion on contrast-enhanced CT (Fig 1a, mid) and an "open-bronchus sign" was noted on high-resolution CT (Fig 1a, left). During CT-guided TTNB, the introducer needle traversed the target lesion, and the needle tip was placed near the pulmonary vein (Fig 1b). The biopsy needle may have damaged the pulmonary vein, leading to a bronchovenous fistula. In addition, the patient was vulnerable to procedure-related cough which was attributed to the "open-bronchus sign", and air could have been aspirated through the introducer needle and bronchovenous fistula.

The clinical manifestations of systemic arterial air embolism are variable as end-organ injury may occur depending on the site of circulatory impairment. Since the first report by Omenaas *et al.* in 1989,[4] many cases have been reported with single organ damage attributable to air emboli. Thus far, simultaneous ischemia of heart and brain has been demonstrated on CT in a limited number of cases.[5, 6] In the case reported here, air emboli were not detected in the cerebral arteries on brain CT. However, symptoms and signs of air embolism developed sequentially with

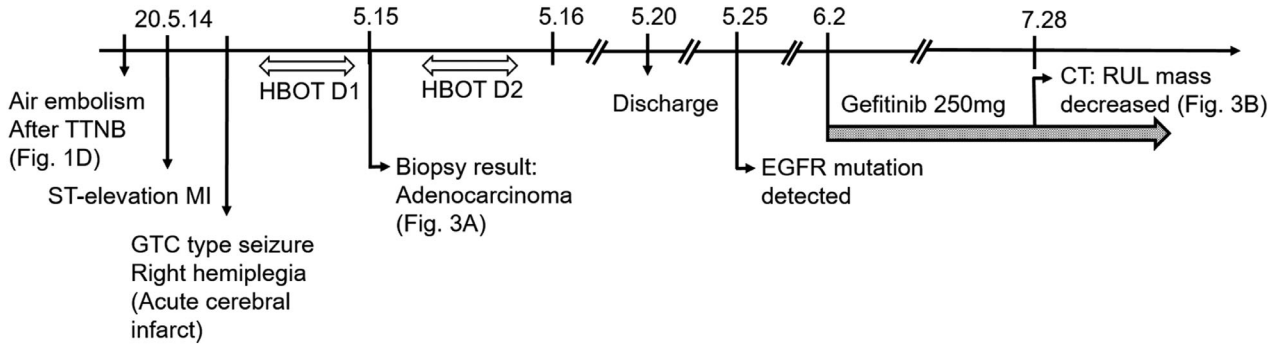

Figure 4 Timeline of embolic event and duration of each treatment. TTNB, transthoracic needle biopsy; MI, myocardial infarction; GTC, generalized tonic-clonic; HBOT, hyperbaric oxygen therapy; EGFR, epidermal growth factor receptor; CT, computed tomography.

progression of air emboli and associated ischemic damage to the involved organs, and the sequelae were confirmed by EEG. Since emboli can get lodged in any organ, the outcome can be fatal if it causes extensive damage to vital organs such as the heart and brain. Therefore, as in this case, multidisciplinary evaluation and management is crucial to improve the overall prognosis in patients.

HBOT is the primary treatment for symptomatic arterial gas embolism and it is important to start this in time because a notable decrease in successful treatment has been previously reported after a few hours of delay.[7, 8] Other supportive therapies such as high flow oxygen and repositioning could be indicated in patients without end organ damage. HBOT corresponded to the indication in this case because the patient showed hemodynamic instability and evidence of end organ damage. In addition, the treatment proceeded without any specific complications for two days.

Recently, liquid biopsy has been widely used to assess genomic information, and has evolved as a promising tool for diagnosis, monitoring and prediction of outcome in lung cancer.[9] However, there are sensitivity limitations in plasma genotyping, and tissue biopsy remains the gold standard for diagnosis and detection of gene mutations. In this case, although the plasma test result was negative, activating *EGFR* mutation was detected by tissue genotyping via TTNB and the patient benefited from EGFR-TKI treatment. A tissue diagnosis is essential for planning the therapeutic strategy and determining the prognosis of lung cancer. However, it is crucial to choose an appropriate biopsy technique considering the risk factors for developing complications.

In conclusion, awareness of air embolism as a complication after TTNB is essential for its early detection and management, and multidisciplinary approaches to systemic complications could potentially improve patient outcome. Recognizing the importance of tissue diagnosis in lung cancer, it is imperative to fine-tune the approaches to reduce the incidence of complications during biopsy procedures as much as possible.

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Disclosure

There are no conflicts of interest relevant to this article.

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