The Pulmonary Manifestations of Generalised Scleroderma (Progressive Systemic Sclerosis)*

LIONEL H. OPIE**
Cape Town, South Africa

Introduction

Two aspects of generalised scleroderma have received much attention in recent years. Firstly, the widespread and sclerotic nature of the disease process has been embodied in the term "progressive systemic sclerosis," proposed by Goetz1 in 1945, and since adopted by other authors. Secondly, connective tissue alterations are now regarded as an integral part of this entity which answers all the criteria of a grave collagen disturbance.

The purpose of this paper is to re-examine the known and possible pulmonary manifestations of systemic sclerosis, as the disease will here be termed, with reference to these newer concepts. Pleural and vascular involvement in allied collagen disorders (e.g. disseminated lupus erythematosus) are well established. The possibility of similar lesions in systemic sclerosis is therefore raised.

Hypertension in the pulmonary circuit, an entity which has recently received wide attention, is known to result from both pulmonary fibrosis and pulmonary arteritis. Systemic sclerosis is an established cause of the former, and full evidence of pulmonary vascular involvement will be presented. The relationship between systemic sclerosis and pulmonary hypertension will accordingly be examined and amplified.

The pulmonary manifestations of systemic sclerosis to be discussed in this paper are:

<table>
<thead>
<tr>
<th>Tissue affected</th>
<th>Pathological process</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Pleura.</td>
<td>Pleural effusion and fibrosis.</td>
</tr>
<tr>
<td>2. Broncho-pulmonary tree</td>
<td>(a) Pulmosclerosis.</td>
</tr>
<tr>
<td>3. Pulmonary vascular bed</td>
<td>(b) Secondary infection, and &quot;spill-over&quot; following esophageal lesions.</td>
</tr>
</tbody>
</table>

Pulmonary hypertension due to:
1. Anoxia (pulmosclerosis).
2. Obstruction (sclerodermatous endarteritis).

Material

The material comprises 12 consecutive cases of systemic sclerosis which presented at Groote Schuur Hospital, Cape Town, during the period 1943-1953. Four of these came to necropsy. These cases include three of Goetz's patients previously reported.1

Case 1 is fully presented elsewhere by Schrire and co-workers.2 The patients were studied by personal examination of clinical protocols.

**From the University of Cape Town and the Groote Schuur Hospital.
radiological and necropsy specimens, and clinical observation wherever possible.

Pleural Effusion and Fibrosis

None of the present group of patients had signs of pleural involvement during life. Dense pleural fibrosis was found in one case at necropsy.

A search of the literature has revealed only three cases with clinical evidence of pleural involvement in systemic sclerosis. Duffy and Bardeley report a unilateral pleural effusion. Yardumian and Kleinerman found bilateral basal dullness revealed as hydrothorax at necropsy. Necropsy confirmed a roentgenogram diagnosis in a patient of Hurly et al.

Post-mortem, evidence of pleural fibrosis has been found in five necropsies. Pleural lesions, whether fibrous or exudative in nature, are thus a rare complication of systemic sclerosis. Fibrosis, when it occurs, is an insidious process, not preceded by symptoms of acute pleurisy (a common feature of disseminated lupus erythematosus). Moreover, the effusions observed clinically in the few cases were not conclusively related to the sclerodermatous process itself.

Pulmosclerosis

Historical Background. Findlay (1891) was the first to remark on the association between pulmonary fibrosis and generalized scleroderma. Two of the 24 necropsy cases reviewed by Lewin and Heller (1895) had macroscopic and microscopic evidence of fibrosis, the radiological recognition of which fell to Murphy and his co-workers half a century later.

In 1945, Pugh ascribed a characteristic radiological appearance to this type of fibrosis, stating that x-ray diagnosis could be made in the absence of clinical data. In the same year Getzowa also gave the first detailed pathological description. She found that lysis of alveolar walls with cystic lesions could occur in addition to the usual "compact" fibrosis. With Dostrovsky, she used the term "pulmosclerosis" to denote progressive systemic sclerosis affecting the pulmonary interstitial tissue. The two types of pathological lesions were called "pulmosclerosis cystica" and "pulmosclerosis compacta" according to their nature.

