Chronic, Massive Thrombotic Obstruction of the Pulmonary Arteries

Analysis of Four Operated Cases

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CHRONIC, massive thrombotic obstruction of the pulmonary arteries has attracted interest recurrently through the years as a neglected cause of pulmonary hypertension of obscure etiology, usually discovered at autopsy.1-10 This form of "cor pulmonale" has been regarded as a rare entity of academic rather than therapeutic interest. Such opinions now require revision. With the advent of pulmonary thromboendarterectomy as a feasible surgical procedure, chronic massive obstruction has become a potentially curable form of heart disease.11, 12 Furthermore, the wider use of pulmonary angiography13, 14 and other diagnostic technics15, 16 has led to the antemortem diagnosis of an appreciable number of such patients in recent years.

In the last 3 years, we have encountered eight patients in whom extensive, chronic thromboembolism was the sole cause of, or the major factor in, the development of pulmonary hypertension. This experience has substantiated our prior suggestion that the possibility of surgical correction would heighten interest in this entity and lead to the discovery of additional cases.11 Four of our eight patients have been operated upon in an attempt to relieve the thrombotic obstruction. In two, thromboendarterectomy was successful, and the patients are alive and well more than 2 years after surgery. In two, surgical correction could not be achieved, and the patients died in the postoperative period. This report recounts our experiences with these four operated cases. It is hoped that this experience will provide further insight into the pathophysiologic and diagnostic features of this entity and assist in the future selection of candidates for pulmonary thromboendarterectomy.

Case Reports

Case 1

K. E., a 41-year-old man, was admitted to the U. S. Naval Hospital, Bethesda, in September 1961, for evaluation of persistent dyspnea on exertion. Mild dyspnea on exertion had appeared in March, following immobilization in a shoulder spica. In July 1961, in another hospital, right femoral thrombophlebitis developed and, despite anticoagulant therapy, he had experienced an episode of right pleuritic chest pain. Thereafter his recovery was uneventful, but mild dyspnea on exertion persisted.

Examination on admission to the Naval Hospital was within normal limits aside from an accentuated pulmonic closure sound, and a holosystolic murmur in the third left intercostal space, which extended through the second sound, was well heard in the back, and increased in intensity with inspiration.

Chest x-ray disclosed a normal-sized heart, prominence of the main pulmonary artery and its primary branches, avascularity of the left upper lobe, and pleural adhesions at the right base. Pulmonary ventilatory studies were unremarkable. Arterial blood gas studies revealed resting and exercise hypoxemia and an abnormally wide arterial to end-tidal carbon dioxide tension difference. Right heart catheterization disclosed a resting pulmonary artery mean pressure of 35 mm. Hg, which rose to 70 mm. Hg during exercise. A pulmonary cineangiogram revealed a filling defect in the distal portion of the right main pulmonary artery, absence of filling of vessels

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Case 2

N. M., a 42-year-old man, was referred to Georgetown University Hospital in March 1962, because of dyspnea on exertion which had persisted since an episode of right lower lobe infarction in February 1961.

Positive physical findings were limited to the thorax. The right diaphragm was elevated, and its motion decreased. Dullness and decreased breath sounds were present at the right base. The heart was not enlarged. A grade-II, late systolic murmur was heard in the pulmonary area, introduced by a faint ejection sound. Just below the left scapula a grade-III systolic murmur was audible, which extended through the second sound, and increased in intensity with inspiration.

Chest x-ray (fig. 2A) disclosed a relatively avascular right lung with small, tapering right main pulmonary artery, contrasted with a plethoric left lung and a dilated left main pulmonary artery. Fluoroscopy demonstrated that the left pulmonary artery was highly pulsatile; the right was non-pulsatile. Electrocardiogram and pulmonary ventilatory studies were unremarkable. Arterial blood studies revealed mild hypoxemia and an abnormal gradient of arterial to end-tidal carbon dioxide tension. At cardiac catheterization the right ventricular pressure was 35-40/3-5 at rest and 50-55/5 during mild exercise. A right ventricular angiogram disclosed no filling of the right pulmonary artery (fig. 2B).

