Treatment of Right Heart Thromboemboli With IV Recombinant Tissue-Type Plasminogen Activator

To the Editor:

We read with interest the recent article by Greco and colleagues (July 1999). Among 30 patients admitted to their ICU with massive pulmonary embolism (PE), they detected 7 patients with right heart thromboembolism (RHTE) who were immediately treated with recombinant tissue-type plasminogen activator. This treatment was followed with rapid resolution of thrombus and improvement of hemodynamic status and echocardiographic parameters of acute right ventricular overload. In our opinion, this study raises two major questions.

First, in patients with massive PE, is the finding of RHTE really a “life-threatening event”? The high mortality rate of 40% was based on pooled case reports or case series. The majority of these patients presented with a dramatic clinical picture of massive PE (New York Heart Association class IV dyspnea, cardiogenic shock), which prompted echocardiographic evaluation. The prevalence of RHTE in nonmassive PE is unknown. In an observational study of 130 patients with massive PE, RHTE was present in 23 patients (18%) and did not carry a higher mortality than in patients without RHTE (30% vs 24%). There was no statistical difference in treatment allocation (heparin vs thrombolysis) between the two groups. RHTE might just represent an incidental finding, the bad prognosis being in fact due to massive PE. Indeed, massive PE complicated by shock has a high mortality rate (18 to 38%) by itself.

Second, what is the efficacy of thrombolytic therapy in the setting of RHTE? The fact that RHTE might not have an isolated prognostic significance raises strong doubts about the relevance of any specific treatment (thrombolytic agents or surgical thromboectomy) other than therapeutic anticoagulation. The study by Greco and colleagues showed disappearance of the thrombus and improvement of different hemodynamic variables. Thrombolytic therapy in PE quickly improves lung scans and angiographic or echocardiographic findings but has not been shown to reduce mortality. Moreover, thrombolytic therapy could double the number with severe bleeding (as compared with patients treated with heparin).

In the study by Casazza et al., 5 of the 18 patients with massive PE and RHTE were treated with anticoagulant therapy and showed disappearance of the thrombus after several days without new symptoms.

In conclusion, we estimate that data on RHTE are too scarce to allow a conclusion on the benefits of thrombolytic therapy over anticoagulation in patients with PE and RHTE but no hemodynamic compromise. However, patients with massive PE and shock should receive thrombolytic treatment whether RHTE are present or not.

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The questions raised by Dr. Procopiou regarding our recent publication in CHEST (July 1999) confirm the great doubts and uncertainties that still exist about management of right heart thromboemboli (RHTE) detected by echocardiography during pulmonary embolism (PE). At the present time, prevalence and treatment of RHTE remain as two major unresolved problems. Prognostic significance, apparently clear and well defined, seems to be emerging as another question.

We know from the literature that detection of RHTE is commonly associated with proximal deep venous thrombosis and massive PE, frequently in cardiogenic shock. This complex clinical condition presents as a severe thromboembolic disease, with a proven high rate of short-term mortality. The retrospective study of Dr. Casazza et al. points out how the bad prognosis of these patients is probably the result of massive PE rather than RHTE itself, so that anticoagulation can be proposed as treatment of choice of RHTE in hemodynamic stability.

In the European Cooperative Study, the heparin group registered a high mortality rate and, although Tavel et al. suggest adding a vena cava filter to heparin infusion in hemodynamically stable patients with RHTE, this novel approach should be confirmed in term of efficacy. Moreover, even if we do not believe that treatment of RHTE with thrombolysis or surgical embolectomy will prevent an unpredictable and catastrophical embolization of these large floating clots in a pulmonary tree, where major embolisms had often previously occurred, we have seen that thrombolysis may favorably affect the clinical outcome of hemodynamically stable patients with massive PE. Thrombolysis over heparin leads to a rapid improvement of pulmonary perfusion and right ventricular function, with a lower rate of recurrent PE and death. Finally, intracranial hemorrhage after PE thrombolysis is an infrequent complication.

We believe, therefore, that thrombolysis can be the first-choice therapy, effective and safe, in this particular condition that we call RHTE syndrome (RHTE plus massive PE and proximal deep venous thrombosis), a critical and high-mortality clinical-instrumental picture. The term “life-threatening event” can reasonably summarize the latter concept. However, until a prospective, multicenter, randomized treatment trial is realized, the debate is far from over.

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To the Editor:

We read with interest the report by Abramson and Gilkeson (July 1999) regarding the benign metastasizing leiomyoma (BML). We report herein our experience of natural decrease of BML in size.

A 52-year-old woman was admitted to our hospital due to abnormal shadows found on chest roentgenograms (Fig. 1, top left), and CT (Fig. 1, bottom left) detected a number of pulmonary nodules in whole lung fields. Her medical history included uterine myomectomy at the age of 43 years. A thorascopic lung biopsy revealed leiomyomatous tumors that were histologically similar to the uterine myoma removed 9 years previously. The final diagnosis was BML. The values of estrogen and progesterone in the resected specimen were 136.9 fmol/mg and 5.6 fmol/mg, respectively.

Although we recommended treatments such as hormone therapy, she strongly refused them. Therefore, she was discharged from hospital on the condition that she would be followed up on an outpatient basis.

After that, she was not seen for about 1 year, and she visited the outpatient department on July 13, 1999. Chest roentgenogram (Fig. 1, top right) and CT (Fig. 1, bottom right) showed significantly reduced tumors in size. When asked if she had noted any prominent changes since leaving the hospital, she informed us that she had undergone menopause. The serum estradiol and serum progesterone levels before menopause were 20.4 μg/dL and 1.5 ng/mL, which decreased to 4.3 μg/dL and 0.3 ng/mL after menopause, respectively. BML is said to be hormone dependent; therefore, the present case suggests that menopause may play a role in the natural decrease of its size.

To the Editor:

The authors present a very interesting case of spontaneous regression of benign metastasizing leiomyoma (BML). BML may contain estrogen and progesterone receptors and is thought to be hormone responsive. The literature includes instances in which pulmonary lesions may regress spontaneously or after hormonal manipulation (surgical oophorectomy and medical treatment such as progesterone or anti-estrogen therapy). In addition, the effects of natural hormonal changes in women (pregnancy, menopause) on tumor growth have been described. For example, a case of a 30-year-old pregnant woman with presumed BML demonstrated spontaneous regression of pulmonary nodules during pregnancy and into the postpartum period. On the other hand, the lesions in our patient showed no significant change in size despite separate 6- to 12-month trials of tamoxifen, progesterone, and an aromatase inhibitor (anastrozole). This occurred in spite of the presence of positive estrogen and progesterone receptors on smooth muscle cells. Although there are cases that

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**FIGURE 1.** Frontal chest radiograph (top left) and CT scan (bottom left) demonstrating a number of pulmonary nodules in whole lung fields. Top right and bottom right: significant improvement 1 year later.