Pulmonary Hypertension Secondary to Chronic Thromboembolism

From the case records of the Hospital of the University of Pennsylvania

Guest Editor: Abass Alavi

Participants: Harold I. Palevsky and David W. Weiss

Pulmonary Section, Department of Medicine and Division of Nuclear Medicine, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

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A 35-yr-old white female was referred to our clinic for evaluation of pulmonary hypertension in September 1984.

CLINICAL HISTORY

In November, 1975, while taking oral contraceptive tablets, she presented with symptoms of acute pulmonary embolism (PE). Pulmonary embolism was confirmed by angiography during which her pulmonary artery pressures were recorded at 75/25 mmHg. She was treated with heparin followed by oral warfarin anticoagulation. A repeat right heart catheterization in January 1976 noted her pulmonary artery systolic pressure to be 38 mmHg. Because of her very active lifestyle and poor compliance, the warfarin was discontinued after 4 mo, and she was maintained daily on aspirin. In May 1977, right heart catheterization recorded resting pulmonary artery pressures of 40/20 mmHg, which increased to 85/30 mmHg during exercise.

She was lost to medical follow-up until early 1984, when she presented with increased fatigability and exertional chest tightness. She stated that she had felt well with no symptoms, even upon exertion, until mid-1983. A ventilation-perfusion lung scan in February 1984 showed a pattern of high probability for PE with multiple large mismatched perfusion defects (Fig. 1). A pulmonary angiogram showed absence of perfusion to the right upper and left lower lobes (Fig. 2). Resting pulmonary artery pressure was 98/35 mmHg. At room air blood gas showed a pH of 7.44, a PO_2 of 57 Torr, and a PCO_2 of 36 Torr. Warfarin anticoagulation was restarted, and she was followed closely as an outpatient. Six months later, a repeat ventilation-perfusion scan was unchanged and symptomatically she had not improved.

She had smoked approximately one pack of cigarettes per day for 17 yr but had stopped in November of 1983 when her exertional dyspnea had progressively limited her activities. She had a history of numerous food allergies and mild exertional asthmatic symptomatology. She had taken oral contraceptive pills for eight years prior to her pulmonary embolus in 1975. Her family history was significant for coronary artery disease on her paternal side. There was no history of pulmonary hypertension known on either side of the family. She denied syncope or presyncope. She had never had hemoptysis and did not have any hoarseness.

Physical examination revealed a well-developed, well-nourished young woman sitting in bed with no distress. Her blood pressure was 108/80 mmHg. Her pulse was 86 and regular. Her respiratory rate was 20 and unlabored. She was afebrile. Her skin was without rashes or lesions. Her neck was supple without adenopathy; the thyroid was not palpable. Her chest exam revealed no dullness to percussion; lung fields were clear to auscultation. Her cardiac exam demonstrated a jugular venous pressure estimated to be 8 cm of water. Her carotids and all other pulses were full and symmetric without bruits. PMI was in the fifth intercostal space in the mid-clavicular line. There was an impulse palpated in the sub-xiphoid region. S1 was normal and S2 was narrowly split but moved normally with respiration; P2 was markedly increased in intensity. No murmurs were appreciated. Her abdominal exam was within normal limits. Her extremities showed a full range of motion without cyanosis, clubbing, or edema.

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For reprints contact: Abass Alavi, MD, Division of Nuclear Medicine, Dept. of Radiology, Hospital of the University of Pennsylvania, 3400 Spruce St., Philadelphia, PA 19104.

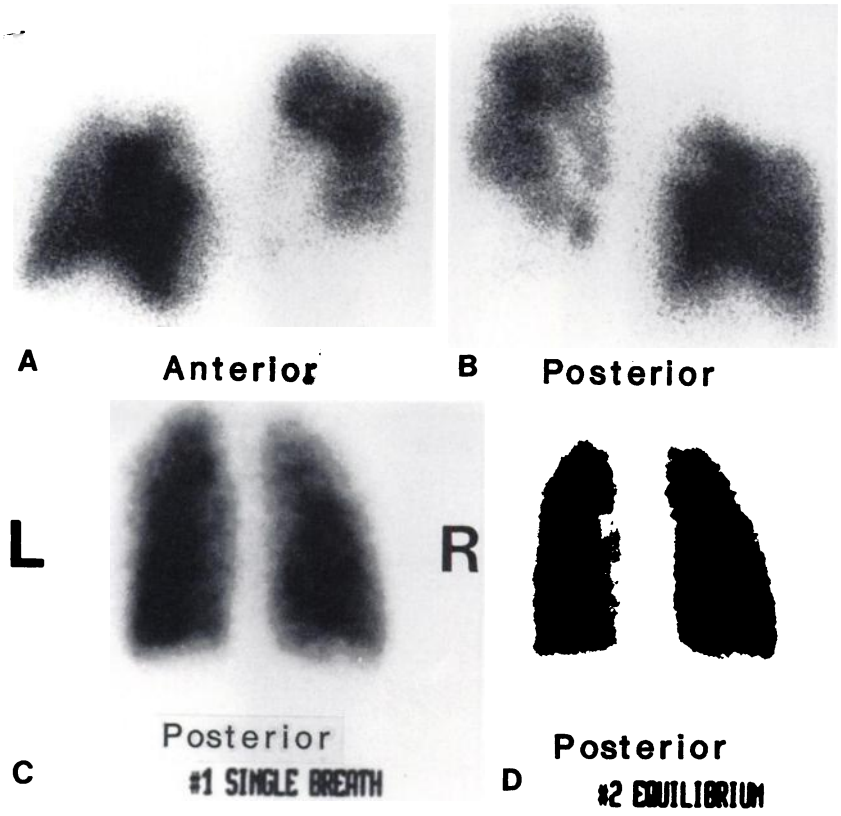

FIGURE 1
Technetium-99m-MAA perfusion scan (A-B). Anterior and posterior views demonstrate large segmental defects involving the right upper and left lower lobes and ^{133}Xe ventilation scan (C-D). Wash-in and equilibration images are within normal limits. Therefore, the multiple mismatched perfusion defects on the perfusion scan carry a high probability for pulmonary embolism.

