after an effort that successfully triggered the ventilator. The relative contributions of rib cage proprioceptors, respiratory muscle spindles, and lung afferents to decreased respiratory rate are not known.

We believe that this case provides interesting insights into the origins of the inhibitory feedback. The longest period between breaths occurred when both lungs were inflated simultaneously. After about 4 s, the ventilator of the transplanted lung delivered a breath that did not inhibit the patient’s inspiration a few seconds later. The transplanted lung was inflated with a relatively large VR, increasing pleural pressure, increasing the hemithorax volume by expanding the rib cage, and depressing the diaphragm. However, the lung inflation did not provide any sensory feedback from the denervated lung. Ventilator-triggered inflation of the transplanted lung was quickly followed by another inspiratory effort, which often triggered only the ventilator to the native lung. After an inspiratory effort that triggered only the ventilator of native lung, the time to the next inspiratory effort was shorter than after an effort that triggered the ventilator to both lungs. We interpret these findings to suggest that although most of the inhibition of inspiration, which occurs with lung inflation, comes from lung receptors transmitted through the vagus nerve (the Hering-Breuer reflex), there is some influence from the respiratory muscles and displacement of the chest wall.

These data also provide some insight about the mechanics of the thorax. If inflating one lung expanded the rib cage bilaterally without displacing the mediastinum and displaced both hemithorax, it would facilitate inflation of the other lung. This is consistent with the findings of Hubmayr and Margulies and Hubmayr et al in dogs and primates, that lungs of unequal size and mechanical properties resist displacement and deformation when exposed to different pressure. In contrast, if inflation of one lung displaces the mediastinum into the other hemithorax, and increased abdominal pressure paradoxically displaced the contralateral hemidiaphragm, it would require more pressure to inflate the other lung.

Inspiratory efforts, which trigger the ventilator to the transplanted lung sometimes also, triggered the ventilator to the native lung, so that both lungs were at end-inspiration simultaneously. When an inspiratory effort triggered only the ventilator to the transplanted lung, the native lung was at a lower volume at the time of end-inspiration of the transplanted lung than when both lungs were inflated. In this situation, peak Paw in the transplanted lung was also lower than when both lungs were inflated synchronously. This demonstrates an interdependence between the two hemithoraces. It takes more pressure to inflate a lung when the opposite lung is at a high volume than when it was at a low volume. That is, the two lungs compete for space in the thorax.

Expiratory flow from the native lung appears to increase slightly when the contralateral transplanted lung is at end inspiration. The pleural pressure applied to the native lung should increase when the contralateral lung is inflated, but the native lung was almost certainly flow limited, so this is an unlikely cause for increased expiratory flow. The increased volume of the contralateral lung should increase longitudinal tension on the airways of the native lung that may increase maximal flow, but we cannot exclude the possibility that there was a small leak from the transplanted lung at peak Paw that increased flow through the endotracheal tube of the native lung. In summary, this case shows that most of the inhibition of inspiration from ventilator-delivered lung inflation is mediated through vagal afferents in the lung and not chest wall afferents.

REFERENCES

Lysis of a Left Ventricular Thrombus With Recombinant Tissue Plasminogen Activator*

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A 23-year-old woman with peripartum cardiomyopathy presented with a 2.1 × 2.5-cm pedunculated, mobile, left ventricular thrombus and evidence of systemic embolization. Due to the patient’s poor left ventricular function, thrombectomy was not a viable option. Treatment with high-dose IV heparin was initially utilized but was unsuccessful as the thrombus appeared to enlarge on echocardiography. An accelerated weight-adjusted dose of recombinant tissue plasminogen activator (rt-PA) successfully lysed the thrombus without evidence of embolization. Although rt-PA has been used for primary lysis of high-risk ventricular thrombi, this is the first documentation of successful lyse of a left ventricular thrombus in a patient with peripartum cardiomyopathy. (CHEST 2001; 120:681–683)

Key words: adult; cardiomyopathy; echocardiography; thrombolysis; thrombus

Abbreviations: AMI = acute myocardial infarction; DCM = dilated cardiomyopathy; LVEF = left ventricular ejection fraction; rt-PA = recombinant tissue plasminogen activator
This case report describes a young woman with peripartum cardiomyopathy who presented with a 2.1x2.5-cm pedunculated, mobile, left ventricular thrombus and evidence of systemic embolization. Although recombinant tissue plasminogen activator (rt-PA) has been used for primary lysis of high-risk ventricular thrombi, this is the first documentation of successful lysis of a left ventricular thrombus in a patient with peripartum cardiomyopathy.

CASE REPORT

A 23-year-old woman with pregnancy-induced hypertension diagnosed at 20 weeks’ gestation and peripartum cardiomyopathy diagnosed 1 month postpartum was admitted to the medical ICU with worsening shortness of breath, fatigue, and bilateral flank pain. The patient was 2 months postpartum and was receiving lisinopril, furosemide, and digoxin for congestive heart failure. An echocardiogram 1 month prior to ICU admission showed a left ventricular ejection fraction (LVEF) of 40%, moderate pulmonary hypertension, mild left atrial enlargement, and mild mitral and tricuspid regurgitation with anteroseptal and inferior wall hypokinesis.

