transferred to the intermediate ICU with a diagnosis of presumed sepsis. He required dopamine for only 5 h. An ECG performed for a complaint of chest pain that morning showed ST-segment elevation in leads 1, aVL, V₅, and V₆ with a smaller degree of elevation in lead 2. Cardiology consultation was obtained. Subsequent ECGs performed over the following days showed a return of the ST segments to baseline, with nonspecific ST- and T-wave changes. Serial cardiac enzymes were as follows:

Based on the elevated creatine kinase (CK) and ECG changes, the patient was transferred to the ICU with the diagnosis of acute myocardial infarction. He was started on heparin and nitrates. Clinical examination was consistent with congestive heart failure, and captopril was added for afterload reduction. An echocardiogram showed a mildly dilated left ventricle, diffuse LV hypokinesis, and a moderately depressed LV ejection fraction. The right ventricle was poorly seen, but mild dilation and depressed function was suspected. A left pleural effusion was identified as well. On the eighth hospital day, a cardiac catheterization was performed and was normal. The patient was discharged after 10 days in the hospital in stable condition, to be followed up by cardiology as an outpatient.

This patient would appear to conform quite closely to the clinical and laboratory picture which characterized the patients in the report by Blum et al. The only departure in this particular case is the initial presence of global, rather than regional wall motion abnormalities and depressed LV (and perhaps RV) function on echocardiogram. This may be explained by the fact that our patient appeared to be truly septic before the onset of the cardiac event. Therefore, sepsis-associated myocardial depression may have been superimposed on dysfunction due to ischemia/infarction.

Our patient did quite well with conservative management and never received thrombolytic therapy. We agree that it would be most useful to obtain angiographic data prospectively in future patients who appear to have infective myocardial infarction, before the institution of thrombolysis, and we would suggest that in young patients without obvious coronary risk factors who present with a similar picture, that approach be taken unless clinically unfeasible at the time. It would also seem reasonable to perform endomyocardial biopsy at the same time to rule out the possibility of myocarditis, especially if no evidence of thrombosis is apparent on the angiogram.

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To the Editor:

The patient presented here had a global ischemia, perhaps reflecting true classical myocarditis with left ventricular (LV) depression. At a later date, when he developed the acute myocardial infarction pattern, an echocardiogram was not performed and may be in this stage, the myocardium would have a regional contraction defect as our patients.

The enigma is to differentiate between true classical myocarditis and acute myocardial infarction when there is a global contraction defect. Therefore, the case presented here is not quite typical of that "syndrome."

It is well-known that infection and especially sepsis cause stimulation of the immunologic system by monocyte liberating cytokines such as tumor necrosis factor (TNF), interleukin (IL)-1B, IL-6, and IL-8. The IL-1, for example, directly and indirectly activates platelets and causes them to be in "a hypercoagulable state," to secrete platelet-aggregating factor and other growth factors that activate the clotting proteins. It is well-known that infection and especially sepsis cause stimulation of the immunologic system by monocyte liberating cytokines such as tumor necrosis factor (TNF), interleukin (IL)-1B, IL-6, and IL-8. The IL-1, for example, directly and indirectly activates platelets and causes them to be in "a hypercoagulable state," to secrete platelet-aggregating factor and other growth factors that activate the clotting proteins and the "clotting cascade" through Von Willebrand's factor, fibrinogen, fibrinogen, and other adhesive molecules.

The global, rather than regional wall motion abnormality and depressed LV function, can be caused by cytokines that are secreted by monocytes and lymphocytes during sepsis and cause myocardial depression. For example, TNF and IL-6 are secreted from monocytes and macrophages, and IL-2 is secreted from T-lymphocytes and natural killer cells.

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Pulmonary Vascular Lesions in Chronic Thromboembolic Pulmonary Hypertension

To the Editor:

In the March issue of Chest, Moser and Bloor claim that plexogenic (sic) lesions occur in the small pulmonary arteries of patients with chronic thromboembolic pulmonary hypertension. The first consists of a circumferential dilatation of a pulmonary artery branch close to its origin from a parent artery. In this dilated segment, there is destruction of the arterial wall with pronounced thinning of the media, loss of smooth muscle cells, disappearance of the internal elastic lamina, and sometimes also the external elastic lamina. The second element is a plexus of narrow silt-like channels within the dilated segment. These channels which are lined by cells with hyperchromatic nuclei resemble a vascular plexus. The distal part of the plexiform lesion...
drains into a dilated and thin-walled vessel, the wall of which usually consists of a single elastic lamina.

