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Progressive generalised scleroderma: respiratory failure from primary chest wall involvement

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This patient showed rapidly progressive generalised scleroderma without systemic involvement which involved the chest wall and intercostal muscles and finally resulted in death from respiratory failure. No abnormal pulmonary pathology was demonstrated.

Case report

A 73-year-old woman presented with an eight-month history of swelling of the right leg. The calf and ankle were found normal, but there was non-pitting swelling of the thigh of "woody" consistency. Both flanks were firm with cutaneous thickening. There were no other abnormal physical findings. A cutaneous biopsy confirmed the diagnosis of scleroderma.

The chest radiograph was normal and initial lung function tests within normal limits—FEV_1 1·60 l (1·61 l), FVC 1·75 l (2·06 l), FEV_1/FVC 91% (72%), TLC 4·31 l (4·2 l), VC 1·99 l (2·27 l), RV 2·32 l (1·88 l), transfer factor 5·46 $mM.min^{-1}.kPa^{-1}$ (7·92 $mM.min^{-1}.kPa^{-1}$), normal values being shown in brackets. The electrocardiogram showed an old inferior myocardial infarction. The ESR was 19 mm in one hour and antinuclear factor positive.

Three months later sclerodermatous changes were noted in the skin of the left leg with more widespread involvement of the anterior abdominal wall extending up to the lower costal margins. Chest radiograph and lung function tests were again within normal limits and barium swallow showed no evidence of oesophageal involvement.

Treatment was started with oral penicillamine 250 mg bd. Despite three months of therapy, however, sclerodermatous changes had extended to involve the entire chest wall, and the left inguinal region. Neck movement was restricted and the arms could not be raised above the head. Oral prednisolone 40 mg daily was added to the treatment regime, but with little objective improvement. A short course of azathioprine was given, but discontinued because of a marked leucopenia and thrombocytopenia.

Eight months after presentation the patient became somnolent with shallow respiration. Arterial blood gas estimations showed hypoxia and hypercapnia with Po_2 5·0 kPa, Pco_2 9·3 kPa, and H^+ 62 nM. Arterial oxygen saturation, as determined by ear oximeter, was 52–62%. Forced hyperventilation, however, reversed these changes (fig 1) to Po_2 12·1 kPa, Pco_2 5·1 kPa, H^+ 44 nM, and an arterial oxygen saturation of 90%. Chest radiograph was again normal and the alveolar-arterial oxygen difference within normal limits (2·28 kPa). Spirometry showed a reduction in FEV_1 to 0·90 l and FVC to 1·00 l. A doxapram infusion was started to stimulate respiratory effects but had minimal effect. Continuous nocturnal recording of arterial oxygen saturation by ear oximetry showed values as low as 44% during doxapram infusion, but rising to 95% on waking. The most powerful stimulus to respiration was the use of the bedpan. Twenty-four per cent oxygen by face mask was used with some benefit on oxygen tension without increasing hypercapnia. Finally, both medroxyprogesterone 300 mg daily and dexamphetamine daily were commenced, but with little effect. She became increasingly somnolent, comatose, and died within a week in respiratory failure.

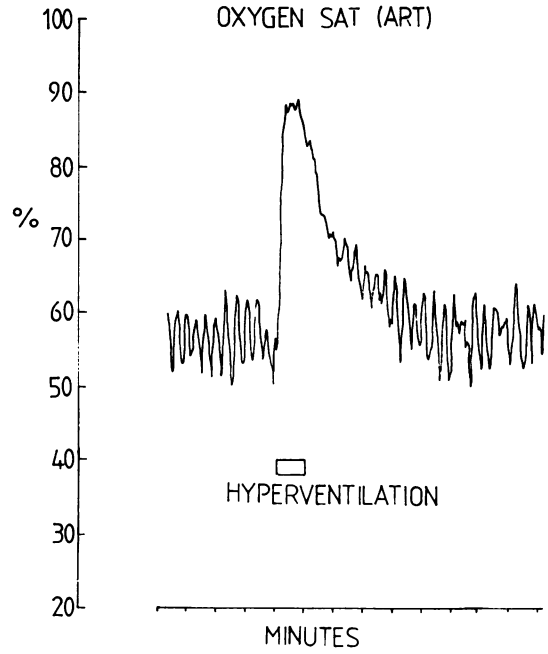

Fig 1 *Continuous recording of arterial oxygen saturation by ear oximetry at rest and during a period of voluntary hyperventilation.*

