CASE REPORT

Massive Fatal Pulmonary Emboli with Fibrinolytic Therapy

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SUMMARY A case is described in which massive fatal pulmonary emboli followed the initiation of thrombolytic therapy. Several important issues regarding anticoagulation and fibrinolytic therapy are addressed, including the possibility of anticoagulant failure and the risks of using fibrinolytic therapy in the setting of recent and remote thrombotic disease.

IN 1-2% of patients with deep vein thrombosis (DVT), pulmonary emboli develop despite therapy with heparin.1 Episodes of DVT successfully treated with anticoagulant therapy may still result in venous valvular incompetence and lead to postphlebitic syndromes characterized by ulceration, varicosities and edema. Studies of thrombolytic agents suggest that early use of these drugs for extensive venoocclusive disease may preserve venous valvular competence and produce more rapid resolution of pulmonary emboli.2,3 However, the role for thrombolytic therapy is undefined in cases where extensive DVT composed of segments of varying ages exists. It has been assumed that the creation of a systemic fibrinolytic state would protect against the development of pulmonary emboli as progressive lysis of the thrombus occurred.4,5 We have recently observed a case in which administration of the fibrinolytic agent streptokinase for extensive DVT was followed rapidly by death from massive pulmonary embolism.

Case Report

A 32-year-old white male engineer was transferred from a referring hospital for further evaluation of chest pain, syncope and left leg pain. There was no personal history of cardiovascular risk factors or family history of premature atherosclerosis, thromboembolic disease or sudden death.

Physical examination revealed a well-developed, well-nourished man in no acute distress. Vital signs, cardiac, thoracic and abdominal examinations were normal. Examination of the extremities revealed intact peripheral pulses, but there was tenderness to compression in the left calf. Calf circumferences were equal. No definite venous cord was palpated.

Laboratory Findings

The complete blood count, the platelet count, the prothrombin time (PT), the activated partial thromboplastin time (aPTT), liver function tests, electrolytes, BUN, creatinine, CPK, glucose, cholesterol and uric acid were all normal. Antinuclear antibody (ANA) was less than 1:40 (normal). T-wave inversion was noted in ECG leads V1-V5 and III. A technetium-99 scan for myocardial infarction was negative. A two-dimensional echocardiogram, including examination of the mitral valve, was normal.

Hospital Course

Eight days before death, a venous Doppler examination suggested left-calf vein obstruction. Venography confirmed the presence of left popliteal vein occlusion and several filling defects in the anterior and posterior tibial veins. Normal runoff was observed in the femoral and iliac veins (fig. 1). A bolus of heparin was administered and followed by a continuous infusion at a rate of approximately 1000 U/hour. This maintained the aPTT between 1½ and 2½ times the control.

On the seventh day of heparin therapy, 2 days before death, oral warfarin was added to the therapeutic regimen. On the day before his death, the patient complained of increased pain in his left leg and thigh. Repeat venous Doppler examination suggested left common and superficial femoral vein as well as popliteal and calf vein obstruction. A ventilation-perfusion lung scan revealed multiple subsegmental perfusion defects with normal ventilation. Repeat venography revealed extensive DVT of multiple veins in the left calf and “complete” thrombosis of the left popliteal and femoral veins. The only venous drainage from the extremity was via the long saphenous vein. Faint opacification of the left iliac vein was present and suggested the presence of a large intraluminal thrombus (fig. 2).

In view of the proximal extension of the DVT during heparin therapy indicative of the formation of fresh thrombosis, streptokinase was administered. Vitamin K₁ (10 mg) was given intravenously and heparin was discontinued. After these maneuvers, the PT, aPTT, and thrombin clotting time (TCT) were normal. One hour later, streptokinase, 250,000 U, was given intravenously and followed by a constant infu-
sion of 100,000 U/hour. Four hours after initiation of fibrinolytic therapy, the TCT had prolonged to 25 seconds (control 14) and plasminogen was undetectable in the patient’s plasma.4

One hour later, the patient experienced a transient episode of apnea, shortness of breath and substernal chest pain. He then sustained a cardiopulmonary arrest from which he could not be resuscitated.

The postmortem examination showed massive (saddle) proximal and bilateral distal pulmonary emboli. Pulmonary infarction, 7–10 days old, was noted in both lungs. A large tubular embolus was coiled in the right ventricle of the heart. Additional clots could be milked from the left thigh.

Discussion

Several major issues regarding anticoagulation therapy are raised by this case, in which establishment of the thrombolytic state was dramatically and temporally related to sudden death secondary to autopsy-proved massive pulmonary emboli. Despite administration of heparin, the patient’s DVT became more extensive. Although this may not represent heparin failure—plasma heparin levels were not determined and the clinical response to a large dose of heparin was not tested—it does confirm that “therapeutic” aPTTs do not necessarily indicate a therapeutic antithrombotic state. The administration of vitamin K1 before thrombolytic therapy might have contributed to the patient’s thromboembolic complications. However, extensive DVT was present before administration of vitamin K1.

The best therapeutic approach to extensive, intraluminal iliac vein thrombosis is unknown. The outcome of this case suggests that a more prudent course of action would be to interrupt the vena cava, increase the dose of heparin, or both. The temporal relationship of this patient’s death secondary to massive pulmonary embolism and initiation of a thrombolytic state with streptokinase indicates that thrombolytic therapy is not without risk. Such therapy may be inappropriate when there is a combination of new and old thrombus in the deep venous system. Lysis of younger, plasmin-sensitive areas of the thrombus may liberate large segments of older thrombus that are resistant to lysis. These thrombi could then embolize, causing cardiovascular compromise and sudden death.

References

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