These features are not shown in the article by Moser and Bloor. Occasionally, difficulty may be encountered in distinguishing between an organized recanalized thrombus and a plexiform lesion. Pulmonary arteries containing organized and recanalized thrombi usually have intact internal and external elastic laminae whereas these structures are destroyed at the sites of plexiform lesions.

Plexiform lesions have never been described in patients with chronic thromboembolic pulmonary hypertension or thrombosis of the major pulmonary arteries. In contrast, recanalized thrombi are seen in the small pulmonary arteries in 65 percent of patients with thrombosis of the main pulmonary arteries.

The concluding statement by Moser and Bloor that the occurrence of plexiform lesions in a lung biopsy does not exclude the diagnosis of chronic thromboembolic pulmonary hypertension is not justified by the findings illustrated in their article.

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To the Editor:

We thank Dr. Kay for expressing his views. However, we respectfully disagree with his conclusions, for the reasons enumerated below.

In our article, we grouped together under the term “plexogenic,” lesions which others have subgrouped into “plexiform” or “angiomatoid” lesions. We, and other experienced pathologists who reviewed these lesions, think they are clearly plexiform lesions, not recanalized thrombotic lesions. Further, these lesions are consistent with the definition of such lesions used in two other, related studies by Lloyd et al and Pietra et al. We curiously find Dr. Kay’s assertion that, based on Yaginuma’s paper, plexiform lesions occur only in vessels 100- to 150-μm diameter when Pietra’s report, of which Dr. Kay was a co-author, indicates that such lesions were present in vessels 100- to 300-μm diameter.

Substantial literature exists indicating that plexiform lesions are not specific to primary pulmonary hypertension. In addition to the several references in our paper documenting this, we note that early experimental studies by Liebow and his colleagues indicated that the plexiform lesions arise from phenomena related to increased pressure and flow, phenomena which occur in multiple clinical contexts.

We certainly cannot accept the statement that such lesions have never been found in patients with chronic thromboembolic pulmonary hypertension. As we pointed out in our paper, the references cited by Dr. Kay (Presti B, et al, Hum Pathol 1990; 21:601-06; Wagenvoort CA, Mooi WJ, Biopsy pathology of the pulmonary vasculature, 1989; and Harris P, Heath D, Human pulmonary circulation, 1986), which we carefully reviewed, do not contain adequate hemodynamic or microscopic information to allow one to reach such a conclusion. Importantly, which patients had chronic, major vessel thromboembolic pulmonary hypertension is not clear. Indeed, as we indicated, the only paper which included clearly defined patients with CT-E PH did indicate that “dilatation lesions” were common.

Therefore, we stand strongly behind our concluding statement which is, to reiterate it, that the diagnosis of potentially surgically remediable chronic, major vessel thromboembolic pulmonary hypertension should not be deterred by the finding of small vessel “pulmonary hypertensive” lesions on lung biopsy, including plexogenic lesions. Certainly, all would agree that the most frequent lesions in the small arteries of pulmonary hypertensive patients are muscular hypertrophy, intimal proliferation, and thrombosis—and such lesions lack differential diagnostic value.

The “bottom line,” as our large experience documents, is that lung biopsy findings cannot and should not be relied on to distinguish among the various pulmonary hypertensive disorders. Such reliance can be particularly harmful to patients with chronic major vessel thromboembolic pulmonary hypertension if it dissuades physicians from pursuing diagnostic studies that could lead to a correct diagnosis and a potential surgical cure by pulmonary thromboendarterectomy. We expect that ongoing research will, ultimately, define those mediators which induce medial hypertrophy, intimal proliferation, thrombotic lesions, and the vessel injury which plexogenic lesions represent. As these insights are gained, physicians must diligently pursue the differential diagnosis of pulmonary hypertensive states because the therapy of the various forms deviates so widely. In this differential diagnostic pursuit, in our view, the small vessel arterial changes available from lung biopsy are of limited—if any value and, if wrongly interpreted, they can deflect physicians from the correct diagnosis.

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