Hayman and Hunt (1952) collected 27 cases of pulmonary fibrosis, in generalised scleroderma recognised radiologically, adding one of their own. Since then Harper has mentioned another case, bringing the total in the English literature to 29. Towards the end of 1952 Deenstra and Jansen of Holland published six cases while the Polish investigators Chodyn and Smigielski reported two. The diagnosis of pulmosclerosis is therefore still relatively infrequent.

Case 1: A colored (mulatto) male of 50 was admitted to hospital in May, 1952. For 15 years he had been coughing severely with the production of large quantities of mucoid sputum. Eight years prior to admission the first symptom suggestive of systemic sclerosis appeared—Raynaud's phenomenon affecting the fingers and toes. Ulceration and calcinosis of the fingers with increased skin pigmentation developed simultaneously. Dyspnea on exertion, of three years' duration, was not accompanied by paroxysmal nocturnal dyspnea. Actual sclerosis of the skin (cutaneous scleroderma) was only manifested one year before admission. This had involved the fingers to give typical sclerodactyly.

Examination revealed few respiratory signs. Excursions were poor but equal, with scattered crepitations on auscultation.
<table>
<thead>
<tr>
<th>Reported by</th>
<th>Cough</th>
<th>Dyspnea</th>
<th>Sputum</th>
<th>X-ray pulmosclerosis</th>
<th>Necropsy pulmosclerosis</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altschule et al.¹⁰</td>
<td>yes</td>
<td>yes</td>
<td></td>
<td>yes</td>
<td>—</td>
<td>impaired pulmonary function preceded x-ray fibrosis</td>
</tr>
<tr>
<td>Bevans²⁰</td>
<td>no</td>
<td>mild</td>
<td>no</td>
<td>no</td>
<td>gross</td>
<td>anatomical findings out of all proportion to clinical signs</td>
</tr>
<tr>
<td>Dostrovsky³</td>
<td>yes</td>
<td>chronic bronchitis</td>
<td>network of cavities</td>
<td>cystic pulmosclerosis</td>
<td>cystic lesions resembled tuberculosis on x-ray</td>
<td></td>
</tr>
<tr>
<td>Kanee⁴</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>moderate sclerosis</td>
<td>—</td>
<td>soft tissue changes may obscure x-ray fibrosis</td>
</tr>
<tr>
<td>Spain and Thomas⁵</td>
<td>yes</td>
<td>yes</td>
<td>much mucoid</td>
<td>yes</td>
<td>cystic and compact lesions</td>
<td>intercurrent infection cause of cough and sputum</td>
</tr>
<tr>
<td>Weiss et al.¹⁰ Case 1</td>
<td>yes</td>
<td>cardiac dyspnea</td>
<td>—</td>
<td>no</td>
<td>focal fibrosis</td>
<td>necropsies revealed evidence of pulmosclerosis not detected clinically</td>
</tr>
<tr>
<td>Weiss et al. Case 2</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td>i. pulmosclerosis preceded cutaneous scleroderma ii. x-ray picture resembled pneumoconiosis</td>
</tr>
<tr>
<td>Wigley et al.¹³</td>
<td>—</td>
<td>yes</td>
<td>—</td>
<td>yes</td>
<td>—</td>
<td>reported finding of &quot;sclerobacillus&quot;</td>
</tr>
<tr>
<td>Wuerthele-Caspe et al.¹⁶</td>
<td>yes</td>
<td>—</td>
<td>yes</td>
<td>yes</td>
<td>—</td>
<td>pulmonary manifestations antedated sclerodactyly by fourteen years</td>
</tr>
<tr>
<td>Present series: Case 1</td>
<td>yes</td>
<td>yes</td>
<td>much mucoid</td>
<td>yes</td>
<td>gross compact pulmosclerosis</td>
<td>x-ray lesion in absence of symptoms</td>
</tr>
<tr>
<td>(Schröer²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 2</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>—</td>
<td>x-ray lesion in absence of symptoms</td>
</tr>
<tr>
<td>Case 3</td>
<td>yes</td>
<td>yes</td>
<td>due to heart involvement</td>
<td>yes</td>
<td>necropsy revealed pulmosclerosis not detected otherwise</td>
<td></td>
</tr>
</tbody>
</table>

The sign — denotes absence of data
Figure 1 (Case 1): The pulmonary artery and primary and secondary branches are usually prominent. The diffuse method used in the right lower lung fields of the chest is shown. Stain: V. Gienon. Magnification: 460X.