Laboratory data demonstrated normal electrolytes and normal liver function tests. Her hemoglobin was 15.0, white count 10,100 with a normal differential, and erythrocyte sedimentation rate was 4 mm/hr. An LE prep, Rheumatoid factor, and ANA were all negative.

Chest x-ray showed a relatively normal-sized heart with prominent central and main pulmonary artery segments. The vessels appeared slightly pruned peripherally and there was a suggestion of hypovascularity in the right upper lobe (Fig. 3).

EKG demonstrated sinus rhythm with frequent PACs. There was evidence of bi-atrial enlargement, an incomplete right bundle branch block, and right ventricular strain pattern.

Pulmonary function testing revealed a vital capacity of 4.09 L, which was 118% of predicted and an FEV_1 of 2.67 L, which was 93% of predicted. Her FEV_1/FVC ratio was 65%. The D_LCO was 16 ml\min\Torr, 63% of predicted. PFTs were interpreted as demonstrating mild airway obstruction with hyperinflation and a mild gas transfer abnormality. A room air blood gas demonstrated a pH of 7.46, a PO_2 of 66 Torr and PCO_2 of 30 Torr.

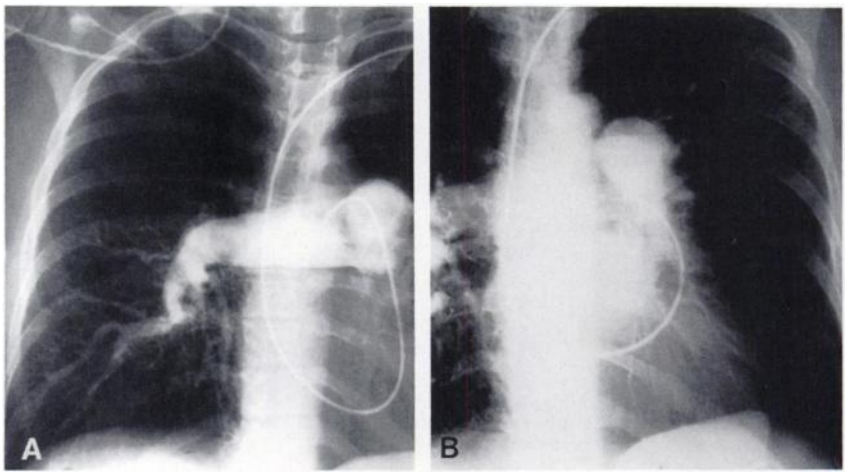

FIGURE 2
Right-sided pulmonary arteriogram (A) from Swan-Ganz catheter injection. Note lack of perfusion of the right upper lung is clearly demonstrated. Left sided pulmonary arteriogram (B) from Swan-Ganz catheter injection in which left lower lobe perfusion is significantly reduced.

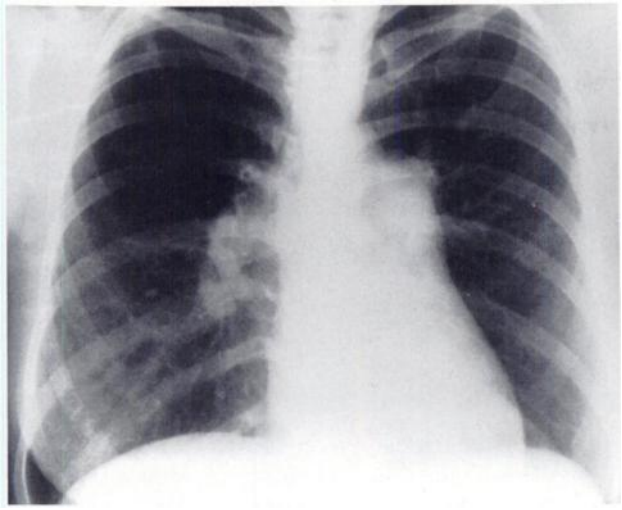

FIGURE 3
PA chest film. Hypovascularity of the right upper lung and left lung base is present. The cardiac silhouette is normal in size. Central pulmonary arteries including the main pulmonary artery are prominent.

During this hospitalization, a right heart catheterization was performed, which demonstrated a right ventricular pressure of 100/4 mmHg and a pulmonary artery pressure of 100/46 mmHg with a mean pulmonary artery pressure of 66 mmHg. The pulmonary capillary wedge pressure was 6 mmHg. The cardiac output was 3.04 l/min. With supine exercise, the pulmonary artery pressure increased to 137/59 mmHg with a mean pressure of 91 mmHg. At the time of exercise, cardiac output rose slightly to 4.04 l/min. During the right heart catheterization, the patient also was tested with a variety of vasodilator agents. The most beneficial appeared to be nifedipine, which slightly lowered the resting mean pulmonary artery pressure and slightly increased the cardiac output. Nifedipine also appeared to block the exercise-induced increase in pulmonary artery pressure. Further work-up included a repeat ventilation-perfusion lung scan which appeared unchanged when compared with previous studies.

While hospitalized, the patient was diagnosed as having severe pulmonary hypertension, which was minimally responsive to vasodilator agents. The review of the ventilation-perfusion lung scans and the available pulmonary angiogram suggested that large pulmonary emboli, seen on the ventilation-perfusion scan, might be responsible for her pulmonary hypertension. She deferred further evaluation and was discharged on nifedipine and warfarin.

