and across subgroups according to age, gender, prior statin use, or co-morbidities (diabetes, metabolic syndrome, or hypertension, with the exception of patients with no hypertension). C-reactive protein was also measured. It decreased significantly more with atorvastatin (-5.2 vs. -36.4% , $p < 0.0001$). Adverse events were similar in the two groups.

Conclusions: Intensive treatment with atorvastatin 80 mg halted progression of coronary atherosclerosis in the full cohort and all 22 prespecified subgroups. Significant differences be-

tween progression rates favoring atorvastatin over pravastatin were observed for primary and secondary efficacy measures.

Consideration of intensive treatment with 80 mg atorvastatin is warranted in secondary prevention, particularly for patients at high risk of morbid events.

Comment (Steven Nissen, M.D.): The main message is that you can reduce the atherosclerosis progression rate essentially to zero, but to do that you have to use the highest dose of a high-efficacy statin.

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Short Communication

A Case of Paradoxical Embolism “in situ” Associated with Massive Pulmonary Embolism: Role of Echocardiography

ANDREW D. SUMNER, M.D., RICK HENDERSON, B.S.,* DEENA MARTIN, B.S.,* VINCENT L. SORRELL, M.D.*

Division of Cardiology, Department of Medicine, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania; *Division of Cardiology, Department of Medicine, Brody School of Medicine, East Carolina University, Greenville, North Carolina, USA

Summary: A 49-year-old man was admitted in transfer for further management of a pulmonary embolism (PE) and possible mitral valve vegetation. Transthoracic echocardiography performed at our institution showed evidence of right ventricular (RV) enlargement and dysfunction. Within the right atrium was a serpentine mobile thrombus which traversed the interatrial septum at the level of the fossa ovalis and extended into the left atrium to the level of the anterior mitral valve leaflet. Because of the patient's dyspnea, RV dysfunction, and large clot burden, thrombolytic therapy was considered and would have been administered had the thrombus in situ not been identified. In light of the thrombus in situ and the concern about possible systemic embolization with thrombolytic therapy, the patient underwent successful surgical thrombectomy. This case highlights the importance of echocardiography in the management of patients with PE. We believe that all pa-

tients should undergo echocardiography prior to receiving thrombolytic therapy for pulmonary emboli. Careful interrogation of the interatrial septum for the presence of a thrombus in situ is warranted. Thrombectomy should be considered in individuals with PE who have a thrombus in situ.

Key words: pulmonary embolus, paradoxical embolus, echocardiography, thrombus in situ

Introduction

Pulmonary embolism (PE) is a relatively common and often lethal disease.¹ Early diagnosis and treatment can be life saving.¹ Use of thrombolytic therapy is often advocated when a PE is associated with hemodynamic compromise or right ventricular (RV) dysfunction.^{2–4} Echocardiography can be useful in the diagnosis and management of PE and its complications.^{5–7} We present a case of PE associated with RV dysfunction complicated by a paradoxical embolus in situ. Echocardiography was central to diagnosing this complication, and information from the echocardiogram altered treatment.

Case Report

A 49-year-old man was admitted in transfer for further management of a PE and possible mitral valve vegetation. The

Address for reprints:

Andrew D. Sumner, M.D.
Associate Professor of Medicine, Division of Cardiology
Penn State Milton S. Hershey Medical Center
500 University Drive, P.O. Box 850, MC H-047
Hershey, PA 17033-0850, USA
e-mail: asumner1@psu.edu

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patient presented to an outside hospital because of worsening dyspnea on exertion, syncope, chest pain, and bilateral leg pain. His past medical history was significant for idiopathic urticaria and two episodes of deep vein thrombosis following a lumbar discectomy performed 14 years previously. He had not been on long-term anticoagulation and had no family history of a hypercoagulable state. His medications on presentation were ranitidine 150 mg p.o., b.i.d., cetirizine 5 mg p.o. daily, and hydroxyzine 25 mg p.o., t.i.d.