Figure 2 (Case 1): Long section; gross compact pulmonary arteries. There is also cardiomegaly. Figure 2 (Case 2): Long section; compact pulmonary arteries but no vascular changes. Stain: V. Gienon.
Repeated sputum examinations for M. tuberculosis were negative. For the rest the picture was that of cardiac failure, predominantly "right-sided." There was extensive edema of the legs, arms, trunk and face. X-ray films of the chest showed cardiomegaly and the changes of pulmonary hypertension (fig. 1). The pulmonary artery was prominent, and its primary secondary branches showed marked enlargement. The diffuse mottling throughout the lung fields, and more marked at the right base, suggested compact pulmosclerosis. The electrocardiogram showed the changes of right ventricular hypertrophy. Skin biopsy established cutaneous scleroderma. On cardiac catheterization an abnormally raised pulmonary arterial pressure was found. The pressure in the main pulmonary artery was 47 mm. Hg. (normal mean, 8-19 mm.)*

The clinical diagnosis was progressive systemic sclerosis, with pulmosclerosis and pulmonary hypertension.

* Figure 3 (CASE 1): Ulceration of the finger-tips in systemic sclerosis.—Figure 4 (CASE 2): Sclerodactyly in an advanced case of systemic sclerosis. Note the shiny skin which is thickened and gives the appearance of hidebinding. The finger nails are curved but built-up nail beds of true clubbing are absent. There is an associated arthritis in this case.
The patient deteriorated and died from paralytic ileus in July, 1952.

At necropsy both lungs were bound to the chest wall by strong fibrous adhesions which obliterated the pleural cavities. The right lung weighed 655 G. (normal average: 550 G.), the left 640 G. (normal average: 450 G.). Both were extremely tough and white but not edematous. On gross section these features were attributable to severe fibrosis, apparently involving the interstitial tissue. This was most marked at the lung bases where great pressure failed to make any indentation. The mediastinal connective tissue was enormously increased, being tough, white and difficult to sever. Histologically the extreme pulmonary fibrosis was confirmed (fig. 2). The extraordinary degree of fibrosis suggested some contributory cause, but none could be found. The collagen content of the fibrous tissue stained poorly with van Gieson's stain. The acellular hyalin type of fibrosis was similar to that found in the skin. In spite of macroscopic pulmonary arterial atheromatosis, the arterioles did not show abnormal intimal or medial changes (fig. 3).

The necropsy diagnosis was progressive systemic sclerosis with cutaneous scleroderma, compact pulmosclerosis, pulmonary hypertension, pericardial and pleural fibrosis, right ventricular hypertrophy, myocardial degeneration, ascites, atrophy of the liver and leukoplakia of the esophagus.

The pulmosclerosis in this patient is reasonably viewed as the cause of his pulmonary symptoms; its presence was recognized radiologically, and established at necropsy.

**Case 2:** This patient, a white male born in 1904, had many stigmata of the systemic sclerosis syndrome when seen at the Out-Patients' Department in December, 1953. Raynaud's phenomenon of the hands, sclerodactyly, scleroderma of upper limbs only, and dysphagia constituted the clinical picture. At no time were there pulmonary or cardiac symptoms. Chest x-ray films revealed changes compatible with pulmosclerosis.

The generalized increase of lung markings was of scattered reticulate pattern. Sarcoidosis, although most unlikely in the full clinical context, could not be excluded on chest x-ray films alone in view of the prominent hilar shadows.

The presumptive pulmosclerosis in this patient was asymptomatic and only revealed radiologically.

**Case 3:** A white spinster of 44 was hospitalised with a history starting 22 years previously with Raynaud's phenomenon. Sclerodactyly had proceeded to scleroderma of the face and neck 20 years before admission. Dysphagia, calcinosis and ulceration of the ears were of 16 years duration.