She was able to maintain her usual work and social activities for several months. In the early spring of 1985 she began to re-experience increasing dyspnea and fatigue. The development of significant peripheral edema resulted in her re-admission.

On admission in May 1985, her blood pressure was 98/76 mmHg, resting pulse 108 bpm, and respiratory rate 20. Notable in her physical exam was a jugular venous pressure of ~13 cm of water. Her lungs were clear to percussion and auscultation. On examination of her cardiovascular system, she had a palpable subxiphoid right ventricular impulse and a palpable pulmonary artery segment and second heart sound in the second left intercostal space. S1 remained normal, however, P2 had increased further in intensity and the splitting of S2 had narrowed. There was no S3. A murmur of tricuspid regurgitation was present. Her abdomen was nontender with a liver span of 9 cm. Her extremities demonstrated mild bipedal edema.

Laboratory evaluation again revealed normal electrolytes. Her gamma GT was 81 (up from 28 at the time of her previous admission), LDH 395, and her hemoglobin was 15.2. An EKG demonstrated sinus tachycardia with bi-atrial enlargement and incomplete right bundle branch block along with findings of right ventricular hypertrophy with strain.

Chest radiograph demonstrated some enlargement of the cardiac silhouette, particularly of the right heart, when compared with previous studies (Fig. 4). There were markedly dilated main and central pulmonary arteries. As in the past, the suggestion of hypovascularity of the right upper and left lower lung fields remained noticeable.

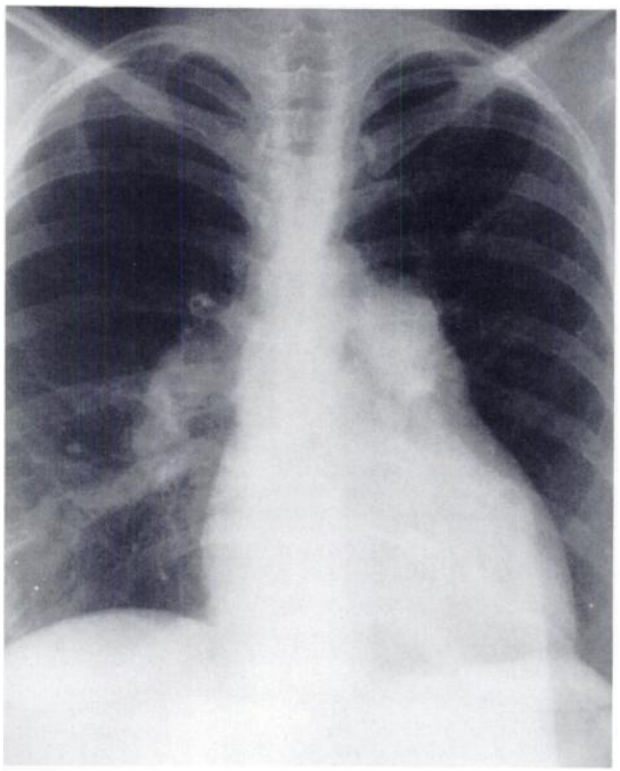

FIGURE 4
PA chest film. Enlargement of the cardiac silhouette has occurred since the earlier examination. Further increase in size of the central pulmonary arteries is also evident. Hypovascularity of the right upper lung and left lung base persists.

Pulmonary function tests were essentially unchanged. The room air blood gas now demonstrated a pH of 7.52, a PCO_2 of 33 Torr, and a PO_2 of 55 Torr.

Cine angiograms of the pulmonary vascular bed revealed a complete obstruction of flow to the right upper lobe and considerable diminution of flow to the left lower lobe (Fig. 5). The mean pulmonary artery pressure was 65 mm, unchanged since the last exam. During this admission she was seen in consultation by the cardiothoracic surgical service, and it was decided that she was an appropriate candidate for pulmonary thromboendarterectomy. The patient agreed to undergo surgical intervention because of her deteriorating health.

On June 17, 1985, she underwent pulmonary thromboendarterectomy for the removal of organized, unresolved pulmonary thromboemboli (Fig. 6). This procedure was performed on cardiopulmonary bypass using deep hypothermia and periods of circulatory arrest. The surgery went smoothly, and she did remarkably well during her postoperative period. A postoperative chest film showed a less prominent cardiac silhouette and central pulmonary arteries. Some patchy densities in the left upper lung base were thought to represent reperfusion edema (Fig. 7). Final Swan-Ganz measurements demonstrated pulmonary artery pressures of 55/30 with a much improved cardiac output. She was discharged on the 11th postoperative day. She was restarted on warfarin before discharge. Marked improvement of chest x-ray findings also occurred by the time of her discharge, with considerable reduction in the cardiac silhouette even from her immediate postoperative study. Although mild prominence of the central pulmonary arteries persisted, this too was much improved from both pre- and immediate postoperative films. Lung vascular patterns had returned to normal (Fig. 8).

She did very well after the surgery with considerable improvement in her exercise tolerance and lifestyle. One year after the surgery a repeat right heart catheterization and pulmonary angiography revealed small amounts of residual chronic thrombus. Her pulmonary artery pressure was 44/20 mmHg with a mean pressure of 30 mmHg. Cardiac output was slightly over 5 l/min. A room air blood gas demonstrated a pH of 7.42, a PCO_2 of 36 Torr and a PO_2 of 95 Torr.

Following the last comprehensive clinical laboratory evaluation, the overall impression was one of remarkable alleviation of right heart failure and the signs and symptoms of progressive pulmonary hypertension.

