Pulmonary Venous and Arterial Hypertension due to Chronic Fibrous Mediastinitis

Hemodynamics and Pulmonary Function

By James T. Botticelli, M.D., Donald P. Schlueter, M.D., and Ramon L. Lange, M.D.

Although chronic fibrous mediastinitis is responsible for 8 to 23% of the cases of superior vena caval obstruction, it may also compress or obstruct other mediastinal structures. Involvement of the tracheobronchial tree, pulmonary artery, esophagus, aorta, and coronary arteries has been reported. Obstruction of pulmonary veins, however, is uncommon and may not be recognized as a cause of pulmonary hypertension.

This report describes the clinical findings, the abnormal hemodynamic and ventilatory functions, and pathological material in a case of complete or partial obstruction of the superior vena cava, the bronchial tree, and pulmonary veins with associated pulmonary hypertension and diffuse interstitial fibrosis. Repeated observations, including hemodynamic and pulmonary function studies, were made over a 3-year period. The presumptive diagnosis of pulmonary vein obstruction secondary to chronic fibrous mediastinitis was confirmed by thoracotomy following which the patient's condition has remained stable for 10 months.

Report of Case

R. B., a 35-year-old truck driver, was admitted to the hospital on May 2, 1962, complaining of severe hemoptysis. At age 18, he noted neck vein distention and increasing shirt collar size. Since age 21, he had been subject to frequent "colds" characterized by cough productive of clear sputum, dyspnea with exertion, and a sensation of chest "congestion" and heaviness.

The pulse rate on admission was 76, blood pressure was 108/80 mm Hg; respiratory rate, 16 and body temperature 99.6 F. The patient had a "bull neck" appearance and markedly distended, nonpulsatile neck veins. Collateral venous patterns were prominent over the anterior chest wall. Inspiratory and expiratory wheezes were noted in all lung fields, and the inspiratory phase was prolonged. The heart size was normal. No murmurs were heard, but fixed splitting of the second sound at the base was noted along with accentuation of the pulmonic closing sound. There was no clubbing, cyanosis, or edema.

Hemoglobin concentration was 12.8 g per 100 ml. A serologic test for syphilis was nonreactive. Sputum smears and cultures for acid-fast organisms were negative as were cultures for fungi. The histoplasmin skin test caused a + reaction, but results of tuberculin tests with PPD and OT and other fungal skin tests were negative. Complement fixation studies were nonreactive for blastomycosis, coccidioidomycosis, and both the yeast and mycelial phases of histoplasmosis. Electrocardiogram revealed right axis deviation and right ventricular hypertrophy.

Slightly increased bronchovascular markings and normal pulmonary artery were present on a routine chest x-ray taken in 1955. Chest x-ray taken on admission showed marked increase in bronchovascular markings with bilateral nodular densities and partial atelectasis of the left lower lobe (fig. 1 left). No evidence of major bronchial obstruction was found at bronchoscopy. Esophogram and intravenous pyelography were normal. A bronchogram of the left lung revealed compression of the left lower lobe bronchi with some distal atelectasis (fig. 1 right).

The long duration of superior vena caval obstruction without evidence of malignant disease, radiographic evidence of pulmonary fibrosis, and right ventricular hypertrophy suggested a diagnosis of chronic fibrosing mediastinitis with asso-
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Associated pulmonary fibrosis and cor pulmonale. Spirometric studies indicated moderately severe ventilatory impairment, and cardiac catheterization and angiography confirmed the diagnosis of pulmonary hypertension and superior vena caval obstruction (tables 1 and 2).

The patient was discharged to the care of his physician. He was readmitted on January 7, 1965, because of right lower chest pain and dyspnea. He related that he had been able to work only intermittently, as during the preceding 18 months, exertional dyspnea and easy fatigue had increased.

The patient appeared acutely ill, cyanotic, and

![Figure 1](http://circ.ahajournals.org/)

Left. Chest roentgenogram made in 1965. Diffusely increased interstitial markings and enlarged pulmonary artery may be noted. Except for the right pleural effusion, there was no change from 1962. Right. Bronchogram of left lower lobe made in 1962 demonstrates compression of major bronchi and some atelectasis.