There was neither clinical nor radiological evidence of any pulmonary disease until orthopnea and cyanosis preceded death with signs of bilateral bronchopneumonia. At necropsy the alveolar walls were found to be thickened and fibrosed. The diagnosis

![Figure 5](image_url)

**FIGURE 5 (Case 4):** Electrocardiogram shows right axis deviation with tall, spiked P-pulmonale waves in limb-lead 2.
of compact pulmosclerosis was thus made microscopically in the absence of any suggestive clinical or radiological evidence.

The Entity of Pulmosclerosis. In support of the term "progressive systemic sclerosis," Goetz\(^1\) stressed that induration and sclerosis may occur in any organ, including the lungs, where the interstitial tissue is involved. Pulmosclerosis embodies the concept of a specific sclerotic process, progressive in nature, as a part of a widespread syndrome—systemic sclerosis.

In particular do the findings in Case 1 support the concept of pulmosclerosis, for identical histological changes were present in both skin and lung.

Comparison with Other Reported Cases. The relation of these cases to pulmonary hypertension is dealt with below; discussion is here limited to pulmosclerosis. The pertinent features are presented in tabular form and compared with those in nine other reported cases (table 1). On the

FIGURE 6 (CASE 4): Graph recorded one year after fig. 5. Right heart strain with low voltage.
basis of these data, the following points are offered in the clinical recognition of pulmosclerosis.

Time of Onset During Systemic Sclerosis. The insidious nature of the sclerotic process is revealed by the numerous necropsies showing varying degrees of histological pulmosclerosis not evident during life. This is exemplified by Case 3 of the present series.

The time of onset bears no constant relation either to the radiological evidence of pulmosclerosis or, in keeping with other visceral lesions,\textsuperscript{10} to the external manifestations of systemic sclerosis.

Impaired pulmonary function may precede radiological evidence of pulmosclerosis.\textsuperscript{11} On the other hand, radiological pulmosclerosis may be present without symptoms or signs\textsuperscript{17} (as in Case 2), clinical pulmonary impairment only manifesting later.

External evidence of systemic sclerosis such as Raynaud's phenomenon, sclerodactyly, cutaneous scleroderma, calcinosis, and ulceration may all be absent when pulmosclerosis is already visible radiologically.\textsuperscript{18} Case 1 presented with pulmonary symptoms fully seven years before Raynaud's phenomenon, ulceration and calcinosis appeared. Actual sclerodactyly and cutaneous scleroderma developed another seven years later. This stresses that finger examination in cases of obscure lung fibrosis should include attention to "numbness," "ulcer-like sores" (fig. 3), and sclerodactyly (fig. 4), in addition to clubbing. This simple clinical observation may greatly aid in the differential diagnosis of such a case.

Radiological Diagnosis of Pulmosclerosis. The description of Hayman and Hunt\textsuperscript{7} is classic. The sclerosis starts as diffuse mottling and interlacing linear shadows confined to the lower lobes and indistinguishable from lipid pneumonia or bronchiectasis. It advances to a diffuse, netlike shadow throughout the lower two-thirds of both lung fields, more dense towards the bases and usually sparing the apices. In addition, scattered irregular mottled shadows are described. Bronchograms are usually within normal limits.

Other authors confirm this description, but of late there have been several descriptions of apical involvement,\textsuperscript{6,8,9} and in some cases the pneumonias are closely simulated.

Involvement of the hilar, bronchial and mediastinal lymph nodes, so frequently found in sarcoidosis, has not been reported in cases described in the literature. However, prominent hilar shadows which closely resembled adenopathy were present in Case 2.

When cystic changes occur, they may be advanced enough to be visible on x-ray film, and may resemble tuberculosis.\textsuperscript{6} In other cases the radiological appearance is a diffuse mottling, indistinguishable from that found in compact pulmosclerosis. Tomography, however, reveals the cystic character of the change. Cystic pulmosclerosis is yet another cause of "honeycombing" of the lungs.