PULMONARY HYPERTENSION

Pulmonary arterial hypertension is an end result of multiple etiologies and pathologic processes in which the consequence is an increase in pulmonary vascular resistance. Disorders causing pulmonary hypertension may generally be classified into six categories:

1. Passive or post-capillary obstruction, which results from a limitation to pulmonary venous outflow by disorders such as fibrosing mediastinitis, mitral stenosis, or left heart failure.
2. Hyperkinetic, due to high flow states such as left to right intracardiac shunts.
3. Obstructive, as in pulmonary embolism.
4. Obliterative, as in both obstructive and restrictive pulmonary parenchymal diseases.
5. Vasoconstrictive, as seen in acute hypoxia or in some patients with sclerodoma.
6. Idiopathic, or primary pulmonary hypertension when no etiology for the increase in pulmonary vascular resistance and increased pulmonary arterial pressures is identified.

In each of these categories, a major decrease in the volume and/or distensibility of the pulmonary vascular bed limits its ability to accommodate right heart output.

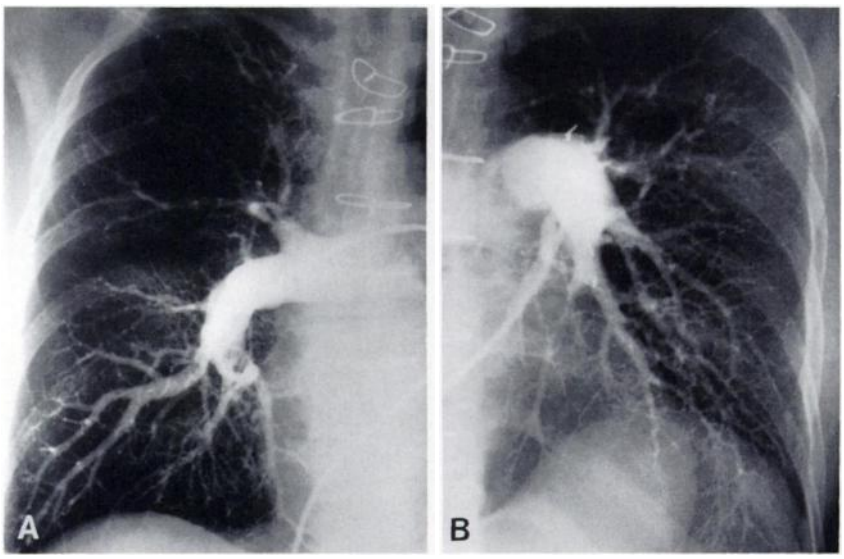

FIGURE 5
Right-sided pulmonary arteriogram (A) has a complete and technically optimal arteriogram revealed near complete obstruction of flow to the right upper lobe. Left-sided pulmonary arteriogram (B) in which significant diminution of flow to the left lower lobe is present. This is particularly notable in the basal segments laterally and posteriorly.

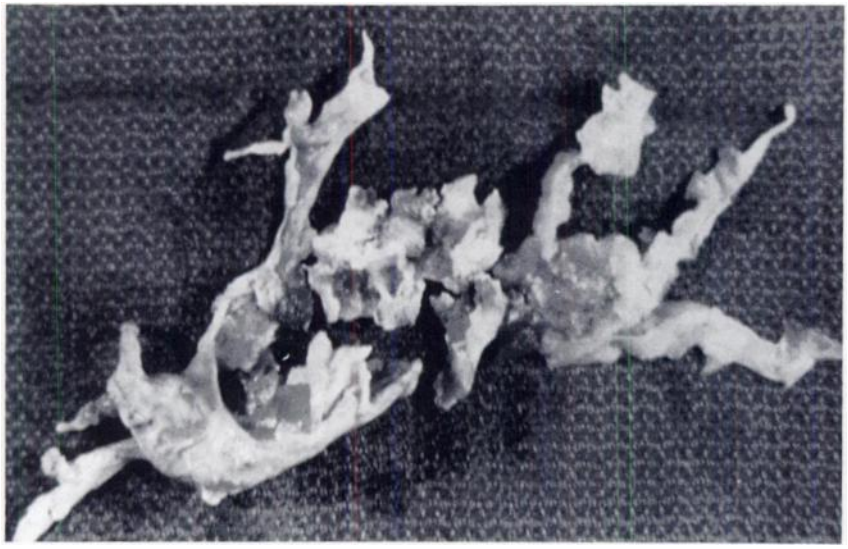

FIGURE 6
Surgical specimen with contents of the occluded vasculature removed at thromboendarterectomy. The organized material represents a large branching thrombus.

Significant increases in pulmonary arterial pressure must be present for the signs and symptoms of pulmonary hypertension to develop. The normal pulmonary vasculature has a considerable reserve capacitance and can accommodate large increments in pulmonary blood flow without corresponding changes in pulmonary arterial pressure (*1*). With disease states, this capacitance is progressively compromised, and small increases in pulmonary blood flow result in significant increments in pulmonary arterial pressure. Widespread pulmonary vascular disease must be present before the patient develops resting pulmonary hypertension. When symptoms do develop, they occur first during exertion, usually as dyspnea, chest pain, or presyncope or syncope. With progression of the disease process, exercise tolerance is progressively diminished, and symptoms occur at lower levels of exertion or even at rest (*2*).

