Using Contrast Material-enhanced Echocardiography to Identify Abnormal Pulmonary Arteriovenous Connections in Patients With Hypoxemia*

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The phenomenon of abnormal pulmonary arteriovenous connections in patients with acquired lung disease rarely has been reported. We report three patients with acquired lung disease and hypoxia that did not respond to the administration of 100 percent oxygen. Contrast-material-enhanced echocardiography demonstrated intrapulmonary right-to-left shunting in all three patients. These cases suggest that patients with hypoxia due to acquired lung disease may be screened by contrast-enhanced echocardiography to identify the presence and the location of anatomic right-to-left shunts. (Chest 1992; 102:1690-92)

Contrast-material-enhanced echocardiography can demonstrate intrapulmonary shunting in patients with known or suspected pulmonary arteriovenous fistulas. The prevalence of coexistent pulmonary arteriovenous connections in patients with hypoxemia is not known. We report three cases in which contrast-enhanced echocardiography has suggested the presence of unsuspected pulmonary arteriovenous connections.

METHODS

During the past ten years, 50,000 echocardiograms were performed in this hospital. In three cases, contrast-enhanced echocardiography revealed delayed appearance of contrast in the left atrium (LA). These cases were selected for review. The patients’ hospital charts were obtained, and clinically relevant data were extracted.

Contrast-enhanced echocardiography was performed according to a standard protocol. Six milliliters of agitated iodocyanine green dye was injected into a peripheral vein. Images were recorded using transthoracic two-dimensional echocardiography. The time interval and number of cardiac cycles between the appearance of microbubbles in the right atrium (RA) and the subsequent appearance of microbubbles in the LA were recorded. Intrapulmonary shunting was considered to be present when microbubbles appeared in the LA three or more cardiac cycles after their first appearance in the RA.

CASE REPORTS

CASE 1

A 63-year-old man with cirrhosis was admitted for dyspnea. Physical examination was significant for jugular venous distention, bilateral rales, a systolic flow murmur and pitting edema of the lower extremities. With the patient breathing room air, an arterial blood sample revealed a PaO2 value of 40 mm Hg. There was little improvement after the patient breathed 100 percent oxygen (PaO2 value of 60 mm Hg). A chest x-ray film revealed cardiomegaly and increased interstitial markings. A perfusion lung scan was interpreted as low probability for pulmonary embolism. A Doppler echocardiogram revealed no abnormalities. During contrast-enhanced echocardiography, microbubbles entered the LA from the pulmonary veins (PVs) eight cardiac cycles (5 s) after their appearance in the RA (Fig 1).

CASE 2

A 51-year-old female smoker with pulmonary hypertension and a history of high blood pressure controlled with medications was admitted with dyspnea. Physical examination revealed a blood pressure of 110/70 mm Hg, jugular venous distension, clear lungs, a systolic murmur and mild pitting edema. With the patient breathing room air, an arterial blood sample revealed a PaO2 value of 43 mm Hg with minimal improvement after the patient breathed 100 percent oxygen (PaO2 value, 50 mm Hg). A chest x-ray film revealed cardiomegaly with clear lung fields. Pulmonary function tests revealed small-airway disease and a decreased carbon monoxide diffusion capacity. A ventilation-perfusion scan was interpreted as low probability for pulmonary embolism. The pulmonary artery pressure was 88/48 mm Hg and the pulmonary capillary wedge pressure was 24 mm Hg. An echocardiogram showed markedly dilated right-sided chambers compressing left-sided chambers. There was reversed early-to-late transmural flow velocity and decreased mitral valvular closing velocity consistent with impaired left ventricular diastolic filling. The ejection fraction was 63 percent. The Doppler study revealed mild to moderate tricuspid regurgitation. No intracardiac shunt was noted. Contrast-enhanced echocardiography revealed microbubbles entering the LA from the PVs three cardiac cycles (2 s) after their appearance in the RA.