X-ray appearances in Cases 1 and 2 could not be considered pathognomonic of pulmosclerosis. In view of this and the numerous other conditions such as idiopathic pulmonary fibrosis, radiation fibrosis, chronic asthma,
pneumoconioses, periarteritis nodosa, miliary tuberculosis, berylliosis, degenerative vascular lesions, lymphatic carcinomatous spread, pancreatic achylia, lymphomas and sarcoidosis which may all radiologically simulate pulmosclerosis at some stage, it is difficult to agree with Pugh who states that the diagnosis of pulmosclerosis may be made by x-ray film alone. Pulmosclerosis is but one cause of diffuse x-ray mottling. If such mottling be found in a patient with systemic sclerosis, the presumptive diagnosis of pulmosclerosis may be made.

Secondary Infection and “Spill-Over” Lesions

Respiratory reserve and function may be limited even in the absence of pulmosclerosis by purely mechanical factors such as sclerosis in the overlying skin, calcinosis of the soft tissues, fibrous pleurisy and mediastinitis (Case 1), and the passive congestion consequent on scleroderma heart disease. Adding the hazards of dysphagia, one would expect broncho-pulmonary infection to be a major mechanism of death in systemic sclerosis. Three of the five patients who died in this series suffered from terminal secondary infection. It is concluded that this may well be a frequent and formidable complication of advanced systemic sclerosis.

Complications secondary to the esophageal changes (ulceration and dilatation) have been noted twice. In Harper’s patient the “spill-over” from an extensively affected esophagus caused recurrent pneumonic episodes. The x-ray film of Steiner’s patient showed both multiple peribronchial miliary-sized foci and a left lower lobe abscess, also attributable to “spill-over” from an atonic esophagus.

Pulmonary Hypertension

Historical Background. Pulmonary hypertension in certain clinical states was inferred by Moschowitz who first propounded the concept in 1927. The term then lapsed into obscurity and for many years was kept alive only by pathological reports such as those of Parker and Weiss and Gilmour and Evans. East revived the clinical concept in 1940, and it was a short step from Cournard and Ranges’s introduction of cardiac catheterisation in man, to actual measurement of the pulmonary arterial pressure.

McMichael gave the two chief causes of pulmonary hypertension of pulmonic origin as:

(a) obstruction of pulmonary vessels;
(b) anoxia associated with chronic lung disease.

In systemic sclerosis there are thus two possible causes for the development of pulmonary hypertension. Anoxia from pulmosclerosis offers one explanation. Vascular obstruction is the other main cause of pulmonary hypertension. Although Brenner (1935) did not mention systemic sclerosis as a cause of disease of the pulmonary arteries, yet Notthafft had described marked sclerodermatous thickening of the pulmonary arteries in 1898. Kraus (1924) found chiefly endarteritis. Similar findings are reported by other workers.
That the two mechanisms may operate individually is illustrated by two cases of the present series.

Case 1: In this case, described above, the ante-mortem diagnosis of pulmonary hypertension was confirmed at necropsy. The minimal endarteritis and gross pulmosclerosis (fig. 2) suggest anoxia as the causal factor.

Case 4: A white spinster of 51 was admitted to hospital as a "black cardiac."

For 37 years she had been suffering from Raynaud's phenomenon of the fingers and toes. For the last 19 years dysphagia had gradually been increasing in severity. Fifteen years prior to admission the skin over the fingers hardened with resultant tapering (sclerodactyly). The sclerosis of the skin spread upwards to involve the upper arms and chest. One year before admission a new series of symptoms arose. Breathlessness on exertion and excitement was accompanied by cyanosis and swollen ankles. The cyanosis developed to such an extent that the patient described herself as "completely black." This was more marked on lying down.

On examination a few basal crepitations and ronchi were heard. The venous pressure was raised—15 cm. above the sternal angle. Blood pressure: 110/90 mm. Hg. There was an apical triple rhythm. The liver was enlarged. Urinalysis showed a trace of albumin. Blood values were: Hb: 97 per cent, R.B.C.: 5 million, W.B.C. 12,000. X-ray films of the chest showed the heart and especially the right atrium to be enlarged. The large pulmonary artery with unusually prominent left and right main branches was associated with peripheral oligemia. Electrocardiograms taken a year previously (fig. 5) had shown right axis deviation with tall sharp P waves in lead 2 (P pulmonale). This had progressed to right heart strain with low voltage at the present admission (fig. 6). Kymography showed blunting of the cardiac excursions. The Wassermann reaction was negative. The clinical diagnosis was progressive systemic sclerosis producing Ayerza's syndrome.