### Table 1

<table>
<thead>
<tr>
<th>Catheter position</th>
<th>Pressure, mm Hg</th>
<th>1962 CO₂ vol %</th>
<th>SO₂ %</th>
<th>Pressure, mm Hg</th>
<th>1965 CO₂ vol %</th>
<th>SO₂ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subclavian vein</td>
<td>15*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right atrium</td>
<td>3/0</td>
<td>2*</td>
<td></td>
<td>78/0</td>
<td>4*</td>
<td></td>
</tr>
<tr>
<td>Right ventricle</td>
<td>70/0</td>
<td>35*</td>
<td></td>
<td>78/23</td>
<td>40*</td>
<td>9.08</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>70/18</td>
<td>5.81</td>
<td>52.8</td>
<td>78/23</td>
<td>40*</td>
<td>9.08</td>
</tr>
<tr>
<td>Pulmonary artery wedge</td>
<td>8.01</td>
<td></td>
<td></td>
<td>78/23</td>
<td>40*</td>
<td>9.08</td>
</tr>
<tr>
<td>Left atrium</td>
<td>18*</td>
<td></td>
<td></td>
<td>78/23</td>
<td>40*</td>
<td>9.08</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>88/0</td>
<td>5*</td>
<td></td>
<td>78/23</td>
<td>40*</td>
<td>9.08</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>100/58</td>
<td>72*</td>
<td></td>
<td>105/56</td>
<td>72*</td>
<td></td>
</tr>
<tr>
<td>Cardiac index, L/min/m²</td>
<td>2.53</td>
<td></td>
<td></td>
<td>3.25</td>
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<tr>
<td>Systemic vascular resistance</td>
<td>28.00</td>
<td></td>
<td></td>
<td>21.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total pulmonary resistance</td>
<td>12.3</td>
<td></td>
<td></td>
<td>5.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary postcapillary resistance</td>
<td>6.8</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

*Mean pressure.

†End-diastolic pressure.

Circulation, Volume XXXIII, June 1966
Hemodynamic and Pulmonary Function Studies

Angiography was done in 1962. Following injection of contrast material into the subclavian vein, marked collateral circulation was demonstrated, with no opacification of the superior vena cava. Inferior vena caval injection revealed enlargement of the main pulmonary artery, without evidence of constriction of major pulmonary arteries. In addition, reduced distribution of contrast material was evident in the left lower and in portions of the left upper lobe.

Hemodynamic studies from 1962 and 1965 are presented in table 1. These confirm the presence of superior vena caval obstruction since subclavian vein pressure exceeded right atrial and inferior vena caval pressure. Marked pulmonary hypertension without evidence of right heart failure and normal cardiac output were found at the time of both studies.

In 1965, the pulmonary artery wedge pressure was 18 mm Hg in the left upper lobe and also in the left lower lobe. The mean left atrial pressure (transseptal technique) was 0. Since the pressure gradient from the pulmonary artery to the left atrium was 40 mm Hg and that from the "pulmonary capillary" to the left atrium was 18 mm Hg, approximately half of the total pressure gradient, and therefore pulmonary vascular resistance was located between the pulmonary capillary bed and the left atrium. With exercise, a marked increase in pulmonary artery (105/38 mm Hg) and pulmonary artery wedge (31 mm Hg) pressures occurred (figs. 2 and 3). At rest, only slight variation in arterial systolic pressure was seen despite considerable respiratory variation in the pulmonary artery wedge pressure which was not apparent in the left atrium. Aside from artifacts produced by catheter movement, the pulmonary artery wedge tracing lacked pulsatile characteristics and did not resemble the left atrial pressure. With exercise, considerably more respiratory variation could be seen in wedge and arterial systolic pressures (fig. 2).

Indocyanine-green indicator-dilution curves (fig. 4), following injection into the pulmonary artery, revealed an 8-second appearance time and normal contour. Injection into pulmonary artery branches of the left upper and lower lobes resulted in indicator-dilution curves with appearance times corresponding to those obtained on main pulmonary artery or inferior vena caval injection. However, there was marked prolongation of the curve suggesting delayed washout of indi-
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cator from the lung segments which had received the bolus of indicator.