CASE 3

A 69-year-old woman who had a history of hypertension, sarcoid lung disease (with the diagnosis based on hilar adenopathy, an elevated serum angiotensin-converting enzyme level, severe restrictive physiology and a good clinical response to steroid therapy) and pulmonary embolism was admitted to the hospital because of worsening dyspnea. Physical examination was significant for jugular venous distention, bilateral rales, a holosystolic murmur and severe pitting edema of the lower extremities. With the patient breathing

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Identification of Abnormal Pulmonary AV Connections (Dansky, Schwinger, Cohen)
room air, an arterial blood sample revealed a $P_{O_2}$ value of 34 mm Hg, which did not totally return to normal after breathing 100 percent oxygen ($P_{O_2}$, 79 mm Hg). A chest x-ray film demonstrated cardiomegaly, bilateral infiltrates and increased pulmonary vascular markings. A pulmonary angiogram did not show the presence of a pulmonary embolism. Right atrial and pulmonary capillary wedge pressures both were 10 mm Hg and the pulmonary artery pressure was 76/30 mm Hg. A Doppler echocardiogram revealed a severely dilated RA and right ventricle with right ventricular hypokinesis and moderate tricuspid regurgitation. The left ventricular size was normal with a normal ejection fraction. There was no evidence of intracardiac shunting. Contrast-enhanced echocardiography revealed microbubbles entering the LA from the PVs eight cardiac cycles (4 s) after their appearance in the RA.

**Discussion**

Ventilation-perfusion mismatch is the predominant mechanism responsible for hypoxemia in lung disease. The results of arterial blood sampling after inhalation of 100 percent oxygen often can aid in distinguishing right-to-left shunting from ventilation-perfusion mismatch. Inhalation of 100 percent oxygen improves arterial oxygenation in patients with ventilation-perfusion mismatch or diffusion impairment but has minimal or no effect on arterial oxygenation in patients with right-to-left shunts.

Contrast-enhanced echocardiography is useful for the detection of intrapulmonary shunts. In patients with a septal defect, microbubbles often can be seen entering chambers of the left side of the heart in less than three cardiac cycles after their appearance in the right side of the heart. Alternatively, in patients with intrapulmonary shunts, microbubbles can be seen emanating from the PVs after a time delay of at least three cardiac cycles.

These three patients are the only ones we studied who underwent contrast-enhanced echocardiography in which delayed appearance of contrast in the LA occurred. Serial arterial blood samples suggested the presence of a right-to-left shunt, and no intracardiac shunts were detected. Even though angiographic evidence of a pulmonary arteriovenous fistula was not obtained in the three cases reported herein (a pulmonary arteriovenous malformation was not seen on the pulmonary angiogram in case 3), the contrast studies do suggest the presence of acquired precapillary arteriovenous communications in the lungs. The shunts may be diffuse and microscopic; therefore, pulmonary angiography may not detect their presence. Intrapulmonary shunting due to abnormal arteriovenous connections may have contributed significantly to our patients’ hypoxemia. Unfortunately, all three patients died, and the families refused autopsy examinations.

The prevalence of potential pulmonary arteriovenous connections in the normal and diseased lung is not known. The majority of pulmonary arteriovenous malformations are congenital. Previous studies have described acquired pulmonary arteriovenous malformations in patients with chronic obstructive pulmonary disease, cirrhosis, actinomycosis, schistosomiasis, metastatic cancer and cavopulmonary shunts. Miller et al identified 22 patients with chronic obstructive pulmonary disease and anatomic intrapulmonary shunting visualized by perfusion scintigraphy. Balchum et al described a series of four patients with
chronic obstructive pulmonary disease and arteriovenous connections which were confirmed by pulmonary angiography. Other investigators claim that vascular shunts may be present in patients with pulmonary emboli and primary pulmonary hypertension. Anatomic pulmonary arteriovenous shunts occur in a variety of lung diseases. Two of the patients we have presented had documented pulmonary hypertension. One may speculate that the development of pulmonary hypertension is the common pathway leading to the development of arteriovenous malformations in the lungs.

The sensitivity and specificity of contrast-enhanced echocardiography for detecting abnormal intrapulmonary vascular channels have not been defined. A limitation of this report is that our database is unable to identify patients with hypoxemia who are not responsive to 100 percent oxygen and who did not have intrapulmonary shunts. A carefully designed study is needed to determine the incidence of late appearance of microbubbles in the LA of patients with acquired lung disease and the relationship between this phenomenon and the response of arterial oxygen tension to inhalation of 100 percent oxygen. Transesophageal contrast-enhanced echocardiography, which provides better visualization of the PVs, would be an excellent technique to further study this phenomenon.

Contrast echocardiography is an excellent noninvasive test for identifying the location of right-to-left shunting. It may be useful for the detection of unsuspected pulmonary arteriovenous connections. One may consider the use of contrast echocardiography in the evaluation of hypoxic patients, particularly when arterial oxygen saturation fails to respond adequately to the administration of 100 percent oxygen.

REFERENCES