Death in predominantly "right-sided" cardiac failure occurred two weeks after admission.

At necropsy the lungs showed no macroscopic abnormality. Microscopically there was no pulmosclerosis. Changes in the arterioles were striking (fig. 7). The medial hypertrophy and intimal endarteritis obliterans closely resembled the changes caused by systemic hypertension in the systemic arterioles. Visceral vessels showed similar changes. The endarteritis was especially marked in the hepatic arterioles. The heart showed right atrial dilatation and right ventricular hypertrophy. There were no abnormalities in the valves or coronary arteries, and no congenital defects. Histologically there was myocardial degeneration equally affecting both sides of the heart.

The necropsy diagnosis was progressive systemic sclerosis with cutaneous sclero-

FIGURE 7 (CASE 4): Lung Section: marked endarteritis obliterans in the absence of pulmosclerosis. Stain: H. and E. Magnification: 450X.
derma, pulmonary endarteritis obliterans in the absence of pulmosclerosis, chronic cor pulmonale and "right-sided" cardiac failure.

Comment on Cases 1 and 4. Case 1 illustrates the clinical pattern described by Brill. For a varying length of time the "pulmonary phase" dominated, merging imperceptibly into the "cardiac phase."

Case 4, on the other hand, had no pulmonary phase and showed similarity to "primary" pulmonary hypertension. The chief difference is that the arteriolar changes associated with "primary" hypertension are of unknown etiology, if present, whereas the endarteritis in Case 4 was sclerodermatous in origin. (Similar vascular changes were found in other organs—as well as in the three other necropsy cases in this series.) The intense cyanosis is reminiscent of the "cardiacos nigros" of Ayerza. In a thorough review of the subject, Leopold23 ascribes such cyanosis to a combination of pulmonary parenchymatous pathology and polycythemia, neither of which were present in this case. Clinically, the cause of this cyanosis was considered to be a right-to-left shunt through a patent foramen ovale, caused by right atrial hypertrophy in severe pulmonary hypertension. This possibility was excluded at necropsy. Similar cyanosis has rarely been found in association with endarteritis resulting from pulmonary sarcoidosis. Progressive fibrosis and cor pulmonale are other pulmonary manifestations of sarcoidosis resembling systemic sclerosis. The arteritis of sarcoidosis is not, however, an entity per se, but is consequent on involvement of the pulmonary vascular bed by granulation tissue.

Criteria for Diagnosis of Pulmonary Hypertension. The most recent upper limits of normal pulmonary arterial pressure are those of Fowler9—29/13 mm. Hg. Although exact diagnosis of pulmonary hypertension can only be obtained by cardiac catheterisation, careful correlation of clinical findings with pressure data has resulted in a much more confident bedside diagnosis.

In severe pulmonary hypertension some or all of the following signs suggest the diagnosis. The reduced cardiac output causes a small peripheral pulse and cold extremities. There is usually a giant 'a' wave in the jugular pulse due to right atrial hypertrophy. A striking left parasternal lift due to right ventricular hypertrophy will be noted on palpation.