In May 1962, during cardiopulmonary bypass...

Figure 1

standby, a large fibrothrombotic mass, occupying the entire right main pulmonary artery with ramifications into secondary and tertiary branches, was removed. Brisk “back-bleeding” occurred from the middle and lower lobes, but not from the upper lobe. The patient tolerated the procedure well and returned to work in 1 month. Since that time, dyspnea on exertion has been minimal. The pulmonary systolic murmur has disappeared, but the left subscapular murmur persists. Chest x-rays have disclosed a decrease in left lung plethora and restoration of right middle and lower lobe vascular shadows. Angiogram 7 months after surgery confirmed restoration of right middle and lower lobe blood flow, but no flow to the right upper lobe (fig. 2C). A recent pulmonary radioscop (fig. 3) has revealed this same pattern plus a left upper lobe defect in the region of the persistent “pulmonary” murmur.

Case 3

F. S., a 56-year-old man, was admitted for the first time to Georgetown Hospital in August 1963, because of progressive dyspnea for 10 years. Two years before admission he was hospitalized with acute dyspnea, which improved with digitalis, diuretics, and salt restriction. Six months before admission, effort dyspnea worsened. Three weeks before admission dyspnea at rest and episodic cyanosis appeared. He denied pleuritic chest pain, hemoptysis, and thrombophlebitis.

Physical examination disclosed a blood pressure of 100/80, pulse of 88 per minute, and respirations of 38 per minute. Chest and diaphragmatic motion were decreased; resonance was increased. Moderate cardiomegaly was present. A right ventricular lift was palpable. An accentuated pulmonic closure sound, a ventricular diastolic gallop, a grade-II ejection murmur along the left sternal border, and a short, harsh systolic murmur in the second left intercostal space near the sternal edge were heard. There was slight pretibial edema, but no evidence of arterial or venous disease.

Electrocardiogram revealed right ventricular hypertrophy. Chest x-ray disclosed bilateral pleural thickening, a left lower lobe infiltrate, reduced vascularity of the left upper lobe, enlargement of the central pulmonary arterial

**Figure 2**

A, left. Chest x-ray of March 1962, in case 2, demonstrating avascular right lung with small pulmonary artery shadow; prominent left pulmonary artery with dilated branches. B, center. Preoperative pulmonary angiogram demonstrating absence of filling of right main pulmonary artery and its branches. C, right. Pulmonary angiogram 7 months after right thromboendarterectomy demonstrating right main pulmonary artery with middle and lower lobe branches. The right upper lobe arteries are not opacified.

**Figure 3**

Pulmonary radioscans with macroaggregated RISA in case 2, approximately 2 years after surgery. Note defect in right upper lobe (corresponding to figure 2C) and peripheral left upper lobe defect in area of persistent murmur.
shadows, and generalized cardiomegaly. Right heart catheterization disclosed a mean pulmonary arterial pressure of 32 mm. Hg. Pulmonary ventilatory studies disclosed mild obstructive emphysema. Despite intensive therapy, the patient developed progressive right ventricular failure. In February 1964, the gradient of arterial to end-tidal carbon dioxide tension was found to be wide. Pulmonary angiography revealed total obstruction of the right middle and lower lobe, and left superior pulmonary artery branches (fig. 4). The mean pulmonary artery pressure was then 43 mm. Hg.

At thoracotomy in April 1964, hypotension developed during induction of anesthesia which was accentuated by temporary occlusion of the right main pulmonary artery and forced abandonment of the procedure. Hypotension persisted and the patient died 2 hours later.

Postmortem examination revealed marked right atrial and ventricular hypertrophy. In the antero-septal portion of the right ventricular wall was a 0.6 by 1.3 cm. white mass which extended upward through the pulmonary valve into the pulmonary artery. Microscopic examination revealed this to be a fibrosarcoma. The main pulmonary artery and primary branches were markedly dilated. The inferior branch of the right main pulmonary artery was totally occluded by an organized thrombus 1.5 cm. in length beyond which the vessel was patent. The superior branch of the left main pulmonary artery was occluded by old thrombus, which extended into segmental and subsegmental branches. Scattered throughout all lobes were small infarcts of all ages. The thromboemboli were entirely throm-
botic in nature except for two small emboli that contained tumor cells. No pulmonary or distant metastases were present.

