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Radiological Reasoning: *Pulmonary Embolism—Thinking Beyond the Clots*

Abstract

Objective

We discuss the CT findings in a case of pulmonary embolism complicated by paradoxical embolism in a patient with a patent foramen ovale and atrial septal aneurysm.

Conclusion

When confronted with a case of pulmonary embolism on CT, besides evaluating the extent of pulmonary artery occlusion, the radiologist should examine the cardiovascular system to identify any unsuspected underlying or associated conditions.

Case History

A 60-year-old woman with no significant medical history had resection of a 5-cm non–small cell lung carcinoma of the left lower lobe. This required a pneumonectomy because the tumor encased the left pulmonary artery. Two days after surgery, while attempting to ambulate, the patient became acutely short of breath and hypoxic. Due to the clinical suspicion for pulmonary embolism, CT pulmonary angiography was performed (Fig. 1). (At this point, if the abstract has not been reviewed, we encourage the reader to examine the CT images to formulate a diagnosis before proceeding further.)

CT

The CT scan shows subcutaneous emphysema with air and fluid in the left pneumonectomy space. There is a central area of hypoattenuation in the interlobar branch of the right pulmonary artery and in the pulmonary artery to the right middle lobe. Multiple segmental pulmonary arterial filling defects are also present in the right lower lobe. The atrial septum appears deformed with curvature convex toward the left atrium. In the upper abdomen, there is a large wedge-shaped area of hypoattenuation in the spleen and a small subtle area of decreased enhancement in the medial aspect of the superior pole of the left kidney.

Expert Discussion (Dr. Maldjian)

The left-sided subcutaneous emphysema and air and fluid in the left pneumonectomy space are expected postoperative findings and do not require further discussion. The filling defects in the pulmonary vessels represent pulmonary emboli. Normally, the short-axis diameter of the right ventricle is about equal to that of the left ventricle. In this case, the right ventricle is dilated compared with the left ventricle. This finding on CT in association with pulmonary embolism may indicate right ventricular dysfunction secondary to the acute elevation of pulmonary artery pressure [1]. The right atrium is also dilated, which is probably due to the elevated right-sided cardiac pressures.