![FIGURE 8: The pulmonary early systolic click (X), best heard in the pulmonary area (PA) and associated with a closely split and much accentuated second sound (2). A reduplicated first sound (lr) precedes the systolic click (X) which is followed by a pulmonary systolic murmur (sm). From a case "primary" pulmonary hypertension.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21272/ on 06/21/2017)
<table>
<thead>
<tr>
<th>Reported by</th>
<th>Clinical</th>
<th>X-Ray</th>
<th>E.C.G.</th>
<th>Necropsy</th>
<th>Likelihood of pulmonary hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chodyn and Smigielaki Case 1*</td>
<td>P₂ loud</td>
<td>compact sclerosis</td>
<td>right axis deviation</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Chodyn and Smigielaki Case 2</td>
<td>P₂ loud</td>
<td>compact sclerosis</td>
<td>right axis deviation</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Dostrovsky Case 1*</td>
<td>—</td>
<td>cystic sclerosis</td>
<td>—</td>
<td>compact &amp; cystic lesions</td>
<td>occlusion sufficient to impair circulation</td>
</tr>
<tr>
<td>Humphreys</td>
<td>—</td>
<td>—</td>
<td>right axis deviation developed</td>
<td>diffuse fibrosis</td>
<td>—</td>
</tr>
<tr>
<td>Kanee*</td>
<td>—</td>
<td>moderate fibrosis</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Kerley**</td>
<td>—</td>
<td>pulmonary arteries enlarged; peripheral oligemia; heart of “cor pulmonale” type</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Kraus***</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>diffuse fibrosis</td>
<td>marked endarteritis</td>
</tr>
<tr>
<td>Author &amp; Case</td>
<td>Illness</td>
<td>Findings</td>
<td>Description</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>---------</td>
<td>----------</td>
<td>-------------</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Linenthal and Talkov\textsuperscript{a} 
Case 2 | right-sided heart failure | prominent hilar markings; pulmonary "conus" enlarged | — — — — possible |
| McMíchael\textsuperscript{b} 
Case 1 | death in right-sided failure | extensive diffuse fibrosis | right axis deviation — — — likely |
| Matsui\textsuperscript{c} 
Case 1 | P\textsubscript{2} loud | — | present endarteritis right heart and pulmonary artery dilated likely |
| Matsui 
Case 2 | — — | — | present endarteritis right heart grossly hypertrophied and dilated likely |
| Matsui 
Case 3 | — — | — | — right heart & pulmonary artery dilated doubtful |
| Matsui 
Case 4 | P\textsubscript{2} grossly accentuated | — | present endarteritis right heart enlarged likely |
| Murphy\textsuperscript{d} 
Murphy\textsuperscript{e} | P\textsubscript{2} loud fibrosis | — | extensive fibrosis endarteritis — doubtful |
| Nottahff\textsuperscript{m} | P\textsubscript{2} loud fibrosis | — | present media greatly thickened right heart enlarged likely |
| Spain and Thomas\textsuperscript{f} | right-sided heart failure | pulmonary arteries prominent; fibrosis | change from left to right axis deviation present moderate right heart enlarged case proven by cardiac catheterization |
| Present series: 
Case 1 (Schrire\textsuperscript{g}) | right-sided heart failure | pulmonary arteries prominent; fibrosis | marked right ventricular hypertrophy gross sclerosis normal arterioles right ventricular hypertrophy case proven by cardiac catheterization |
| Case 4 (Goetz) | right-sided heart failure; black cardiac | pulmonary arteries prominent; peripheral oligemia | right axis deviation absent gross endarteritis obliterans right ventricular hypertrophy pulmonary hypertension virtually certain |

The — sign denotes absence of data.
Auscultation reveals an accentuated pulmonary second sound and recently Leatham and Vogelpoel\textsuperscript{24} have described an added click-like sound occurring in early systole and best heard in the second and third left intercostal spaces. This they term the pulmonary early systolic click (fig. 8). In a series of 50 patients with this sign, 44 had pulmonary hypertension.

In the presence of emphysema the clinical diagnosis is much more difficult and can often only be inferred when a triple rhythm and "right-sided" failure supervene.

Electrocardiographic right ventricular hypertrophy and pulmonary hypertension have been correlated by Johnson and Taquini and their co-workers. Zuckerman and his colleagues believe that a diagnosis of chronic cor pulmonale is often arrived at by electrocardiography in the absence of definite clinical findings. Furthermore, the "P pulmonale" is closely related to pulmonary hypertension.

The radiological changes of pulmonary hypertension are due to obstruction to the blood-flow at the level of the smaller arteries and arterioles. This results in enlargement of the pulmonary artery and its left and right main branches, in contrast to the peripheral oligemia. The degree of such changes is in close relationship to the actual pulmonary artery pressure.

