tissue of lung cancer patients. *Am J Respir Crit Care Med* 2008; 177: 337–341.
3 Carpagnano GE, Palladino GP, Gramiccioni C, *et al.* Exhaled ERCC-1 and ERCC-2 microsatellite alterations in NSCLC patients. *Lung Cancer* 2010; 68: 305–307.
4 Felip E, Rosell R. Testing for excision repair cross-complementing 1 in patients 172 with non-small-cell lung cancer for chemotherapy response. *Expert Rev Mol Diagn* 2006; 7: 261–268.
5 D'Agostini F, Izzotti A, Balansky R, *et al.* Early loss of FHIT in the respiratory tract of rodents exposed to environmental cigarette smoke. *Cancer Res* 2006; 66: 3936–3941.
6 Mao L, Lee JS, Kurie JM, *et al.* Clonal genetic alterations in the lungs of current and former smokers. *J Natl Cancer Inst* 1997; 89: 857–862.
7 Beane J, Sebastiani P, Liu G, *et al.* Reversible and permanent effects of tobacco smoke exposure on airway epithelial gene expression. *Genome Biol* 2007; 8: R201.
8 Sozzi G, Veronese ML, Negrini M, *et al.* The FHIT gene 3p14.2 is abnormal in lung cancer. *Cell* 1996; 85: 17–26.
9 Siafakas NM, Tzortzaki EG, Sourvinos G, *et al.* Microsatellite DNA instability in COPD. *Chest* 1999; 116: 47–51.
10 Ito H, Matsuo K, Wakai K, *et al.* An intervention study of smoking cessation with feedback on genetic cancer susceptibility in Japan. *Prev Med* 2006; 42: 102–108.

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EBUS-TBNA in the differential diagnosis of pulmonary artery sarcoma and thromboembolism

To the Editors:

Pulmonary artery sarcoma is a rare tumour of the cardiovascular system. It is often misdiagnosed as acute or chronic pulmonary thromboembolism because its clinical presentation and radiological findings are similar to those of thromboembolism. The diagnosis of pulmonary artery sarcoma by endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has not been reported. Herein, we report two cases with mass-like lesion in the pulmonary artery. The lesions were safely approached by EBUS-TBNA, and the tissues obtained by EBUS-TBNA were sufficient to diagnose pulmonary artery sarcoma and thromboembolism.

A 79-yr-old female with hypertension and atrial fibrillation presented with sudden-onset left chest and shoulder pain. She had taken warfarin for atrial fibrillation, but the warfarin had been discontinued for 1 week because of a scheduled endoscopy. We performed chest computed tomography (CT), which revealed an extensive intraluminal low-attenuated mass- like lesion involving the entire luminal diameter of the left main and left lower lobar pulmonary artery (fig. 1a). D-dimer was 0.94 $\mu g \cdot mL^{-1}$ (reference value <0.4 $\mu g \cdot mL^{-1}$). Positron emission tomography (PET)-CT with ^{18}F-fluorodeoxyglucose (FDG) showed increased FDG uptake, with a maximum standardised uptake value (SUV max) of 18.6 in the left main pulmonary artery (fig. 1c). For a tissue diagnosis, EBUS-TBNA was performed targeting the mass-like lesion encasing the pulmonary artery (fig. 1d). The sonograph revealed a round heterogeneous mass with distinct margin that include some necrotic area. The cytopathological examination confirmed spindle cell malignancy with vimentin and CD31 expression by immunohistochemistry (fig. 1e and f); this was compatible with pulmonary artery sarcoma. She underwent a left pneumonectomy (fig. 1b) and final pathology revealed pulmonary artery sarcoma $4.5 \times 2.0 \times 2.0$ cm in size with marked nuclear pleomorphism and mitotic count of 15/10 high-power fields. 6 months after surgery she is alive without complications or relapse.

A 68-yr-old female with hypertension presented with dyspnoea and syncope. Chest CT revealed a 2.6×3.1 cm mass-like density in the left main pulmonary artery trunk occupying the entire luminal diameter and extending to the left lower lobe pulmonary artery (fig. 2a). The possibility of pulmonary artery sarcoma was not excluded because the mass-like density in the pulmonary artery was distributed asymmetrically and the left lower lobe pulmonary artery bulged out by the mass. Although the D-dimer level was 11.83 $\mu g \cdot mL^{-1}$ and only mildly increased FDG uptake (SUV max 3.5) was noted, D-dimer can be elevated in