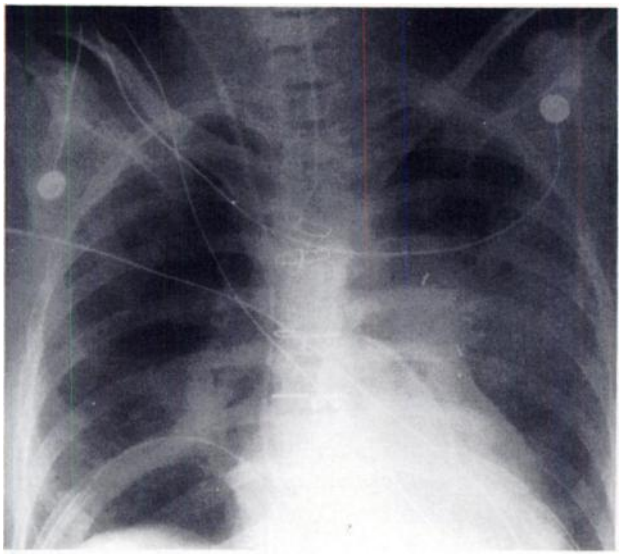

FIGURE 7
On portable AP chest film, a postoperative study reveals interval decrease in size of the cardiac silhouette and central pulmonary arteries. Patchy airspace disease has developed in the left base postoperatively, probably due to reperfusion edema.

Examination of the patient while at rest, particularly before pulmonary hypertension becomes severe, is often interpreted as normal unless the examiner has reason to suspect the presence of pulmonary hypertension. The difficulty in early diagnosis is compounded by the inability of currently available noninvasive screening techniques to detect small increases in pulmonary arterial pressures. Consequently, suspicion of the presence of pulmonary hypertension is often delayed until abnormalities in the chest radiograph or electrocardiogram are present and the suspicion confirmed by right heart catheterization.

Symptoms

There are no symptoms which are specific for pulmonary hypertension (*3,4*). Because of this, and also due to the similarity of the symptoms to those of concurrent and underlying disease processes, there is often a long delay between the time when symptoms appear and when the diagnosis of pulmonary hypertension is established.

The most common symptom associated with pulmonary hypertension is exertional dyspnea (*4*). As with complaints of easy fatigability, the dyspnea found in pulmonary hypertension, initially occurring only with exertion, is often attributed to anxiety or being "out of shape."

Syncope, or pre-syncope (light headedness during exertion) is another common symptom in pulmonary hypertension. Generally, it occurs in patients with more advanced disease and higher pulmonary arterial pressures.

Angina-like chest pains occur in approximately one-half of patients with more severe pulmonary hyperten-

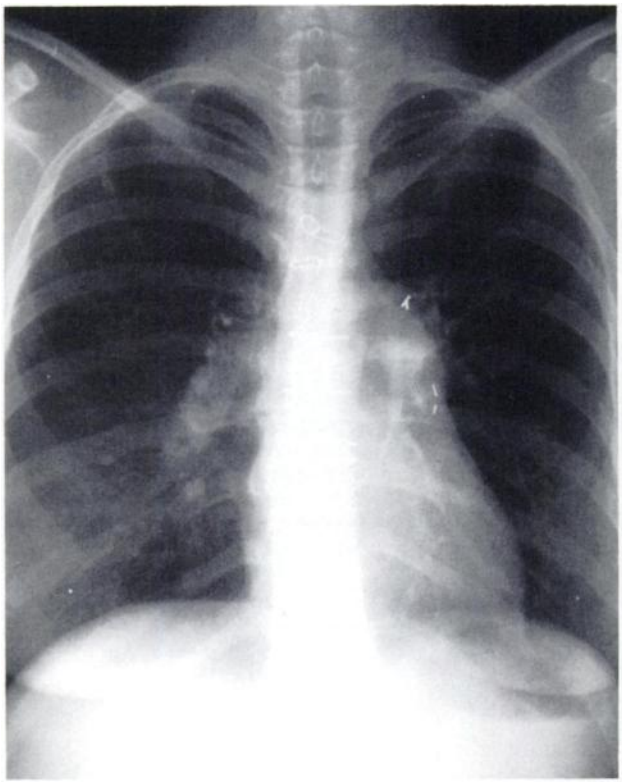

FIGURE 8
PA chest film. A follow-up chest film by the time of discharge demonstrated a nearly normal cardiac silhouette size. Although the main pulmonary artery remains prominent, it has significantly decreased in size from the preoperative study. Significant interval resolution of the oligemia in the right upper lung and left lung base also has occurred.

sion; the pain is similar to that typical of left ventricular ischemia and is generally felt to represent right ventricular ischemia. Hemoptysis can occur in all forms of pulmonary hypertension and is felt to result from abnormally dilated vessels consequent to the increased intravascular pressures.

Peripheral edema, early satiety, and epigastric or right upper quadrant fullness or discomfort may develop as the right heart fails (cor pulmonale).

Signs

The physical signs of pulmonary hypertension are the same no matter what the underlying pathophysiology (*3–5*). Early on, the jugular, venous pulse is characterized by a large A-wave. As the right heart fails, the V-wave becomes predominant. The right ventricle is usually palpable near the lower left sternal border, and pulmonary valve closure may be palpable in the second left intercostal space.

On auscultation, the second heart sound is often narrowly split and varies normally with respiration; P2 is accentuated (*6*). A sharp systolic ejection click may be heard over the pulmonary artery. As the right heart fails, a right atrial gallop is usually present, and tricuspid insufficiency develops. Because of the large pressure gradient across the tricuspid valve in pulmonary hypertension, the murmur is high pitched and may not exhibit respiratory variation. These findings are quite different from those usually observed in tricuspic valvular disease. A murmur of pulmonic regurgitation also is frequently detected.

Diagnostic Studies

With the exception of cardiac catheterization, available diagnostic techniques do not detect early pulmonary hypertension (*3,6*). However, the finding of right ventricular hypertrophy on either an electrocardiogram or an echocardiogram, or the finding of right heart enlargement or of prominent central pulmonary arteries on a chest radiograph should raise concern about the presence of pulmonary hypertension and should prompt further investigation (*3,7–10*).