Pathology

At necropsy the sclerodermatous changes of the skin were noted. The lungs showed evidence of recent pulmonary oedema, but no fibrosis macroscopically. Pleurae and pericardial sac were normal. There was no evidence of pulmonary embolism. All three coronary vessels were moderately affected by atheroma and there was minimal fibrosis in the left ventricle. There was no evidence of systemic sclerosis affecting the oesophagus or major organs, and the diaphragm was macroscopically normal.

Skin biopsies showed the appearances microscopically of scleroderma with marked fibrous thickening of the dermis with replacement fibrosis of subcutaneous fat and lymphoid aggregates. The epidermis was normal with sparse atrophic sweat ducts.

Sections of the intercostal muscles (fig 2) showed muscular atrophy with interfibre oedema, replacement fibrosis, and focal aggregates of chronic inflammatory cells with perivascular cuffing. Foci of fat globules were present among the muscle fibres, associated with lymphocytic aggregates. These changes are consistent with sclerodermatous infiltration of the intercostal muscles.

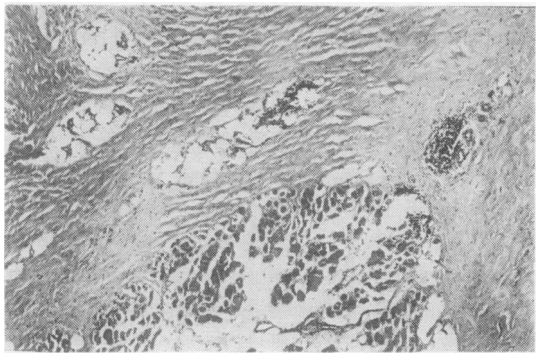

Fig 2 *Section of intercostal muscle taken at necropsy showing foci of fat globules associated with lymphocyte aggregates and muscular atrophy with replacement fibrosis and interfibre oedema. Note focal aggregates of chronic inflammatory cells with perivascular cuffing (H and E, original magnification ×50).*

The brain was fixed and sections taken from the brain stem, hypothalamus, thalamus, and cerebral cortex. Apart from slight generalised gyral atrophy, no abnormality was found.

Sections of lung showed no evidence of interstitial fibrosis.

Discussion

Respiratory failure resulting from chest wall involvement, in the absence of lung fibrosis, is a rare complication of scleroderma. Sparing of the lung is the exception rather than the rule,[1] and even in the presence of cutaneous involvement of the chest wall, reductions in pulmonary compliance have been attributed entirely to pulmonary fibrosis.[2]

The patient, however, represents an example of the rare condition of progressive generalised scleroderma which differs from systemic sclerosis in that cutaneous involvement affects the trunk, abdomen, and thighs rather than the face, hands, and feet and systemic involvement is unusual.[3] Generalised involvement, including chest wall infiltration, in this condition has been reported in only one of 44 cases.[4] One of 10 cases of scleroderma was found by Hughes and Lee[5] to have reduced vital capacity and normal diffusing capacity in association with extensive chest wall involvement. Death from respiratory failure has not been reported.

The combination of a terminal reduction in vital capacity with chest wall involvement and alveolar hypoventilation, without abnormality in pulmonary histology or gas exchange, would suggest this patient's respiratory failure was mechanical in origin. An unusual feature, however, was the apparent lack of hypoxic drive to respiration at low arterial oxygen saturations. The diaphragm appeared spared from fibrous infiltration and voluntary hyperventilation was effective in reversing hypoxia and hypercapnia, suggesting a possible additional primary failure in respiratory drive. Therapeutic measures, however, had minimal effect and no neuropathological basis for primary alveolar hypoventilation was detected. Alternatively, fibrous infiltration and destruction of afferent and efferent nerve terminals within the chest wall may have contributed. Mechanical involvement of the chest wall and intercostal muscles would appear therefore to have led to a vicious cycle of increasing hypercapnia, somnolence, and hypoventilation, possibly exacerbated terminally by a central defect in respiratory drive, and finally death from respiratory failure.

References

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