Case 4

W. R., a 37-year-old man, was admitted to Walter Reed Army Hospital in January 1964, because of severe congestive heart failure. He had developed varicosities of the right leg following an injury in 1946, and required venous ligation and stripping in 1960. In early 1961, he developed hemoptysis, mild dyspnea on exertion, ankle edema, and a nonproductive cough. In November 1961, physical signs of pulmonary hypertension, right ventricular hypertrophy, and failure were found. Chest x-ray demonstrated cardiomegaly, marked enlargement of the main pulmonary arterial branches, and relative avascularity of the right upper lobe (fig. 5A). Right heart catheterization disclosed a mean pulmonary artery pressure of 60 mm. Hg with no evidence of valvular disease or intracardiac shunt. The patient was discharged, well compensated, on digitalis, diuretics, and anticoagulant drugs.

During the next 2 years, dyspnea on exertion and right ventricular failure slowly progressed. In January 1964, the patient was markedly dyspeic, with a right pleural effusion and peripheral edema. A prominent jugular venous A wave, right ventricular lift, accentuated pulmonic closure sound, right ventricular diastolic gallop, and murmurs of pulmonic and tricuspid insufficiency were noted. Electrocardiogram indicated right atrial enlargement, right ventricular hypertrophy and “strain.” Chest x-ray disclosed cardiomegaly, right pleural effusion, and avascularity of both lung fields. The lower portion of the right pulmonary arterial shadow had become attenuated since 1961 (fig. 5B). A lung radioscan showed reduced blood flow to the right lung and left lower lobe. Right heart catheterization disclosed a resting mean pulmonary artery pressure of 70 mm. Hg. Pulmonary angiogram revealed no right upper lobe filling, markedly diminished filling of right middle and lower lobe vessels, abrupt termination of the lingular pulmonary branch, and delayed, poor left lower lobe filling (fig. 6).

At thoracotomy in April 1964, the right side was approached first. Extensive, vascular pleural adhesions were encountered. Exploration of the right pulmonary artery disclosed occlusions of all tertiary branches which were not thought to be remediable. The procedure was terminated because of persistent hypotension. This persisted postoperatively, and the patient died 36 hours after surgery.

Postmortem examination disclosed marked right atrial and ventricular dilatation and hypertrophy.

Figure 6

Pulmonary angiogram, case 4. Note marked dilatation of main pulmonary arteries with absence of right upper lobe filling, sharply reduced filling of right middle and lower lobes, and poor lingular and left lower lobe filling.

Scattered small, healed peripheral infarcts were present in both lungs. Old thrombotic lesions were present in all tertiary pulmonary arterial branches of the right lung and of the left lower lobe, and in 50 per cent of those of the left upper lobe. In each instance, the thromboocclusive lesions extended only 0.5 to 1.0 cm. with normal pulmonary arterial vessels beyond.

Discussion

The exploration of any new area inevitably produces as many questions as answers. The application of thromboendarterectomy to patients with chronic thrombotic pulmonary arterial occlusion certainly has done so. Yet the experience to date has supplied enough basic answers to encourage further pursuit of the problem. Perhaps the central question answered is that extensive, well-organized thrombi, which have obstructed major pulmonary vessels for months to years, can be removed successfully. Furthermore, the “reclaimed” lung areas seem able to accept safely this sudden return of blood flow and to resume adequate respiratory function. However, our experience also has indicated that technical feasibility
and operative success are not synonymous. An early diagnosis is essential if the patient is to have sufficient cardiopulmonary reserve to withstand the surgery required. Early diagnosis requires a strong suspicion of the disorder, based upon familiarity with its characteristic clinical features, and the verification of this clinical suspicion by appropriate laboratory studies.