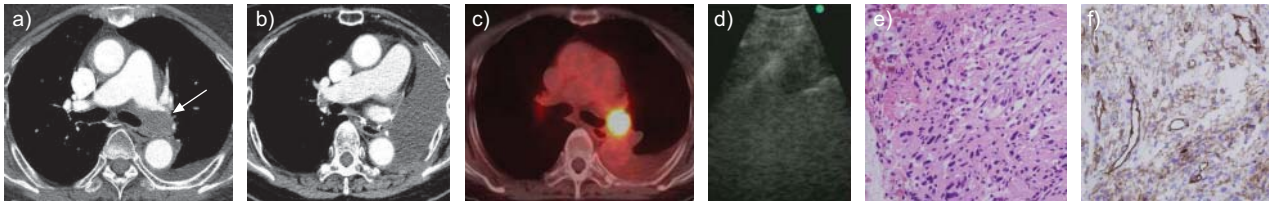

FIGURE 1. Chest computed tomography (CT), positron emission tomography (PET)-CT with ^{18}F-fluorodeoxyglucose (FDG), endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and pathological specimens from EBUS-TBNA in case 1. a) CT scan showing an intraluminal low-attenuation lesion in the left main pulmonary artery. b) The lesion (sarcoma) was resected completely after a left pneumonectomy. c) PET-CT showing increased FDG uptake (maximum standardised uptake value of 18.6) in the intraluminal lesion of the left main pulmonary artery. d) EBUS showing a heterogeneous mass near the left pulmonary artery with the needle inserted in the mass. e) The histological examination revealed poorly differentiated spindle-cell malignancy (haematoxylin and eosin stain $\times 100$). f) Tumour cells show focal but definite immunoreacitivity for CD31 (immunostaining $\times 200$).

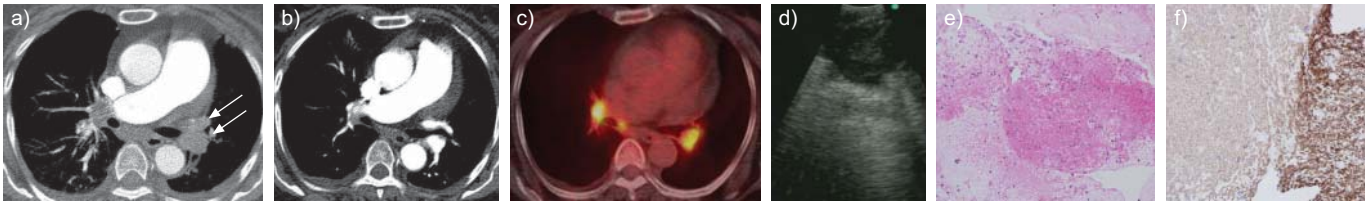

FIGURE 2. Chest computed tomography (CT), positron emission tomography (PET)-CT with ^{18}F-fluorodeoxyglucose (FDG), endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and pathological specimens from EBUS-TBNA in case 2. a) CT scan revealed a mass-like density in the right and left main pulmonary artery extending to the left lower lobe pulmonary artery. b) The mass (thrombus) disappeared after anticoagulation therapy for 6 weeks. c) PET-CT showed mildly increased FDG uptake (maximum SUV 3.5) in the left lower lobe pulmonary artery lesion. d) EBUS-TBNA was performed for the round mass-like lesion in the left pulmonary artery. e) The fibrin clot and organisation suggest a thrombus (haematoxylin and eosin stain ×40). f) Glut1 expression in the thrombus and red blood cells (immunostaining ×100).

malignancy and relatively low FDG uptake is also possible in sarcoma [1]. The endobronchial ultrasound (EBUS) showed round homogeneous mass with distinct margin and EBUS-TBNA was performed for the mass-like lesion in the left lower lobe pulmonary artery (fig. 2d). The pathology did not show any evidence of malignancy, and instead revealed fibrinous exudates and blood clot suggesting an organising thrombus with diffuse glucose transporter 1 (Glut1) expression (fig. 2e and f). She was also diagnosed with protein S deficiency, with a protein S level of 50% (reference value 70–140%). As the pathological diagnosis suggested pulmonary artery thrombus, she was treated with anticoagulation, and the mass-like lesion disappeared after 6 weeks (fig. 2b).

Pulmonary artery sarcoma is often misdiagnosed as pulmonary thromboembolism [2]. This can lead to inappropriate therapy, such as prolonged anticoagulation or thrombolysis, and can delay surgery, which is the only definitive treatment modality. Therefore, pulmonary artery sarcoma should be included in the differential diagnosis of pulmonary thromboembolism because early, complete resection is mainstay of the treatment [2].

