We describe here a case of a 45-year-old male patient who, 3 years after allogeneic bone marrow transplantation for chronic myelogenous leukemia, developed a rapidly evolving pulmonary picture consisting of increasing exertional dyspnea, dry cough, and wheezing. The patient did not show any improvement following treatment with inhaled bronchodilators. A chest radiograph showed normal findings. On bronchoscopic examination, the major conducting airways were found to be mildly inflamed. Since the patient had an oxygen saturation rate of 82% with a PaO₂ of 51 mm Hg (on room air) that was increased to 90 mm Hg under oxygen enrichment (4 L/min), we decided to limit our diagnostic sampling to BAL, without performing a transbronchial biopsy.

BAL was carried out on the medium lobe with three cycles of the instillation and immediate reexpiration of 50 mL of physiologic saline solution at 37°C. An unusual resistance to fluid instillation was noticed during the maneuver and the subsequent reexpiration allowed the retrieval of only 20% of the volume instilled. Within minutes of the end of the procedure, the patient suddenly developed severe respiratory failure with an oxygen saturation rate of 68% and pain in the right chest. Diminished breath sounds were perceived on the right hemithorax, and pneumothorax (PNX) was diagnosed. Chest tube drainage was performed and the patient was put under mechanical ventilation in the ICU, where he eventually died 2 days later.

At autopsy a tear was seen on the visceral pleura of the medium lobe. Pathologic examination disclosed a picture compatible with bronchiolitis obliterans, with mild peribronchiolar infiltration consisting of lymphocytes and plasma cells. The bronchiolar lumen had varying degrees of narrowing with focal lumen obliteration by fibrosis. No alterations suggesting graft versus host disease in extrapulmonary organs were detected. The alveolar spaces were free of any significant change and no signs suggesting an infectious process were seen. According to the chronology of the events, it seems likely that PNX had a precipitating effect on the ongoing respiratory failure and was probably induced by BAL.

In light of the extreme rarity of fatal complications occurring as a consequence of BAL, we believe that the case described deserves attention. Bronchoscopy and BAL were fully indicated in this case, but looking at the remarkable resistance encountered in fluid instillation, it seems advisable not to insist on delivering the solution when an unusually high pressure is found.

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Use of Pulsed-Wave Doppler Echocardiography to Measure Changes in MPAP

Is Further Validation Required?

To the Editor:

The article published in CHEST by Kiely et al (September 1996) and the accompanying editorial raise the possibility that angiotensin II receptor antagonists may attenuate acute hypoxic pulmonary vasoconstriction (AHPV) in man, in the presence of an activated renin-angiotensin system. Both articles point out that angiotensin II receptor antagonists may have the potential to relieve hypoxic vasoconstriction in patients with cor pulmonale. Although there is clearly cause for optimism, there are a number of concerns. First, the degree to which acute hypoxic vasoconstriction contributes to the modest elevation of pulmonary arterial pressure in cor pulmonale secondary to COPD is uncertain. Most studies have reported only a trivial acute fall or no acute fall in pulmonary arterial pressure with high concentrations of inspired oxygen. Furthermore, invasive studies in conscious rats have demonstrated no effect of captopril or the type I angiotensin II receptor antagonist, losartan, on the magnitude of AHPV. Similar results have been obtained in the dog with the nonspecific angiotensin II antagonist, saralasin. In the chronically hypoxic rat model, we found that captopril and losartan significantly attenuated the hemodynamic structural changes of pulmonary hypertension, without affecting AHPV. It is now well established that angiotensin II has growth-promoting effects in vascular smooth muscle cells. This suggests, at least in the rat, that the inhibition of angiotensin II-mediated pulmonary vascular remodeling by angiotensin inhibitors is more important than inhibition of AHPV by this class of drugs.

A further reason for caution is the use of pulsed-wave Doppler echocardiography to measure changes in mean pulmonary arterial pressure (MPAP). Although a significant correlation exists between the MPAP and the pulmonary acceleration time (PAT) measured by Doppler, there is considerable variability between simultaneous measurements in an individual. In addition, although the PAT correlates with MPAP, a very small change in PAT can give a large calculated change in MPAP. Furthermore, the PAT can be affected by other factors, such as cardiac contractility. It is possible that in the study by Kiely et al., the inhibition of angiotensin II during activation of the renin-angiotensin system had a direct effect on the heart. The use of pulsed-wave Doppler echocardiography to measure changes in MPAP, possibly resulting from agents that also act on the myocardium, requires further validation.