The results of pulmonary function studies are shown in table 2, and are compatible with com-
bined restrictive-obstructive ventilatory impairment of progressive severity. The lack of im-
provement with inhalation of isoproterenol in both studies ruled out reversible bronchoconstriction.

**Figure 2**

Elevated pulmonary artery wedge pressure (PAW) with moderate respiratory variations may be noted. With exercise, the wedge pressure rose from 18 to 31 while the femoral arterial pressure also increased. Respiratory variation in pressure is present in the femoral arterial tracing.

**Figure 3**

Pressure recording during pull back from left ventricle to left atrium demonstrates low atrial and ventricular diastolic pressures with little respiratory variation.
The indicator-dilution curve sampled from the femoral artery following injection into the main pulmonary artery has a normal contour. That following injection into the left upper lobe segment, however, demonstrates nearly the same appearance time, but markedly delayed washout of indicator suggesting markedly diminished flow in the lung segment receiving most of the injectate.

Marked abnormality of ventilation-distribution was demonstrated since the dynamic lung compliance was markedly decreased with respiratory rates increasing from 25 to 160 per minute (table 3). The nonelastic resistance (airway plus tissue) was considerably elevated in inspiration and expiration. Both the elastic and nonelastic work were moderately increased and could be related to the increased retractive force of the lung due to fibrosis (elastic) and to the severe airway obstruction (nonelastic). Arterial blood gas studies (table 4) indicate slight arterial unsaturation at rest (91%). With exercise, there was a further decrease in arterial oxygen saturation to 89%, despite a considerable increase in ventilation ($O_2V$ 40). The carbon monoxide diffusion capacity was reduced to 58% of the predicted value.

**Operative Findings**

The possibility that the pulmonary venous obstruction might be correctable led to surgical exploration. Dense vascular adhesions were encountered and the superior vena cava was completely occluded throughout its entire length. The lungs, which were firm and somewhat nodular, failed to collapse. All right pulmonary veins were severely narrowed in their extrapericardial segments. The lung parenchyma was woody hard for 2 to 5 cm into the hilar region. Palpation of the left hilum yielded similar characteristics. The intrapericardial segments of pulmonary veins were free from adhesions and collapsed partially with each diastole. Insertion of a catheter into the smaller radicles of the pulmonary veins via the left atrial appendage revealed pressures as high as 40 mm Hg in the smaller tributaries with gradual reduction to 0 as the catheter was withdrawn into the left atrium. Since no operable locus of venous obstruction was found, the procedure was terminated.

Biopsies of the pericardium and subpleural areas of the right middle lobe showed an extreme degree of fibrous thickening which, in some areas, was markedly vascular. The pleural fibrosis extended into the interlobular and interalveolar septa (fig. 5). Most of the vessels showed significant hypertrophy of the walls, and the smaller branches of the pulmonary artery had an increased number of nuclei, indicating intimal hyperplasia (fig. 6). Granulomata were not found in the biopsy material, and treatment with meth-

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Mechanics of Respiration</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Normal 1962 1965</td>
</tr>
<tr>
<td>Static compliance, L/cm $H_2O$</td>
<td>0.22 ± 0.05 0.19 0.16</td>
</tr>
<tr>
<td>Dynamic compliance, L/cm $H_2O$</td>
<td>0.18 ± 0.04 - 25 bpm 0.139</td>
</tr>
<tr>
<td>Nonelastic resistance, cm $H_2O/L/sec$</td>
<td>1.5 – 3.0 5.18* Inspiration 6.41</td>
</tr>
<tr>
<td>Work of breathing, kg-m/min</td>
<td>1.2 – 0.6 0.022 Nonelastic 3.72</td>
</tr>
<tr>
<td>Total</td>
<td>1.8 – 0.6 0.139 Elastic 3.92</td>
</tr>
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</table>

*Interrupter method.
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Table 4

<table>
<thead>
<tr>
<th></th>
<th>Predicted</th>
<th>1962 Exercise</th>
<th>Rest</th>
<th>1965 Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_{O_2}$, %</td>
<td>94</td>
<td>86</td>
<td>91</td>
<td>89</td>
</tr>
<tr>
<td>pCO$_2$, mm Hg</td>
<td>35 - 44</td>
<td>38</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.38 - 7.42</td>
<td>-</td>
<td>7.41</td>
<td>7.41</td>
</tr>
<tr>
<td>HCO$_3$, mEq/L</td>
<td>24 - 30</td>
<td>-</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>$O_2V$</td>
<td>25 - 35</td>
<td>-</td>
<td>-</td>
<td>40</td>
</tr>
<tr>
<td>$D_LCO_2$, cc/mm Hg/min</td>
<td>26</td>
<td>-</td>
<td>-</td>
<td>15</td>
</tr>
</tbody>
</table>

enamine silver and Ziehl-Neelson stains failed to reveal fungi or acid-fast organisms.