On physical examination he appeared minimally dyspneic. His blood pressure was 137/87 mmHg with a heart rate of 83 beats/min. His respiratory rate was 20/min. He had coarse breath sounds bilaterally, elevated jugular venous pulsations, a prominent fourth heart sound, a grade II/VI holosystolic murmur at the base, and bilateral lower extremity edema, greater in the left leg than in the right. His neurological exam was normal and there was no evidence of systemic arterial embolization.

PaO₂ on room air was 48 mmHg. An electrocardiogram showed normal sinus rhythm with nonspecific T-wave changes. A ventilation-perfusion scan performed at the referring institution showed bilateral perfusion defects consistent with bilateral PE. Two-dimensional transthoracic echocardiography from the outside institution was reported to show RV enlargement with a mobile mass in the right atrium and a mass on the atrial side of the anterior mitral valve leaflet. Lower extremity venous duplex examination revealed venous thrombosis in the superficial femoral and popliteal veins. There was no evidence of venous thrombi in the right leg.

Transthoracic echocardiography performed at our institution showed evidence of RV enlargement, RV dysfunction, plethora of the inferior vena cava, small left ventricular cavity size, and ventricular interdependence (Figs. 1, 2). Right ventricular systolic pressure was estimated to be at least 50 mmHg by Doppler echocardiography. Within the right atrium was a serpentine mobile echogenic structure consistent with thrombus (Fig. 3). It traversed the interatrial septum at the level of the fossa ovalis and extended into the left atrium to the level of the anterior mitral valve leaflet. Because of the patient's dyspnea, RV dysfunction, and large clot burden, thrombolytic therapy was considered and would have been administered had the thrombus in situ not been identified. In light of the thrombus in situ and the concern about possible systemic embolization with thrombolytic therapy, the patient was referred for surgical thrombectomy. At surgery, a 12 cm thrombus that extended across the fossa ovalis into the left atrium was removed from the right atrium (Fig. 4). An 8 cm thrombus was also removed from the distal main and right pulmonary arteries. The patient's postoperative course was uneventful. He was therapeutically anticoagulated and discharged home on postoperative Day 11.

Discussion

Echocardiography is a noninvasive imaging test often used in the management of patients with PE. Although it is not recommended as a routine test for diagnosing suspected PE,² it

FIG. 1 Apical four-chamber transthoracic echocardiogram demonstrating dilated right heart with small left ventricular cavity. RV = right ventricle, LV = left ventricle, RA = right atrium, LA = left atrium.

FIG. 2 Parasternal short-axis transthoracic echocardiogram. The right heart is dilated and there is flattening of the interventricular septum in systole and diastole suggesting right ventricular pressure and volume overload. Abbreviations as in Figure 1.

FIG. 3 Subcostal four-chamber echocardiogram. The right heart is dilated. A thrombus is visualized in the right atrium and traverses the interatrial septum at the level of the fossa ovalis extending into the left atrium (thrombus identified by arrows). Abbreviations as in Figure 1.

FIG. 4 Thrombus removed from patient's right atrium and pulmonary arteries at the time of surgical thrombectomy.

does provide information useful in the diagnosis of patients with unexplained dyspnea or syncope, is helpful in identifying patients with PE who are at high risk, and is useful in helping guide thrombolytic therapy in high-risk patients.^{2-4, 6, 7}

Large pulmonary emboli cause an abrupt increase in pulmonary artery pressure and increase RV afterload. This often produces the echocardiographic findings of RV dilatation and hypokinesis, abnormal motion of the interventricular septum, tricuspid regurgitation, and plethora of the inferior vena cava.⁵ It is not surprising that our patient exhibited these echocardiographic findings given his large bilateral pulmonary emboli. Of note, our patient had global dysfunction of the RV free wall, and the RV apex was not spared. McConnell *et al.* described the phenomena of free RV wall dysfunction with relatively normal contraction of the RV apex as a useful sign for helping to distinguish between RV dysfunction due to PE (normal RV apical function) and dysfunction due to other causes such as pulmonary hypertension.⁸ In our patient, apical RV dysfunction existed with documented PE. Absence of the McConnell sign may have been due to the possibility that our patient had acute or chronic PE, or that the sensitivity of the sign is not 100%.