Keywords: cardiopulmonary imaging, embolism, heart

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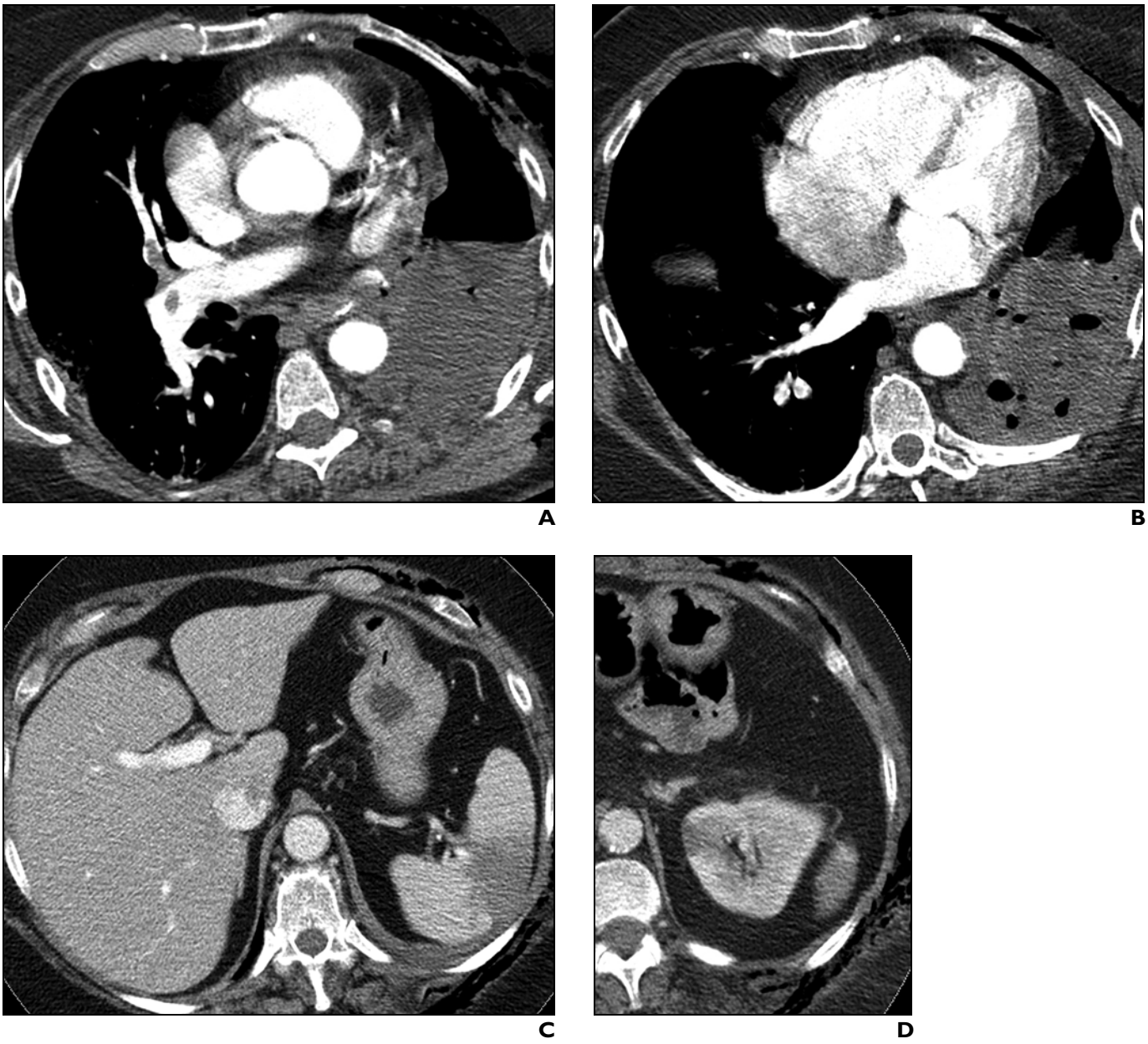
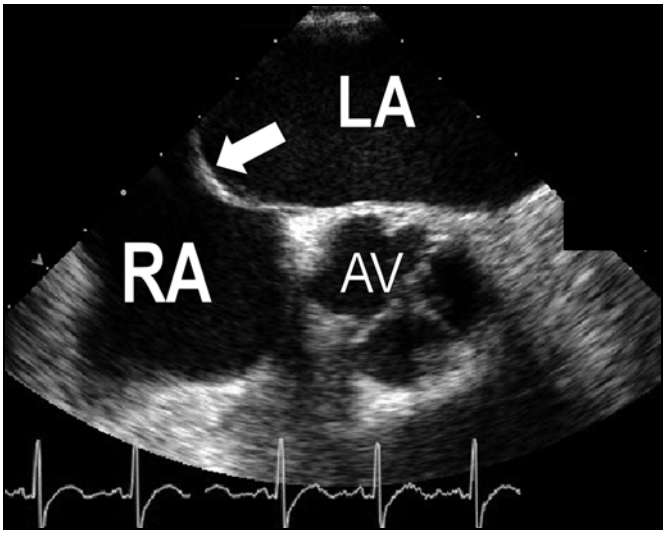


Fig. 1—60-year-old woman who developed acute dyspnea and hypoxia 2 days after left pneumonectomy. Images are from CT pulmonary angiography.
A–D, CT images at level of right interlobar artery (**A**), at level of cardiac chambers (**B**), through upper abdomen (**C**), and at level of superior pole of left kidney (**D**).