Various diagnostic methods are used to differentiate these two diseases. Symptoms and signs such as weight loss, fever, anaemia and digital clubbing are subtle clues [3]. CT findings favouring pulmonary artery sarcoma include: a low-attenuation filling defect, heterogeneous enhancement of a mass occupying the entire luminal diameter of the main or proximal pulmonary artery, and extravascular spread of the lesion [4]. Enhancement of an intraluminal filling defect with gadolinium-diethylenetriamine pentaacetic acid on magnetic resonance imaging has been suggested as a sensitive way of differentiating a tumour mass from a thrombus [5]. Pulmonary artery sarcoma has a higher SUV for the FDG uptake on PET than pulmonary embolism [6]. However, a definite diagnosis can still only be made with a pathological examination. In our cases, CT could not differentiate the diagnosis. The relatively high SUV (3.5) on PET-CT in a thrombus was also noted, which could be explained by Glut1 expression by red blood cells [7].

EBUS-TBNA has been used to stage mediastinal lymph nodes in lung cancer. Moreover, it can approach the tumour itself if located adjacent to the bronchus and can diagnose other various diseases, such as tuberculosis and sarcoidosis [8]. A pilot study demonstrated the possibility of detecting pulmonary embolism using EBUS [9]. Although the use of EBUS-TBNA in pulmonary artery sarcoma has not been reported, we felt that it was appropriate and safe for our cases because the mass was in contact with the main bronchus and it was too central for a percutaneous approach. Diagnosis of pulmonary artery sarcoma on small biopsy has also been reported previously [10]. We obtained sufficient core tissue in both cases without complications, and the proper tissue diagnosis was made. In our cases, the EBUS-TBNA needle went through the pulmonary arterial wall to the mass occupying artery. There might be a concern about the safety of the transarterial puncture; however, transarterial approach was safe in our cases, as reported previously [11].

Our cases suggest that EBUS-TBNA is a safe, feasible approach to the differential diagnosis of pulmonary artery sarcoma and pulmonary thromboembolism. EBUS-TBNA can be used as a diagnostic option for pulmonary artery sarcoma according to the tumour location, although additional experience is required before it is used in general practice.

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REFERENCES

1 Benz MR, Tchekmedyian N, Eilber FC, *et al.* Utilization of positron emission tomography in the management of patients with sarcoma. *Curr Opin Oncol* 2009; 21: 345–351.
2 Akomea-Agyin C, Dussek JE, Anderson DR, *et al.* Pulmonary artery sarcoma mimicking pulmonary embolism: successful surgical intervention. *Ann Thorac Surg* 1996; 61: 1536–1538.
3 Loredo JS, Fedullo PF, Piovella F, *et al.* Digital clubbing associated with pulmonary artery sarcoma. *Chest* 1996; 109: 1651–1653.
4 Yi CA, Lee KS, Choe YH, *et al.* Computed tomography in pulmonary artery sarcoma: distinguishing features from pulmonary embolic disease. *J Comput Assist Tomogr* 2004; 28: 34–39.

5 Masauzi N, Ichikawa S, Nishimura F, *et al.* Primary angiosarcoma of the right atrium detected by magnetic resonance imaging. *Intern Med* 1992; 31: 1291–1297.
6 Ito K, Kubota K, Morooka M, *et al.* Diagnostic usefulness of 18F-FDG PET/CT in the differentiation of pulmonary artery sarcoma and pulmonary embolism. *Ann Nucl Med* 2009; 23: 671–676.
7 Chung JH, Cho KJ, Lee SS, *et al.* Overexpression of Glut1 in lymphoid follicles correlates with false-positive (18)F-FDG PET results in lung cancer staging. *J Nucl Med* 2004; 45: 999–1003.
8 Medford AR, Bennett JA, Free CM, *et al.* Endobronchial ultrasound guided transbronchial needle aspiration. *Postgrad Med J* 2010; 86: 106–115.
9 Aumiller J, Herth FJ, Krasnik M, *et al.* Endobronchial ultrasound for detecting central pulmonary emboli: a pilot study. *Respiration* 2009; 77: 298–302.
10 Kim JB, Kim SH, Lim SY, *et al.* Primary angiosarcoma of the pulmonary trunk mimicking pulmonary thromboembolism. *Echocardiography* 2010; 27: E23–E26.
11 Wallace MB, Woodward TA, Raimondo M, *et al.* Transaortic fine-needle aspiration of centrally located lung cancer under endoscopic ultrasound guidance: the final frontier. *Ann Thorac Surg* 2007; 84: 1019–1021.