In patients with PE, echocardiography is especially useful in identifying those at high risk of death. Ribero *et al.* performed transthoracic echocardiography on the day of diagnosis in 126 consecutive patients with PE.⁶ After multivariate analysis, RV dysfunction was the most powerful predictor of in-hospital death. Grifoni *et al.* found similar results in their cohort of 209 consecutive patients with PE and normal systemic arterial pressures on admission.⁹ Of these, 15% with PE

and echocardiographic evidence of RV dysfunction developed cardiogenic shock within 24 h of diagnosis or died during the initial hospitalization.⁹ None of the 97 patients with PE who had normal RV function on echocardiography died.⁹

In addition to the presence of RV dysfunction, elevated pulmonary artery systolic pressure estimated on Doppler echocardiography identifies individuals with increased morbidity after PE.¹⁰ Patients with pulmonary artery systolic pressures > 50 mmHg at admission were three times as likely to have persistent pulmonary hypertension and RV dysfunction 6 weeks later compared with patients with normal or mildly elevated pulmonary artery pressures.¹⁰

Our patient's large clot burden, RV dysfunction, and moderate pulmonary hypertension placed him at high risk of death from his PE, and aggressive therapy was felt to be warranted. Thrombolytic therapy would have been administered, but the presence of the thrombus in situ was felt to be a relative contraindication to thrombolytic therapy because of the concern of systemic embolization. The presence of a thrombus located across the fossa ovalis was easily identified in our patient on transthoracic echocardiography. Misinterpretation of this entity as a mitral valve vegetation at an outside institution highlights the importance of a thorough echocardiographic examination as well as an appreciation that thrombus in situ can complicate PE.

The presence of a patent foramen ovale, even in the absence of a thrombus in situ, places an individual at a higher risk of death and arterial thromboembolic complications.¹¹ In 139 consecutive patients with PE, Konstantinides *et al.* found that the presence of a patent foramen ovale doubles the mortality rate compared with patients with a PE and no shunt.¹¹

Thrombolytic therapy should be considered in patients with acute PE who have hemodynamic embarrassment or evidence of RV dysfunction.²⁻⁴ Nonrandomized registry data¹² have shown that thrombolytics decrease mortality when administered to hemodynamically stable patients with PE and RV dysfunction. Unfortunately, no randomized trials have been performed using thrombolytics in this patient group. In a randomized trial of thrombolytics plus anticoagulation versus anticoagulation alone for patients with PE and normal systemic pressures, those with RV dysfunction who received thrombolytics had significantly fewer recurrent PE and significantly improved RV function.³

Our patient would have received thrombolytic therapy had he not had a thrombus in situ across the fossa ovalis. We are aware of no data evaluating the use of thrombolytics in patients with PE and a thrombus in situ across the fossa ovalis. The reported risk of systemic embolization in patients with left-sided cardiac thrombi from other etiologies is variable.¹³⁻¹⁶ In post hoc analysis, Sloan *et al.*¹³ found no increased risk of serious embolic events when thrombolytic therapy was administered for acute myocardial infarction in individuals at clinically high risk for embolization. Derex *et al.* found that the risk of embolism was not increased in stroke patients with a known left ventricular thrombus given tissue plasminogen activator (t-PA).¹⁴ Other researchers, however, have found high rates of systemic embolization when thrombolytics were given to pa-

tients with myocardial infarction and coexisting left ventricular thrombi¹⁵ and to those with prosthetic valve thrombi.¹⁶ It is possible that a mobile paradoxical venous thromboembolus may have more embolic potential than other left-heart thrombi. Because of the perceived high risk of systemic embolization, we elected to treat our patient with surgical thrombectomy. This technique has been used successfully by others in the treatment of patients with PE and thrombi in situ.¹⁷

Conclusions

Echocardiography is an important tool in managing patients with PE. In our patient, it demonstrated RV dysfunction and a thrombus located across the fossa ovalis. We believe that all patients should undergo echocardiography prior to receiving thrombolytic therapy for PE. Careful interrogation of the interatrial septum for the presence of a thrombus in situ is warranted and thrombectomy should be considered in individuals with PE who have a thrombus in situ.

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