**Clinical Findings**

**History**

The most valuable historical clue in this series and others has been episodic or persistent dyspnea—particularly dyspnea on effort—which is not adequately explained by coexisting cardiopulmonary disease. In the current series, dyspnea on effort was present in all subjects for 6 months to 3 years before its etiologic basis was established. The frequency of this symptom is not surprising, since multiple bases for dyspnea exist in embolic occlusion. Chest pain also has been a symptom common in this and other series. However, the chest pain was commonly attributed to other causes, a pitfall emphasized by Carroll in 1950. Hemoptysis did occur eventually in three of our four patients, but in only one was it an early sign. In only one patient was there a clearly documented history of thrombophlebitis.

**Physical Signs**

Physical stigmata of advanced right ventricular hypertrophy and failure are late and nonspecific signs. They point toward massive occlusion only in the absence of other causes of right ventricular compromise. One type of murmur, however, may provide a significant diagnostic clue, namely, a systolic murmur that is maximal over the lung fields, increases in intensity with inspiration, and frequently "spills beyond" the second sound. This type of murmur, which mimics that of pulmonary branch stenosis, is particularly suggestive of thromboembolic disease. It appears related to the same mechanism operative in branch stenosis—turbulence engendered by flow past a constriction in vascular lumen. In one of our patients (case 1), this murmur disappeared following removal of thrombus from the left upper lobe artery. In another (case 2), the maximum intensity of the murmur coincides with an area of diminished flow on the pulmonary radioscan. However, since such a murmur will not occur with total luminal obstruction, its absence does not deter the diagnosis.

**Laboratory Findings**

The chest roentgenogram suggested the diagnosis in each of our four patients. The radiographic clues, often rather subtle, have been reviewed in detail by others. They include (1) avascularity of an entire lung or lung area; (2) a blotchy or irregular vascular pattern in a lung or lung area, indicative of increased bronchial collateral flow; (3) increased vascularity in certain zones contrasted with avascularity in others; (4) disparity in the size of comparable major pulmonary arteries; (5) abrupt tapering ("rat-tail" appearance) or termination of a pulmonary arterial branch; (6) evidence of old or recent pulmonary infarction. Comparison of prior with current x-rays is often helpful, as illustrated by our cases 2 and 4. Fluoroscopy also may assist by disclosing diminished pulsations of a main pulmonary artery or one of its major branches.

The electrocardiogram, which was normal in two of our patients, is of limited value. However, the presence of unexplained right atrial or ventricular hypertrophy can suggest the proper diagnosis. Determination of the lung volumes serves to eliminate intrinsic pulmonary disease (e.g., emphysema) as the basis for the patient's symptoms. The arterial blood gas pattern may provide diagnostic clues. Some degree of hypoxemia was present in each of our patients. Hypoxemia, however, is common in many cardiopulmonary disorders. Of greater differential value is measurement of the arterial to end-tidal ("alveolar") carbon dioxide tension gradient. From an extensive study of normal subjects and patients with cardiopulmonary disease, we view a gradient greater than 25 per cent of the arterial pCO2 level as highly suggestive
of extensive pulmonary vascular obstruction. Such a gradient was present in the three patients in this series in whom it was measured. While the absence of a significant gradient does not exclude the diagnosis,25 its presence is of considerable value in justifying further study.

Another procedure we now employ routinely is lung radioscanning with macroaggregated, radioiodinated human serum albumin.16 This procedure is simple, safe, and has been of great aid in confirming the absence of pulmonary arterial blood flow to a lung area. It is also of considerable assistance in long-term follow-up, as demonstrated by our case 2.

If preceding studies have suggested the diagnosis, right heart catheterization is required to eliminate the presence of significant cardiac lesions. In addition, the pulmonary arterial pressure contour may provide some diagnostic aid in that, in two of our patients, this contour has been similar to that noted in "branch stenosis."21 Pulmonary angiography, however, remains the definitive procedure. Angiography not only confirms the diagnosis of vascular obstruction; it also defines the location of the obstruction. Knowledge of the location of the lesion is vital in selecting those patients in whom surgery is feasible.