Postoperative convalescence was prolonged and complicated by severe respiratory distress related to recurrent right pleural effusion. Chlorothiazide, digitalis, and low sodium diet were not effective, and mercurial diuretics were required along with occasional thoracentesis. Subsequently, it was found that pleural transudation could be prevented by aldosterone inhibition (Aldactone A). During 10 months of observation, the patient's course appears to have stabilized. Although unable to work, he is ambulatory and free of edema.

Discussion

Three of the various obstructive phenomena associated with fibrous mediastinitis are demonstrated in this case: that in the superior vena cava, the tracheobronchial tree, and the pulmonary veins. Aside from the cosmetic effects, superior vena cava obstruction produced no untoward physiological disturbance.

A bronchogram in 1962 showed partial obstruction of the left lower lobe bronchi with some distal atelectasis. Pulmonary function studies are compatible with moderately severe, nonreversible obstructive disease. In particular, the high inspiratory resistance and nonelastic work of breathing are suggestive of fixed airway obstruction which would result from

![Figure 5](http://circ.ahajournals.org/)

Lung parenchyma showing marked thickening of the pleura and interlobular septa by edematous, fibrous, vascular connective tissue. The interalveolar septa are thickened; some alveoli are collapsed; others are distended.
Small branch of the pulmonary artery showing marked concentric proliferation of cells. The adjacent alveoli are lined by cuboidal epithelium of respiratory ducts, and the spaces are filled with large mononuclear cells. bronchial compression. Marked abnormality of ventilation-distribution was demonstrated by the decrease in dynamic compliance with increasing respiratory frequency. The low static compliance noted in 1965 was compatible with pulmonary fibrosis and resulted in an increase in the elastic work of breathing. Three possible causes of pulmonary hypertension in chronic adhesive mediastinitis may be considered. Local pulmonary artery obstruction, functionally resembling coarctation, has been described in a few cases.\textsuperscript{11, 12} The absence of a characteristic murmur and the lack of obstruction of major pulmonary arteries on angiography is strong evidence against this possibility. Furthermore, the microscopic appearance of the distal pulmonary vessels in the lung biopsy show the marked medial hypertrophy associated with pulmonary arteriolar hypertension.\textsuperscript{18} Data from the cardiovascular study suggest that pulmonary hypertension was due to pulmonary venous obstruction since marked elevation of the pulmonary artery wedge pressure was noted. The postcapillary location of vascular obstruction implied by elevation of the “pulmonary-capillary” pressure was confirmed by retrograde pulmonary venous catheterization at the time of surgery. The pulmonary artery wedge pressure is usually normal in cases of pulmonary hypertension due to pulmonary fibrosis.\textsuperscript{19} The normal left atrial and ventricular pressures clearly rule out left heart disease as the cause of pulmonary hypertension and indicate a locus of resistance estimated at nearly 50\% of the total pulmonary resistance in the postcapillary segments of the lesser circulation. The rise in pulmonary artery and wedge pressures with exercise further supports the interpretation of a fixed pulmonary venous resistance. The findings in this case provide an explanation for the hemoptysis which is a frequent accompaniment of pulmonary venous hypertension when due to mitral stenosis or cor triatriatum\textsuperscript{20, 21} or adhesive mediastinitis.\textsuperscript{1, 15–17} In addition, the symptoms of left heart failure and the pleural transudate can
be related to the pulmonary venous and consequent pulmonary capillary hypertension.