The large wedge-shaped defect in the spleen and the small low-attenuation area in the superior pole of the left kidney represent infarcts. These findings in a patient with pulmonary embolism indicate paradoxical embolism. Paradoxical emboli are most commonly caused by an intracardiac communication between the systemic and pulmonary circulations. Patent foramen ovale and atrial septal defect are the two most common cardiac abnormalities associated with paradoxical emboli [2]. Therefore, we should now scrutinize the image through the cardiac chambers. The atrial septum is bulging abnormally toward the left atrium. This finding is consistent with an atrial septal aneurysm (ASA). Bowing of the ASA toward the left atrium indicates that at the instant the image was obtained the pressure in the right atrium exceeded that in the left atrium. This difference in pressure can be transient, related to the phase of the cardiac cycle, but in this case likely reflects acute elevation of the right-sided cardiac pressures.

The significance of an ASA is its association with patent foramen ovale (PFO). Approximately 70% of patients with an ASA also have a PFO [3]. Thus, we can now postulate a diagnosis that



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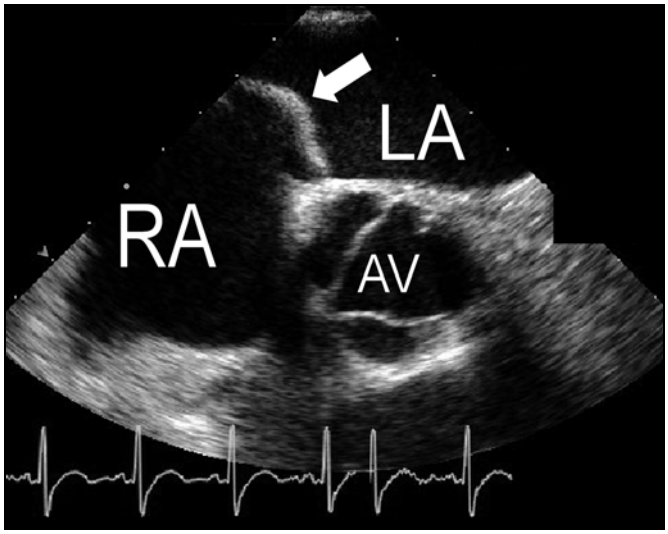

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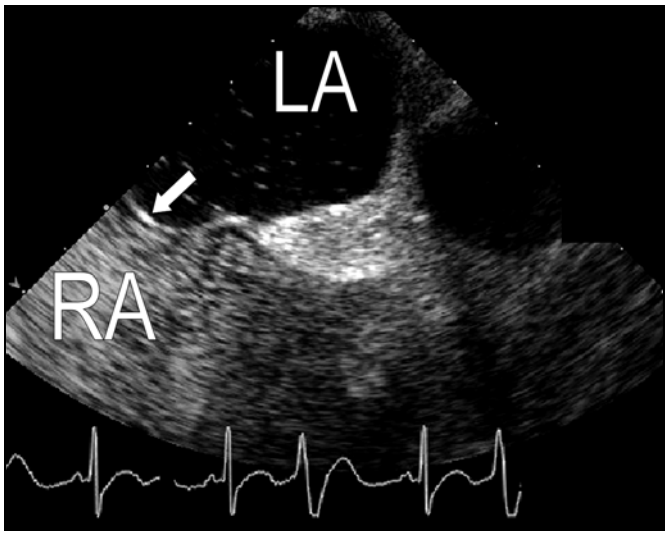

C

Fig. 2—Images from transesophageal echocardiography performed 6 days after CT study show atrial septal aneurysm oscillating throughout cardiac cycle and right-to-left shunt at atrial level after administration of agitated saline. RA = right atrium, LA = left atrium, AV = aortic valve, arrow = atrial septum.
A, Image in diastole shows bulging of atrial septum toward right atrium.
B, Image in systole shows atrial septum bulging into left atrium.
C, Image after administration of saline containing microbubbles shows increased echogenicity in right atrium representing bolus and speckled echoes in left atrium from passage of microbubbles through patent foramen ovale.

explains all of the CT findings. The pulmonary embolism caused elevation of the right-sided intracardiac pressures that resulted in increased right-to-left shunting through a PFO, thereby predisposing the patient to paradoxical emboli.

