Pulmonary Venoocclusive Disease and Failure of Specific Therapy

To the Editor:

We read with interest the article in CHEST (June 2009) by Harch and colleagues, suggesting that pulmonary venoocclusive disease (PVOD) might be the main cause of the lack of response to specific therapy in patients with pulmonary arterial hypertension (PAH). The 80% rate of PVOD in patients with refractory PAH is higher than previously reported. Indeed, Dorfmüller et al. have stated that PVOD could be confirmed by pathologic examination of the lung tissue available from autopsy or explant in 5 of 29 patients (17.2%) with refractory idiopathic PAH. Interestingly, the majority of patients with end-stage PAH had histologic evidence of plexiform arteriopathy. Furthermore, the inclusion of two patients with systemic sclerosis, a condition frequently associated with PVOD-like lesions, may have led to a higher than expected rate of PVOD in the report by Harch and colleagues. We were surprised to read that high-resolution CT (HRCT) scanning of the chest was not helpful in the diagnosis of PVOD. This could be due to the small number of HRCT scans analyzed. Indeed, large series have shown that centrilobular ground-glass opacities, septal lines, and lymph node enlargement are significantly associated with PVOD. Furthermore, patients with PVOD usually present with lower PaO2, diffusing capacity of the lung for carbon monoxide, and oxygen saturation during the 6-min walk test compared to patients with idiopathic PAH. Therefore, a noninvasive diagnostic approach using HRCT scanning of the chest, arterial blood gas measurements, pulmonary function tests, and BAL may be helpful in this difficult patient population.

The authors also indicated that prostanoid analog therapy did not cause pulmonary edema in their PVOD patients and suggested that this might be the consequence of the absence of pulmonary arterial vasodilatation because of arterial intimal fibrosis. These results are in contradiction with those from several reports demonstrating that PVOD patients are at higher risk of the development of severe pulmonary edema with specific PAH therapy, particularly with IV epoprostenol. Of note, the patients reported had a low dosage of prostacyclin, which may explain why pulmonary edema did not occur. Indeed, recent findings have indicated that careful use of PAH therapy may be associated with a lower risk of pulmonary edema in patients with PVOD.

In conclusion, we agree that PVOD may be a major cause of refractory PAH. However, we wish to emphasize that PVOD could be identified early using a noninvasive approach. Such patients may benefit from the careful use of PAH-specific therapy, and eligible subjects should be considered early for lung transplantation.

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Response

To the Editor:

We thank Montani and colleagues for their response to our article, which suggested that pulmonary venoocclusive disease (PVOD) should be considered as an alternative diagnosis in patients with pulmonary arterial hypertension who do not respond to medical therapy. We recognize that the reported rate of PVOD in this study is higher than that previously documented in literature on pulmonary hypertension. This may be attributable to two factors. First, the study was performed in a selected group of patients with pulmonary hypertension who had not responded to medical therapy and for whom, consequently, an alternative diagnosis was more likely. Second, a novel stain using routine smooth muscle actin immunohistochemistry with a Verhoeff elastin counterstain allowed concurrent examination of the vessel elastic lamina and smooth muscle hypertrophy in any one vessel. In conjunction with vessel microanatomical location, this enabled...