Chest x-rays and pulmonary function tests (spirometry, lung volumes, and diffusing capacity) are essential for uncovering intrinsic pulmonary disease or abnormalities of the mediastinum. A ventilation-perfusion lung scan is essential for detecting thromboembolic pulmonary vascular disease that would otherwise appear to be primary pulmonary hypertension, eg., proximal (surgically treatable), organized pulmonary embolism (*11*). Pulmonary angiography is generally reserved for patients with either a clinical history or a lung scan suggestive of pulmonary emboli. Catheterization remains the gold standard for establishing the presence and degree of pulmonary hypertension, for excluding intrinsic cardiac disease and congenital heart anomalies, and for the testing of vasodilator agents.

PULMONARY THROMBOEMBOLIC DISEASE

Pulmonary hypertension, as a consequence of acute pulmonary thromboembolism, is not uncommon and relates to both the amount of the pulmonary vascular bed occluded by clot, and the pre-existing cardiopulmonary status of the patient (*12*).

Chronic thromboembolic occlusion of the pulmonary arterial tree, remains a misunderstood and misdiagnosed cause of chronic pulmonary hypertension. Under this single descriptor, there appears to be two separate syndromes with different patterns of vascular involvement, different pathogenetic mechanisms, and different therapies (*13*). The first is thrombosis, involving only small muscular pulmonary arteries; the second is chronic (unresolved) thromboembolic occlusion of large (segmental or larger) pulmonary arteries.

Thrombosis of Small Pulmonary Arteries

Thrombotic and recanalized lesions of the small muscular pulmonary arteries and pulmonary arterioles are found in specimens from patients with a variety of causes of pulmonary hypertension (*14*) and are the most frequent histologic lesions in primary pulmonary

hypertension (*15*). These thrombotic lesions are found in the absence of identifiable sources of emboli and in the absence of involvement of the larger pulmonary vessels and were previously thought to be from one or more showers of microemboli. Now they are widely held to be the result of in situ thrombosis rather than the result of multiple pulmonary emboli. To account for this postulated in situ thrombosis, attention has focused on injury to the microvascular endothelium or to derangements in the local balance between coagulation and fibrinolysis (*16*).

Histologic proof of the presence of microthrombi in the pulmonary vascular bed does not appear to be of much practical use in patient management. A ventilation-perfusion lung scan is necessary to exclude the entity of chronic proximal pulmonary thromboembolism (*11*) (see next section). Patients with microthromboemboli may demonstrate patchy inhomogeneity in their perfusion scan; however, defects that correspond to anatomic segments or subsegments are not observed. In the majority of patients, pulmonary angiography is unnecessary and does not add to the information obtained from the lung scans. Treatment is empirical and consists of long-term anticoagulation and/or antiplatelet agents. Since these histologic lesions are so common, it has even been suggested that all patients with pulmonary hypertension be treated with anticoagulants.

Large Vessel Pulmonary Thromboembolism

Chronic thromboembolic pulmonary hypertension is an uncommon and frequently under-recognized cause of treatable pulmonary hypertension (*13,14*). Whether this syndrome is due to repeated episodes of PE or to failure of lysis of a single embolic episode with subsequent in situ propagation of the thrombus and clot organization remains uncertain. The combination of occlusion of substantial portions of the pulmonary vascular bed and alterations of the compliance characteristics of the central pulmonary arteries appear to be prerequisites for development of pulmonary hypertension. Symptoms develop insidiously and because of this, high clinical suspicion is necessary in order to establish the diagnosis. Fortunately, the use of ventilation-perfusion lung scanning as a screening test in all patients with unexplained pulmonary hypertension will uncover the presence of this syndrome in those patients of whom it is present. This examination will determine the extent of the vascular occlusion and the potential for surgical treatment. At the time of diagnosis, these thrombi are endothelialized and organized and can no longer be treated with standard anticoagulation or thrombolytic therapy (*13,17*). Only surgical removal of the thrombotic material will allow reperfusion of occluded portions of the pulmonary vascular bed and restoration of the compliance of the pulmonary circulation toward normal.

Studies of the hemodynamic consequences of a known single large pulmonary embolus or of repeated thromboembolic events have failed to document progression to severe pulmonary hypertension and right heart failure (*18*). The patients presenting with the syndrome of pulmonary hypertension as a consequence of chronic thromboembolism are presumed to have had occult pulmonary emboli, which were substantial in size and failed to resolve (*19*). It is likely that these thromboemboli originate in the lower extremities as in the majority of symptomatic pulmonary emboli. However, these emboli, which are likely to have been either clinically occult, or, as in the case of this patient, incompletely treated, may organize and propagate within the pulmonary vascular bed. This accounts for the insidious development of pulmonary hypertension and progression of symptoms.

The progression of pulmonary hypertension and increased afterload to the right heart are a consequence of occlusions of the pulmonary vasculature decreasing the cross-sectional area of the vascular bed and of alterations to the compliance of the central pulmonary vessels. As pulmonary hypertension progressively develops, damage to the microvascular bed of the remaining patent portions of the pulmonary circulation will ensue. These microvascular changes are similar to those which are seen as a consequence of most other causes of pulmonary hypertension (*20*). Suspecting and establishing the presence of chronic thromboemboli will allow for surgical removal of the obstructing lesions and reopening of the pulmonary vascular segments, which have been occluded before irreversible changes have occurred in the small vessels of the remaining portions of the pulmonary circulation.