Clinical Management

After the CT examination, the patient received IV infusion of heparin for systemic anticoagulation. Vascular sonography of the lower extremities performed 2 days later was negative for deep venous thrombosis. Because swelling and erythema of the patient's left arm were noted by the clinical service, vascular sonography of the left upper extremity was also performed, which revealed thrombosis of the cephalic vein extending into the left subclavian vein. The thrombophlebitis was likely a complication from IV cannulation and was deemed the source of the pulmonary emboli.

Transthoracic and transesophageal echocardiography was performed 6 days after CT. An ASA was seen on the transesophageal study (Figs. 2A and 2B), although it was not visible on the transthoracic study. The transesophageal study obtained with saline used as contrast material also confirmed the presence of a PFO (Fig. 2C). No intracardiac thrombi were present. Right ventricular function was normal. The patient recovered uneventfully and was discharged from the hospital after converting to oral warfarin to continue anticoagulation. The final diagnosis was pulmonary embolism and paradoxical embolism with PFO and ASA.

Expert Discussion (Dr. Maldjian)

In most cases, thrombi from the lower extremities are the source for pulmonary emboli, and it is rare to encounter a patient with pulmonary embolism from clots in the upper extremity. Although a

negative sonography examination of the lower extremities does not completely exclude lower extremity veins as a source of emboli, the known thrombus in the upper extremity was the most likely source in this patient. Because the patient had only one lung, it would not require a large amount of embolized clot from the thrombus in the subclavian vein to result in significant compromise of the pulmonary circulation. The patient may also have been at increased risk for thrombophlebitis because a hypercoagulable state is associated with malignancy [4].

The fact that the ASA was visible on only the transesophageal echocardiogram is not surprising because ASAs are commonly missed on a transthoracic study alone [3]. Normal right ventricular function at the time of echocardiography given the appearance on CT likely reflects a good therapeutic response. On echocardiography, the diagnosis of PFO is made using agitated saline (saline containing microbubbles of air) as a sonography contrast agent. The saline is injected IV, and the sonographer looks for passage of microbubbles from the right atrium to the left atrium through the atrial septum. The patient can be asked to cough or bear down (Valsalva maneuver) during the injection; these actions transiently elevate right atrial pressure and increase the amount of shunting through a PFO [5].

Commentary

A definitive diagnosis of paradoxical embolism requires detection of thrombus lodged in the intracardiac defect, most commonly right atrial thrombus crossing a PFO. Such direct observation is rare and is usually limited to sporadic echocardiographic reports [6]. In clinical practice the diagnosis of paradoxical embolism is usually presumptive and requires detection of the following three elements: first, systemic embolism without an apparent source in the left heart or proximal arterial tree (no evidence of atrial fibrillation or severe atherosclerosis of the thoracic aorta); second, venous thrombus or pulmonary embolus as an embolic source; and, third, right-to-left shunting through an abnormal communication between the right and left circulations, such as a PFO, atrial septal defect, or pulmonary arteriovenous malformation [2, 6].

A PFO is the most common abnormal communication between the right and left circulations associated with paradoxical embolism. Both echocardiography and autopsy studies have shown that the prevalence of PFO is approximately 25% [7, 8]. A PFO usually remains physiologically closed as long as the pressure in the left atrium is higher than the pressure in the right atrium. However, common maneuvers, such as inspiration, cough, or Valsalva, can result in transient elevation of right atrial pressure sufficient to allow paradoxical emboli to pass from the right atrium to the left via the PFO [9]. The eustachian valve (valve of the inferior vena cava) may also direct blood return from the inferior vena cava directly onto the PFO, promoting passage of thrombi from the lower extremity veins to the systemic circulation [10]. Echocardiographers can take advantage of this phenomenon as the sensitivity for the detection of a PFO is increased when agitated saline contrast material is injected through a femoral vein rather than an antecubital vein [11].