The diagnosis of pulmonary hypertension in a patient with systemic sclerosis requires careful clinical, electrocardiographic and radiological examination for the features described above. When pulmonary hypertension is an early event the classical signs should be found readily. However, in advanced systemic sclerosis the signs may well be obscured when the disease has extended to involve the neck and chest wall. Thus the giant 'a' wave and left parasternal lift may be hidden, while a small peripheral pulse and cold extremities are common due to the same factors that cause Raynaud's phenomenon. The diagnosis will then largely depend on the auscultatory findings, electrocardiogram and x-ray film. In Cases 1 and 4, the first clues to the development of pulmonary hypertension were, in fact, x-ray films and electrocardiographic findings.

\textit{Incidence of Pulmonary Hypertension in Systemic Sclerosis.} Applying the above criteria, and also necropsy evidence of chronic cor pulmonale, 16 cases of pulmonary hypertension have been culled from the world literature and two added (table II). Of the cases in the literature, one is confirmed by catheterisation, 10 are likely, two possible and three rather doubtful. In no case except that of Spain and Thomas\textsuperscript{4} is pulmonary hypertension specifically mentioned. Most authors overlooked findings now known to be significant. While it is apparent that pulmonary hypertension is by no means a rare complication of systemic sclerosis, it is difficult to judge the frequency of pulmonary hypertension with accuracy in view of the fact that its signs and their significance have been appreciated fully only in recent years. It is to be anticipated that greater regard to the signs of pulmonary hypertension will establish its association with systemic sclerosis more firmly. Nevertheless, on present evidence, pulmosclerosis
would appear to be a more frequent manifestation of systemic sclerosis than pulmonary hypertension.

SUMMARY

Attention is focused on the various pulmonary manifestations of generalised scleroderma (progressive systemic sclerosis). These were investigated in a series of 12 patients suffering from this condition.

Pleural involvement is uncommon in systemic sclerosis, in contrast to its frequency in other collagen diseases.

Pulmonary fibrosis due to systemic sclerosis, although a specific lesion, has no pathognomonic radiological appearance. Three illustrative cases are presented, in one of which sarcoidosis was closely simulated. The true cause of the radiological alterations may be established by giving attention to other stigmata of systemic sclerosis. The value of examination of the fingers for Raynaud's phenomenon, calcinosis, ulceration and sclerodactyly is stressed.

Secondary broncho-pulmonary infection, a frequent complication of systemic sclerosis, may befavoured by several different factors which are listed.

Pulmonary hypertension may be caused either by pulmosclerosis or sclerodermatous endarteritis. Cases are presented to illustrate these two mechanisms.

ACKNOWLEDGMENTS

The writer gratefully records his indebtedness to Prof. R. H. Goetz for his kindness in permitting this work to be carried out in his department and for providing the material for Cases 2, 3, and 4. Further acknowledgments are to Drs. L. Mirvish and V. Schrire for permission to publish the first case, to Prof. J. G. Thompson for the pathological data for Case 1, to Mr. C. C. Goosen for the photographs and photomicrographs, to Prof. Goetz and the editors and publishers of "Angiology" for Figures 5 and 6, to Dr. L. Vogelpoel for Fig. 8 and advice on pulmonary hypertension, and to Drs. M. Sacks and R. Mibashan for their help.

RESUMEN

Se enfoca la atención hacia varias manifestaciones pulmonares del escleroderma (esclerosis progresiva generalizada). Estas fueron investigadas en 12 enfermos con el padecimiento.

El compromiso pleural no es común en la esclerosis generalizada en contraste con su frecuencia en otras enfermedades del colágeno.

La fibrosis pulmonar debida a esclerosis generalizada, aunque es una lesión específica, no tiene aspectos radiológicos patognomónicos. Se presentan tres casos demostrativos en uno de los cuales la sarcoidosis fue simulada muy estrechamente. La verdadera causa de las alteraciones radiológicas puede ser establecida prestando atención a otros estigmas de la esclerosis generalizada.

El valor del examen de los dedos para descubrir el fenómeno de Raynaud, la calcinosis, ulceración y esclerodactilia, son recalzados. La infección broncopulmonar secundaria, una complicación frecuente de la esclerosis generalizada puede ser favorecida por los factores que se enumeran.
La hipertensión pulmonar puede ser causada ya sea por neumonoesclerosis o por endarteritis esclerodermatoso. Se presentan casos que ilustran estos dos mecanismos.

REFERENCES


2. Schrire, V., et al., to be published.