To ensure diagnosis of this entity in those patients in whom it is present, a standardized evaluation should be undertaken in all patients presenting with unexplained pulmonary hypertension (*3,4,7,21*). This work-up includes a chest radiograph, which may show either apparent vessel cutoffs of the lobar or segmental pulmonary arteries or regions of oligemia suggesting vascular occlusion. The EKG will demonstrate findings of right ventricular hypertrophy. Pulmonary function tests are necessary to exclude intrinsic pulmonary parenchymal disease of either obstructive or restrictive types as the etiology of pulmonary hypertension.

The essential test for establishing the diagnosis of unresolved thromboembolism is the ventilation-perfusion lung scan. A normal lung scan is thought to exclude the diagnosis of both acute and unresolved pulmonary thromboembolism. The usual lung scan pattern in most patients with pulmonary hypertension is either relatively normal or diffuse nonuniform perfusion (*11,13,14,19*). When subsegmental or larger perfusion defects are noted on the lung scan, even when matched with ventilatory defects, it is appropriate to consider pulmonary angiography to confirm thromboembolic disease.

Experience in interpretation of pulmonary angiograms is essential for properly establishing the diagnosis. The organized thromboembolic lesions will not appear like the intravascular filling defects seen in acute pulmonary emboli. Rather they appear as unusual filling defects, webs or bands, or completely thrombosed vessels which may resemble congenital absence of the vessel (*19*). In addition, the organized material along a vascular wall which has been recannulized will appear as a scalloped or serrated edge to the lumen. Due to the coexistence of vessel wall thickening and dilatation of the proximal vessels, the contrast-filled lumen of these vessels may be relatively normal in diameter. The distal vessels will demonstrate the rapid tapering and pruning often seen in pulmonary hypertension.

While there has been some reluctance to perform angiography in patients with pulmonary hypertension, the use of selective and subselective injections with small amounts of contrast material have significantly reduced the risks of pulmonary angiography (*22*). Although some risk still remains, the benefit of establishing the presence of a treatable etiology for the pulmonary hypertension clearly outweighs the risks; pulmonary angiography should be performed when the possibility of chronic thromboembolism as the etiology for the pulmonary hypertension is being entertained.

In recent years, computed tomographic scanning, magnetic resonance imaging, two-dimensional echocardiography, and ultrafast computed tomographic scanning have all been actively investigated as noninvasive imaging modalities for diagnosing the presence of organized thrombotic material (*23*). Pulmonary angioscopy has also been proposed as a means for confirming this diagnosis and for determining the proximal extent of the organized clot to assist in planning surgery (*24*).

Standard anticoagulants and thrombolytic agents have not proven successful in treating these patients. Once the diagnosis is established, evaluation for surgical thromboendarterectomy should proceed. Surgical treatment will relieve the obstruction to the pulmonary vascular bed and will result in an increase in pulmonary blood flow and a reduction in pulmonary artery pressure (*19,25*).

The recommended surgical approach to these patients involves median sternotomy and cardiopulmonary bypass. The surgery is performed under deep hypothermia with intermittent periods of circulatory arrest to minimize obscuration of the operative field by back-bleeding from bronchial collaterals and to allow for optimal visualization of the surgical plane between the organized thrombus and the pulmonary arterial wall (*26*).

Patients with clinical evidence for thrombotic arterial obstruction that has been present for at least six months, despite adequate anticoagulations, are candidates for this procedure. In as much as an operative mortality ranging from approximately 6% to 40% has been reported (with the lower figure from more recent series), it is recommended that patients not be considered candidates for this surgery until evidence of resting pulmonary hypertension or functional limitations is present (*19,26,27*). The patient presented here clearly meets both of these criteria and, in fact, has probably passed the stage at which she would have been an optimal surgical candidate.

The immediate postoperative complications from this surgical procedure are related to the development of right ventricular failure, reperfusion pulmonary edema, and arterial hypoxemia. The right ventricular failure is due to the combination of depressed cardiac function in the immediate post-bypass state, perhaps in part due to inadequate myocardial perfusion and preservation during the periods of circulatory arrest and the exacerbation of pulmonary hypertension secondary to vasoconstriction of the pulmonary vascular bed in the immediate postoperative period (*25, 28, 29*).

The reperfusion pulmonary edema, which occurs in the early postoperative course, is often marked by profound hypoxemia (*30*). The etiology of this syndrome is uncertain but it has been suggested that it may in part be due to previously obstructed portions of the pulmonary vascular bed not having been exposed to the high pressures and its inability to tolerate this hemodynamic burden. In addition to these hydrostatic forces, lung permeability defects due to reperfusion phenomena and alterations in pulmonary surfactant may be present (*13*). This syndrome may manifest clinically as pulmonary edema or even lung hemorrhage. The chest radiograph usually demonstrates focal pulmonary infiltrates in the regions distal to the removed thrombotic occlusions. The consequences of this reperfusion injury may be severe and patients may not survive the hypoxemia. However, over time, the lung injury and capillary leak resolve and oxygenation improves.

Since it is uncertain whether pulmonary hypertension in these patients represents failure of the resolution of a single thromboembolic event or recurrent embolic events, they require lifetime anticoagulation after thromboendarterectomy (*13*). Some centers have advocated the placement of inferior vena caval filters in all patients who have undergone thromboendarterectomy but this is not universally accepted (*19*).

Patients usually note immediate improvement in their functional status once they have recovered from the surgery. However, the full benefits of surgery may not be seen for several months. The use of vasodilator agents as an adjunctive therapy in these patients during their postoperative period may be of benefit, but such therapy has not been studied in any controlled manner.