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Ralstonia mannitolilytica and COPD: a case report

To the Editors:

Ralstonia mannitolilytica is a recently established species of clinical significance and was previously known as *Pseudomonas thomasii* or *Ralstonia pickettii* biovar 3/*thomasii* [1]. It has been recovered from the respiratory tract of patients with cystic fibrosis and has also been associated with catheter-associated bacteraemia, recurrent meningitis, infection of a haemoperitoneum, urinary tract infection and post-renal transplant infection. Hospital outbreaks of *R. mannitolilytica* due to contamination of water [2], saline solutions [3] or oxygen-delivery devices [4] have also been reported. However, this bacterium has not been reported in patients with respiratory illnesses other than cystic fibrosis.

Isolate G100 was recovered from a sputum sample from a male, 78-yr-old patient in April, 2010. This patient was presented with cough and gradually worsening dyspnoea for 1 month, but without fever. He received no antimicrobial agents prior to admission. This patient had a 20-yr history of intermittent cough, and chronic obstructive pulmonary disease (COPD) was diagnosed 10 yrs previously. He had also had type II diabetes mellitus for 5 yrs and had been a cigarette smoker for >20 yrs, but had stopped smoking 10 yrs previously. Physical examination revealed a ''barrel-shaped'' chest, reduced breath sounds and crackles. On admission, a full blood count revealed haemoglobin 15.1 $g \cdot dL^{-1}$, white cell count 5.93×10^9 $cells \cdot L^{-1}$ (neutrophils 4.49×10^9 $cells \cdot L^{-1}$ and lymphocytes 1.25×10^9 $cells \cdot L^{-1}$) and platelets 187×10^9 $cells \cdot L^{-1}$. Routine serum chemistry was normal. Blood-gas analysis revealed pH 7.28, oxygen tension 64 mmHg, carbon dioxide tension 80 mmHg, HCO_3^- 37.6 $mmol \cdot L^{-1}$ and arterial oxygen saturation 89%, suggesting type II respiratory failure and respiratory acidosis. High-resolution chest computed tomography on admission revealed barrel-shaped chest and increased lung markings, but no infiltrations. He was diagnosed with an acute exacerbation of COPD and a sputum sample was sent on admission, from which G100 was isolated. The sputum sample was of good quality when examined by microscopy and Gram-negative rods were detected.

G100 was identified as a *Ralstonia* sp. of Centers for Disease Control group II using a MicroScan Walkaway 96 SI automated system (Siemens Healthcare Diagnostics, Deerfield, IL, USA). Species identification was performed by partially sequencing the 16S ribosomal RNA (rRNA) gene amplified with universal primers 27F and 1492R [5]. The 1,405-bp partial 16S rRNA sequence of G100 was identical to that of *R. mannitolilytica* strain AU0428 from a cystic fibrosis patient in the USA (GenBank accession number AY043378) [6], strains LMG 19090 (LBV407; AJ270257) and LMG 19091 (LBV371; AJ270256) from cases of recurrent meningitis and haemoperitoneum infection in Belgium [1], and many uncultured clones (*e.g.* GQ417788) from environmental samples in France.

Random amplification of polymorphic DNA (RAPD) typing has been used previously to determine the clonal relatedness of *R. mannitolilytica* isolates. Using the *R. pickettii* RAPD primers P3 (5′-AGACGTCCAC-3′) and P15 (5′-AATGGCGCAG-3′) [7], 30 *R. mannitolilytica* clinical isolates from Austria have been classified four distinct genotypes [8]. RAPD using P3 and P15 was performed as described previously [7], revealing that G100 belonged to a genotype different from those seen in Austria (data not shown).

G100 was resistant to amikacin, gentamicin, tobramycin, ampicillin, ampicillin/sulbactam, amoxicillin/clavulanate, piperacillin, ticarcillin/clavulanate, cefazolin, ceftazidime, cefoxitin and aztreonam, intermediate to cefotaxime and cefepime, and sensitive to ceftriaxone, piperacillin/tazobactam, imipenem, ciprofloxacin, levofloxacin and trimethoprim/sulphamethoxazole, as determined with the Walkaway system using Negative Combo panel type 31.

Piperacillin/tazobactam (Wyeth, Beijing, China), 4.5 g every 8 h, was initiated as empirical therapy and continued after the culture result was available, since G100 was sensitive to this compound. This patient also received noninvasive ventilation. However, The patient's condition gradually deteriorated. Therefore, after 9 days of therapy, piperacillin/tazobactam was replaced by panipenem/betamipron (Daiichi Sankyo, Beijing, China) but patient's condition did not improve. After 1 month of hospitalisation, the patient received endotracheal intubation and was transferred to the intensive care unit (ICU) due to deteriorating respiratory failure. Various microorganisms, including *Aspergillus* spp., *Candida albicans*, *Klebsiella oxytoca*, *Klebsiella planticola*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, were recovered from the sputum samples collected at different time-points before or after invasive ventilation.