The markedly delayed washout of indicator following segmental pulmonary arterial injection probably reflects decreased flow in the segments receiving most of the injectate. This may be due to partial atelectasis in the case of the left lower lobe, but more likely reflects variations in the degree of pulmonary venous obstruction in various segments with consequent uneven flow distribution. Hurwitz and associates have studied the venous collateral circulation in dogs following pulmonary venous ligation and have shown that collateral veins drain into the azygos system via pleural adhesions and return blood to the right heart. This collateral system is capable of carrying up to 20% of the flow of an unobstructed lung. A significant shunt (left-to-right) is ruled out in this case by the normal contour of the indicator-dilution studies following inferior caval and proximal pulmonary arterial injection.

The vascular changes in the pulmonary arteries closely resemble those reported in mitral stenosis and other forms of secondary pulmonary hypertension. These so-called "protective" lesions have been described in pulmonary lobes with pulmonary venous obstruction while those areas without venous obstruction are spared. Andrews has suggested that interstitial fibrosis is the result of complete, partial, or intermittent pulmonary venous obstruction. His evidence is not convincing, however, since two of his five patients had left atrial enlargement without definite pulmonary venous obstruction, two had mediastinal fibrosis and the fifth had several congenital defects in addition to left pulmonary venous stenosis. Additional reports of congenital pulmonary venous stenosis have described pulmonary fibrosis, and Stovin and Mitchinson have reported a case of pulmonary fibrosis with obstruction of intrapulmonary veins. The rarity of extensive pulmonary fibrosis in mitral stenosis, most cases of atrial thrombosis, atrial myxoma, cor triatriatum, and chronic severe left heart failure suggest that pulmonary fibrosis may not be causally related to pulmonary venous hypertension in man. Reports of animal experiments in which pulmonary fibrosis followed acute pulmonary venous ligation have doubtful application since acute hemorrhage and infection invariably follow acute ligation. A common etiology for pulmonary and mediastinal fibrosis is a more attractive hypothesis.

A common infectious cause for the pulmonary fibrosis and mediastinitis may exist in our case. Histoplasmosis has been frequently implicated in the past decade and is suggested by the 4 + reaction to skin-testing in this patient. Despite the negative complement-fixation studies, negative histological examination, and negative fungus culture, histoplasmosis may be present. On the other hand, a positive skin test alone is inconclusive evidence. Other etiological agents which have been reported, such as tuberculosis, syphilis, and actinomycosis were eliminated from consideration by history and appropriate studies.

Hawk and Hazard pointed out the gross and histological similarity of fibrous mediastinitis, fibrosing retroperitonitis, and Riedel's struma. These conditions may represent variable manifestations of a tissue response to one or more undetermined factors.

**Summary**

A patient with chronic fibrous mediastinitis presented with bronchial, superior vena caval, and pulmonary venous obstruction, pulmonary hypertension, and pulmonary fibrosis. Pulmonary venous obstruction was confirmed at surgery and explains the hemodynamic findings of elevated pulmonary artery and pulmonary wedge pressures despite low left atrial pressure. Pulmonary function studies showed marked alterations in ventilation—distribution, diffusion, work of breathing, and fixed airway resistance.

It is concluded that the pulmonary arterial hypertension was due, in large part, to the pulmonary venous hypertension caused by pulmonary venous obstruction. Unsuccessful surgical intervention has been followed by 10
months of observation during which aldosterone inhibition together with use of chlorothiazide has prevented recurrence of heart failure and pleural effusion.

The relationship between the physiological abnormalities and the patient’s symptoms is discussed along with the possible relationship between pulmonary venous obstruction and pulmonary fibrosis.

Acknowledgments

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An Intellectual Exercise and Challenge to Contemporary Writing

The scientific paper is a fraud in the sense that it does give a totally misleading narrative of the processes of thought that go into the making of scientific discoveries. The inductive format of the scientific paper should be discarded. The discussion which in the traditional scientific paper goes last should surely come at the beginning. The scientific facts and scientific acts should follow the discussion, and scientists should not be ashamed to admit, as many of them apparently are ashamed to admit, that hypotheses appear in their minds along uncharted by-ways of thought; that they are imaginative and inspirational in character; that they are indeed adventures of the mind.—P. B. Medawar: Is the Scientific Paper Fraudulent? Yes; It Misrepresents Scientific Thought. Saturday Review, p. 43 (Aug. 1), 1964.
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