An ASA is a congenital cardiac abnormality characterized by saccular formation of the interatrial septum. Redundant atrial septal tissue results in bulging of the septum into either or both atria during the cardiac cycle. ASA has a high association with PFO: 70% of patients with an ASA also have a PFO. The combination of ASA and PFO also puts the patient at increased risk for cryptogenic stroke likely from paradoxical emboli [3]. It has been theorized that the motion of the ASA promotes paradoxical shunting by enhancing the already preferential orientation of blood flow from the inferior vena cava toward the PFO [12]. Transesophageal echocardiography is considered the best imaging test for the diagnosis of PFO and ASA [5]. Recently, contrast-enhanced dynamic MRI with the Valsalva maneuver has also been shown to be useful in the diagnosis of ASA and PFO [13].

Pulmonary embolism in the setting of a coexistent PFO increases the risk of paradoxical embolism due to elevated right-sided cardiac pressure increasing right-to-left shunting through the PFO [14]. It has been shown that right-to-left shunting through a PFO is increased in acute pulmonary embolism even in hemodynamically stable patients without preexisting cardiopulmonary disease [15]. In their a study of patients with acute major pulmonary embolism, Konstantinides et al. [6] found right-to-left shunting through a PFO to be an independent predictor of adverse outcome. In that study, those patients with a PFO had a significantly higher incidence of death (33% vs 14%) and ischemic stroke (13% vs 2.2%) than those without a PFO [6].

Therapeutic options for paradoxical embolism associated with PFO include anticoagulation, thrombectomy, placement of an inferior vena cava filter (if the source for emboli is from the lower extremity), and closure of the PFO [16]. Recurrent paradoxical embolism in the presence of a PFO and ASA is considered an unequivocal indication for PFO closure [10]. Closure of a PFO can now be accomplished with devices implanted percutaneously [17].

When confronted with a case of pulmonary embolism on CT, besides identifying the extent of pulmonary artery occlusion, the radiologist should examine the cardiovascular system for any associated abnormalities. Dilatation of the right ventricle and interventricular septal shift toward the left ventricle are associated with right ventricular dysfunction secondary to pressure overload. Other signs of pressure overload of the right heart include enlargement of the right atrium and the inferior vena cava [18]. Patients with right ventricular dysfunction after pulmonary embolism have a higher mortality rate than those with normal right ventricular function even if hemodynamically stable at presentation [19, 20]. Therefore, right ventricular dysfunction in patients with pulmonary embolism places them at increased risk and may be an indication for aggressive intervention, such as thrombolytic therapy, as opposed to anticoagulation alone [21].

A PFO on CT pulmonary angiography can manifest as decreased enhancement of the pulmonary artery with early enhancement of the thoracic aorta from augmentation of right-to-left shunting through the defect caused by deep inspiration [22] (although this was not present in our patient). Significant deviation of the atrial septum might indicate an ASA, and as we have seen, this finding should also raise suspicion for a possible coexisting PFO. The cardiac chambers

and systemic arteries should also be scrutinized because paradoxical embolism can have characteristic findings on CT [23–25].

In conclusion, we have presented a case of pulmonary embolism complicated by paradoxical embolism in a patient with an ASA and PFO. Although the diagnosis of pulmonary embolism on CT may be straightforward, it is essential that the radiologist examine the remainder of the cardiovascular system for ancillary findings to diagnose unsuspected underlying conditions. The radiologist should look and think beyond the pulmonary clots.