**Surgical Candidates and Considerations**

When the diagnosis of chronic pulmonary embolic obstruction is established, three questions arise. Is surgery desirable? Is it feasible? What technical-management problems will be faced?

There are three major reasons for considering thromboendarterectomy: hemodynamic, alveolo-respiratory, and " prophylactic." The hemodynamic goal is to prevent or ameliorate right ventricular compromise due to pulmonary hypertension. The alveolo-respiratory objective is to improve respiratory function by removing a large ventilated but unperfused "physiologic dead space." The prophylactic goal is to prevent retrograde extension of the obstruction which might result in further cardiorespiratory deterioration or death. If such indications are not present, we would not consider surgery even though extensive thrombotic obstruction is demonstrable.

If the patient is a surgical candidate, the feasibility of surgery is the next consideration. Feasibility, at this time, is based upon the anatomic location of the obstructive lesions and the general suitability of the patient for major surgery. Currently, patients with lesions located in the primary and secondary (lobar) branches are acceptable candidates. If the blockade is in tertiary branches, the potential benefits of surgery are less and the technical problems considerably increased. We would not now consider such patients as operable.

The general suitability of a given patient for thromboendarterectomy presents complexities that cannot be resolved with precision. For example, in a patient with moderate obstructive emphysema who also has multiple occlusions, it is difficult to quantitate the contribution of each to the patient's symptoms and functional abnormalities. Each such patient must be carefully studied and accepted or rejected for surgery on an individual basis.

It should be noted that we have not mentioned two potential problems that might limit surgical feasibility: (1) inability to achieve thromboendarterectomy in vessels obstructed by old, well-organized thrombi and (2) inoperability due to extension of thrombus into tertiary branches and beyond. Regarding the first point, experience to date suggests that thromboendarterectomy remains feasible despite the presence of organized thrombi months to years of age as demonstrated by our cases 1 and 2 and that of Snyder et al.12 Furthermore, in our two unsuccessful cases, many of the obstructions "peeled" from the vessel wall rather easily with forceps at autopsy. Age alone, therefore, would not seem to prevent surgical success. Marked distal extension of the thrombosis, the second problem, certainly may be encountered. Further experience is required before the frequency of such extension is identified. However, it is encouraging that the great majority of obstructions in our patients extended a short distance with a patent vascular bed beyond.

Finally, there are certain technical consid-
erations that deserve brief mention. The use of cardiopulmonary bypass is one. Our present consensus is that bypass should be available on a standby basis in all cases and is required if extensive bilateral obstruction is to be corrected. We have noted acute electrocardiographic and hemodynamic disturbances in two chronic (cases 1 and 4) and two acute embolic subjects with bilateral involvement when one main pulmonary artery was occluded at the time of surgery. Perhaps bypass should be used in all cases to permit more detailed exploration of the pulmonary arterial tree, but the problems associated with bypass must be balanced against the advantages of its use in each case. Other questions of approach include whether or not ligation of the inferior vena cava should be performed routinely in such patients; how one can best assure that embolic sources do not exist in the right heart chambers; the best postoperative anticoagulant (and possibly fibrinolytic) regimens. Answers to each of these questions require individualization until more experience is accumulated. However, it is already apparent that mobilization of the vasculature itself may present a formidable technical problem because of extensive, highly vascular pleural adhesions. Such adhesions were present in each of our four patients and were a source of major delay and blood loss in two of them. This difficulty can be anticipated in future cases.

Summary

Four patients with extensive, chronic pulmonary arterial thrombotic obstruction, are presented in whom thromboendarterectomy was attempted. The procedure was successful in two, both of whom are alive and well more than 2 years since surgery; it was unsuccessful in two, both of whom succumbed in the postoperative period. The clinical and laboratory diagnostic approach to such patients is discussed. Criteria for selection of operative candidates are reviewed and certain technical decisions considered. It is concluded that selected patients with chronic massive occlusion can be improved significantly by thromboendarterectomy, but further experience is required to improve criteria for the selection of surgical candidates. The poor experience with two patients in advanced right ventricular failure already has indicated that one essential factor in reducing surgical risk is diagnosis prior to overt cardiac decompensation.

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