REFERENCES

1. Fishman AP. Pulmonary circulation. In: Fishman AP, ed. *Handbook of physiology—The respiratory system.* Bethesda,

MD: American Physiology Society, 1985:93–165.
2. Palevsky HI. Exercise and the pulmonary circulation. In: Leff A, ed. *Cardiopulmonary exercise testing.* Orlando, FL: Grune and Stratton, 1986:89–106.
3. Reeves JT, Groves BM. Approach to the patient with pulmonary hypertension. In: Weir EK, Reeves JT, eds. *Pulmonary hypertension.* Mount Kisco, NY: Futura Publishing Co., 1984:1–44.
4. Rubin LJ. Clinical evaluation. In: Rubin LJ, ed. *Pulmonary heart disease.* Boston: Martinus Nijhoff, 1984:107–115.
5. Wood P. Pulmonary hypertension. In: Wood P, ed. *Diseases of the heart and circulation.* 3rd edition. Philadelphia: J.B. Lippincott, 1968:964–985.
6. Perloff JK. Ausculatory and phonocardiographic manifestations of pulmonary hypertension. *Prog Cardiovasc Dis* 1967; 9:303–340.
7. Gregoratos G, Karliner JS, Moser KM. Mechanisms of disease and methods of assessment. In: Moser KM, ed. *Pulmonary vascular disease.* New York: Marcel Dekker, 1979:279–339.
8. Kanemoto N. Electrocardiogram in primary pulmonary hypertension. *Eur J Cardiol* 1980; 12:181–193.
9. Lupi E, Dumont C, Tejada VM, Horwitz S, Galland F. A radiologic index of pulmonary arterial hypertension. *Chest* 1975; 68:28–31.
10. Kanemoto N, Furuya H, Etoh T, Sasamoto H, Matsuyama S. Chest roentgenograms in primary pulmonary hypertension. *Chest* 1979; 76:45–49.
11. Powe JE, Palevsky HI, McCarthy KE, Alavi A. Usefulness of lung scanning in the evaluation of patients with pulmonary arterial hypertension. *Radiology* 1987; 164:727–730.
12. Malik AB, Johnson A. Role of humoral mediators in the pulmonary vascular response to pulmonary embolism. In: Weir EK, Reeves JT, eds. *Pulmonary vascular physiology and pathophysiology.* New York: Marcel Dekker, 1989:445–468.
13. Rich S, Levitsky S, Brundage BH. Pulmonary hypertension from chronic pulmonary thromboembolism. *Ann Int Med* 1984; 108:425–434.
14. Moser KM. Pulmonary vascular obstruction due to embolism and thrombosis. In: Moser KM, ed. *Pulmonary vascular disease.* New York: Marcel Dekker, 1979:341–386.
15. Wagenvoort CA, Wagenvoort N. Primary pulmonary hypertension: a pathologic study of the lung vessels in 156 clinically diagnosed cases. *Circulation* 1970; 42:1163–1184.
16. Voelkel NF, Weir EK. Etiologic mechanisms in primary pulmonary hypertension. In: Weir EK, Reeves JT, eds. *Pulmonary vascular physiology and pathophysiology.* New York: Marcel Dekker, 1989:513–539.
17. Sutton GC, Hall RJ, Kerr IH. Clinical course and late prognosis of subacute massive, acute minor and chronic pulmonary thromboembolism. *Br Heart J* 1977; 39:1135–1142.
18. Reidel M, Stanke V, Widimsky J, Prerovsky I. Long-term follow-up of patients with pulmonary thromboembolism: late prognosis and evaluation of hemodynamic and respiratory data. *Chest* 1982; 81:151–158.
19. Moser KM, Daily PO, Peterson K, et al. Thromboendarterectomy for chronic, major vessel thromboembolic pulmonary hypertension: immediate and longterm results in 42 patients. *Ann Int Med* 1987; 107:560–565.
20. Wagenvoort CA. Lung biopsy specimens in the evaluation of pulmonary vascular disease. *Chest* 1980; 77:614–625.
21. Rich S, Dantzker DR, Ayres SM, et al. Primary pulmonary hypertension: a national prospective study. *Ann Int Med* 1987; 107:216–223.
22. Nicod P, Peterson K, Levine M, et al. Pulmonary angiography in severe chronic pulmonary hypertension. *Ann Int Med* 1987; 107:565–568.
23. Gefter WB, Palevsky HI, Dinsmore BJ, Reichek N, de Roos A, Kressel HY. Identification of chronic thromboembolic pulmonary hypertension with MR imaging. *Radiology* 1988; 169:218.
24. Shure D, Gregoratos G, Moser KM. Fiberoptic angioscopy: role in the diagnosis of chronic pulmonary arterial obstruction. *Ann Int Med* 1985; 103:844–850.
25. Moser KM, Spragg RG, Utley J, Daily PO. Chronic thrombotic obstruction of major pulmonary arteries: results of thromboendarterectomy in 15 patients. *Ann Int Med* 1983; 99:299–305.
26. Daily PO, Dembitsky W, Peterson KL, Moser KM. Modifications of techniques and early results of pulmonary thromboendarterectomy for chronic pulmonary embolism. *J Thorac Cardiovasc Surg* 1987; 93:221–233.
27. Chitwood WR, Jr, Sabiston DC Jr, Weschsler JS. Surgical treatment of chronic unresolved pulmonary embolism. *Clin Chest Med* 1984; 5:507–536.
28. Sabiston DC Jr, Wolfe WG, Oldham HN Jr, et al. Surgical management of chronic pulmonary embolism. *Ann Surg* 1977; 185:699–712.
29. Utley JR, Spragg RG, Long WB III, Moser KM. Pulmonary endarterectomy for chronic obstruction: recent surgical experience. *Surgery* 1982; 92:1096–1102.
30. Levinson RM, Shure D, Moser KM. Reperfusion pulmonary edema after pulmonary artery thromboendarterectomy. *Am Rev Respir Dis* 1986; 134:1241–1245.