References

1. Contractor S, Maldjian PD, Sharma VK, Gor DM. Role of helical CT in detecting right ventricular dysfunction secondary to acute pulmonary embolism. *J Comput Assist Tomogr* 2002; 26:587–591
2. Ward R, Jones D, Haponik EF. Paradoxical embolism: an underrecognized problem. *Chest* 1995; 108:549–558
3. Cabanes L, Mas JL, Cohen A, Amarenco P, et al. Atrial septal aneurysm and patent foramen ovale as risk factors for cryptogenic stroke in patients less than 55 years of age: a study using transesophageal echocardiography. *Stroke* 1993; 24:1865–1873
4. Falanga A. Thrombophilia in cancer. *Semin Thromb Haemost* 2005; 31:104–110
5. Gill EA, Quaife RA. The echocardiographer and the diagnosis of patent foramen ovale. *Cardiol Clin* 2005; 23:47–52
6. Konstantinides S, Geibel A, Kasper W, Olschewski M, Blumel L, Just H. Patent foramen ovale is an important predictor of adverse outcome in patients with major pulmonary embolism. *Circulation* 1998; 97:1946–1951
7. Gill EA. Definitions and pathophysiology of the patent foramen ovale: broad overview. *Cardiol Clin* 2005; 23:1–6
8. Meissner I, Whisnant JP, Khandheria BK, et al. Prevalence of potential risk factors for stroke assessed by transesophageal echocardiography and carotid ultrasonography: the SPARC study. *Mayo Clin Proc* 1999; 74:862–869
9. Wu LA, Malouf JF, Dearani JA, et al. Patent foramen ovale in cryptogenic stroke: current understanding and management options. *Arch Intern Med* 2004; 164:950–956
10. Meier B, Lock JE. Contemporary management of patent foramen ovale. *Circulation* 2003; 107:5–9
11. Cramer SC. Patent foramen ovale and its relationship to stroke. *Cardiol Clin* 2005; 23:7–11
12. Mas JL, Arquizan C, Lamy C, et al. Recurrent cerebrovascular events associated with patent foramen ovale, atrial septal aneurysm, or both. *N Engl J Med* 2001; 345:1740–1746
13. Mohrs OK, Petersen SE, Erkapic D, et al. Diagnosis of patent foramen ovale using contrast-enhanced dynamic MRI: a pilot study. *AJR* 2005; 184:234–240
14. Kasper W, Geibel A, Tiede N, Just H. Patent foramen ovale in patients with haemodynamically significant pulmonary embolism. *Lancet* 1992; 340:561–564
15. Miller RL, Das S, Anandarangam T, et al. Relation between patent foramen ovale and perfusion abnormalities in acute pulmonary embolism. *Am J Cardiol* 1997; 80:377–378
16. Inoue T, Tadehara F, Hinoi T, et al. Paradoxical peripheral embolism coincident with acute pulmonary thromboembolism. *Intern Med* 2005; 44:243–245
17. Carroll JD, Dodge S, Groves BM. Percutaneous patent foramen ovale closure. *Cardiol Clin* 2005; 23:13–33
18. Cheriex EC, Sreeram N, Eussen YF, Pieters FA, Wellens HJ. Cross sectional Doppler echocardiography as the initial technique for the diagnosis of acute pulmonary embolism. *Br Heart J* 1994; 72:52–57
19. Grifoni S, Olivotto I, Cecchini P, et al. Short-term clinical outcome of patients with acute pulmonary embolism, normal blood pressure, and echocardiographic right ventricular dysfunction. *Circulation* 2000; 101:2817–2822
20. Van der Meer RW, Pattynama PM, Van Strijen MJ, et al. Right ventricular dysfunction and pulmonary obstruction index at helical CT: prediction of clinical outcome during 3-month follow-up in patients with acute pulmonary embolism. *Radiology* 2005; 235:798–803
21. Lualdi JC, Goldhaber SZ. Right ventricular dysfunction after acute pulmonary embolism: pathophysiologic factors, detection, and therapeutic implications. *Am Heart J* 1995; 130:1276–1282
22. Henk CB, Grampp S, Linnau KF, et al. Suspected pulmonary embolism: enhancement of pulmonary arteries at deep-inspiration CT angiography—influence of patent foramen ovale and atrial septal defect. *Radiology* 2003; 226:749–755
23. Kim JH, Seo JB, Do KH, et al. Paradoxical embolism detected on CT angiography and treated with temporary inferior vena cava filtration and anticoagulation. *AJR* 2004; 183:1244–1246
24. Delalu P, Ferretti GR, Bricault I, Ayanian D, Coulomb M. Paradoxical emboli: demonstration using helical computed tomography of the pulmonary artery associated with abdominal computed tomography. *Eur Radiol* 2000; 10:384–386
25. Oliver TB, Reid JH. Thoracic aortic dissection that wasn't: CT demonstration of probable paradoxical embolus secondary to unsuspected pulmonary embolus. *Br J Radiol* 1997; 70:840–842