On evaluation, vital signs were as follows: temperature (oral), 39.4°C; heart rate, 130 beats/min; and respiratory rate, 35 breaths/min. The patient was an obese woman in mild distress because of pain, with elevated jugular venous pulsations, tachycardia with an S3 gallop at the apex, and bilateral basilar rales on auscultation. There was moderate, bilateral, lower-quadrant abdominal tenderness without rebound or pain with percussion. Significant laboratory data included the following: total leukocyte count, 21,000/μL with 70% segmented and 6% band cells; alkaline phosphatase, 388 IU/L; aspartate aminotransferase, 407 IU/L; and alanine aminotransferase, 368 IU/L. An ECG showed sinus tachycardia with nonspecific ST-T segment abnormalities, and chest radiograph revealed cardiomegaly with an infiltrate in the left lower lung field consistent with pneumonia. Treatment with broad-spectrum antibiotics was initiated secondary to concerns for a concomitant pulmonary and intra-abdominal infection. A CT of the abdomen showed findings suggestive of partial splenic and right renal ischemic infarction. Two-dimensional Doppler echocardiogram on hospital day 2 revealed severely decreased LVEF (25%) and a 2.1x2.5-cm apical left ventricular thrombus that was mobile and protruding into the left ventricular cavity (Fig 1). Although the patient had no complaints of chest pain, mild elevations in cardiac troponin I isoenzyme were detected. This troponin elevation was believed secondary to embolization into the coronary arteries with resultant microinfarction and worsening left ventricular function. Subsequently, the patient was administered a weight-based heparin infusion. During the following 48 h, she developed a painful and transiently pulseless right lower extremity. A repeat echocardiogram on hospital day 4 revealed evidence of lucency in the center of the thrombus, as well as an attached echo-dense area suggesting further thrombus formation. Due to the high likelihood of continued embolization, in light of a negative finding on CT of the head, the patient was administered (following informed consent) an accelerated, weight-adjusted infusion of rt-PA over the course of 90 min. A follow-up echocardiogram approximately 8 to 10 h later showed near complete resolution of the thrombus. There were no further clinical signs of embolization during or after rt-PA infusion. An echocardiogram on hospital day 8 showed persistently diminished LVEF with global hypokinesis, but no evidence of residual or recurrent thrombus formation. The patient was discharged receiving oral warfarin therapy.

DISCUSSION

The development of intracavitary or mural cardiac thrombi in patients with acute myocardial infarction (AMI), left ventricular aneurysm, and dilated cardiomyopathy (DCM) is well described.1 Although the exact mech-
anism remains unclear, presumably an akinetic segment or globally hypokinetic ventricle leads to stasis and subsequent thrombus formation. For the last 20 years, two-dimensional echocardiography has been effectively and reliably utilized to demonstrate the presence of ventricular thrombi, both mural and intracavitary, with a 36 to 44% incidence of left ventricular thrombosis. However, perhaps the more concerning aspect regarding ventricular thrombosis is not its presence, but the potential for systemic embolization. The morphologic characteristics of the clot itself combined with the contractility of the ventricle are primary determinants of embolic risk. Intuitively, a thrombus that protrudes into the lumen of the ventricle and is subject to the flow of blood vigorously pumped across its surface has a greater propensity to detach and embolize than does a smooth, mural thrombus located in a relatively akinetic wall segment. Haugland et al studied 60 patients with left ventricular thrombus visualized on two-dimensional echocardiography. Of the 27% of patients with evidence of systemic embolization, intracavitary motion combined with protrusion and central echogenic lucency were the three most important characteristics, in descending order, associated with embolization.

Although the incidence, frequency, and embolic potential of left ventricular thrombi has been well studied and documented, there is no generally accepted consensus published regarding its management. Over the last 30 years, the primary therapeutic options have included thrombectomy, anticoagulation, or, more recently, thrombolysis.

Before rt-PA was commercially available in the United States, the two primary thrombolytic agents on the market were streptokinase and urokinase. These agents have been used extensively to treat left ventricular thrombus and, particularly, AMI. Kremer et al described 16 patients with recent AMI and mural thrombi who were treated with urokinase. Successful lysis, which seemed to occur more commonly in soft, newly formed clots, was noted in 10 of 16 patients (62.5%). Two individuals developed hematuria, while another two patients had no detectable change in the size or appearance of the thrombus. Mathey et al likewise reported an approximate 66% rate of complete lysis with urokinase and similar complications of hemorrhage and lack of any detectable thrombolysis. Although both agents are effective plasminogen activators, streptokinase is well-known for its potential for anaphylaxis (approximately 1%) and antibody formation, potentially rendering the drug ineffective in vivo. Urokinase has been removed from the United States market by the Food and Drug Administration due to concerns of impurities in the raw materials.

rt-PA is a highly fibrin-specific serine protease that catalyzes the Arg560-Val561 peptide bond of plasminogen. Since 1991, there have been four separate case reports where rt-PA was utilized for primary lysis of intracardiac thrombi. Krogmann et al successfully lysed a mobile and protruding left ventricular thrombus in a 2-year-old boy with congenital DCM. Kemennu and Riggs likewise used rt-PA for lysis of a large, mobile, and protruding right ventricular thrombus in a 13-year-old girl with congestive heart failure secondary to doxorubicin toxicity. One hour after rt-PA infusion was completed, there was no residual echocardiographic evidence of thrombus and no complications. Janssens et al described successful lysis of right atrial and ventricular thrombi in a patient with peripartum cardiomyopathy and evidence of extensive pulmonary embolism. More recently, Yeh et al reported three separate cases where rt-PA was used successfully to lyse right-sided and left-sided intracardiac thrombi with high-risk features. Two of the patients developed thrombi as a complication of radiofrequency ablation, and one patient had DCM related to chronic supraventricular tachycardia. In all three patients, there were no bleeding or embolic complications during or after administration of rt-PA.

Conclusion

To our knowledge, this is the first documented case in which rt-PA was used for primary lysis of a left ventricular thrombus in a patient with peripartum cardiomyopathy. Particularly when there is evidence of extensive embolization and high-risk echocardiographic features, we feel that early and aggressive thrombolysis with rt-PA is a superior alternative to treatment with streptokinase, urokinase, high-dose heparin, or thrombectomy.

References