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We thank Dr. Morrell for pointing out his data on the lack of effects of captopril and losartan on acute hypoxic pulmonary vasoconstriction (AHPV) in conscious rats. The likelihood is that there are species differences, and this may explain why nonselective angiotensin II receptor blockade with saralasin was found to exhibit activity in humans in terms of attenuating AHPV. Indeed, we have also shown that as occurs with saralasin treatment, AHPV is attenuated by type I angiotensin II receptor blockade with losartan in humans. In this study, subjects were not given furosemide, and so there was no activation of the renin-angiotensin system prior to the administration of losartan. Thus, the criticism from Dr. Morrell regarding the effects of angiotensin II blockade on the mycardium would appear to be invalid. We do, however, agree with Dr. Morrell that there may be an additional effect of angiotensin II receptor blockade in terms of preventing pulmonary vascular remodeling, although this is not supported by any in vivo data in human studies.

In the context of cor pulmonale, the increase in the pulmonary vascular resistance has a dynamic component due to hypoxic vasoconstriction, as well as a more fixed component due to established pulmonary vascular remodeling. We have evaluated patients with hypoxemic cor pulmonale, in whom a 50-ng oral dose of losartan produced a significant fall in both mean pulmonary arterial pressure (mPAP) (13%) and total pulmonary vascular resistance (TPVR) (16%) compared with placebo. Taken together, these studies with saralasin and losartan in healthy volunteers and patients with cor pulmonale show that angiotensin II receptor blockade may have an important effect in modifying the AHPV response in man.

We realize that there are limitations to the measurement of Doppler-derived mPAP using the pulmonary acceleration time (PAT). However, we have shown with our own hands in previous studies that there is in fact little variability between simultaneous measurements in a given individual, with coefficients of variability for PAT, reported as 1.7%4 and 1.1%5 in healthy volunteers, and values of 3.2%6 and 1.9%7 in patients with cor pulmonale. We have also shown a highly significant correlation between Doppler PAT and catheter mPAP over a range of pulmonary arterial pressures.6,7 The main problem with Doppler-derived mPAP is that it does not distinguish between pre- and post-capillary vascular resistance, as it is not possible to measure wedge pressure with this technique.

Dr. Morrell also inferred that changes in cardiac contractility may explain the effects of angiotensin II blockade on the PAT. In this respect, we have recently shown in a dose-ranging study, with infusion of endothelin 1 in healthy volunteers, that marked increases in Doppler mPAP and TPVR occurred in concert with negative inotropic and lusitropic activity.7 Since angiotensin II also has a similar profile in terms of inducing pulmonary vasoconstriction in the presence of negative inotropic-lusitropic effects,8 it is highly unlikely that effects of angiotensin II receptor blockade on the myocardium would explain the associated fall in mPAP. Indeed, if anything, one could argue that antagonizing the myocardial effects of angiotensin II would, if anything, tend to underestimate the effects of angiotensin blockade in terms of attenuating AHPV.

We therefore remain firmly of the opinion that angiotensin II receptor blockade may be implicated in the pathophysiology of acute pulmonary vasoconstriction and that this may be reliably measured using Doppler assessment of pulmonary arterial flow.

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Noninvasive Measurement of Pulmonary Arterial Blood Velocity

Can it Replace Right Heart Catheterization?

To the Editor:

A recent publication1 has concluded that right heart catheterization using pulmonary artery flotation catheters is “associated with increased mortality and increased utilization of resources.” Methods of magnetic resonance imaging (MRI) of large vessels provide morphologic and dynamic flow-related information completely noninvasively and with high spatial and temporal resolution. In the decade since Singer and Crooks2 proposed the measurement of blood flow with such techniques, MRI velocity mapping has been shown to give accurate estimates of total blood flow and velocity profiles.3,4

Five normal adult volunteers were positioned supine in a 1.5-Tesla Signa imager (GE Medical Systems, Milwaukee, Wis) and a series of scout images of the upper torso of each subject was obtained. An optimal transverse plane was chosen which contained a representative cross-section of a side branch of the pulmonary artery. For blood flow velocity measurement, an ECG-gated phase-sensitive imaging protocol was used which provided velocity sensitivities of 0.7 to 5.0 mm/s, and which resulted in five to eight velocity measurements spanning two