THE LUNG SCAN IN α_1-ANTITRYPSIN DEFICIENCY

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The most frequent application of the radioisotope lung scan has been as an aid in the diagnosis of pulmonary embolism. In addition, reports have appeared describing abnormal scan patterns in mitral valve disease (*1*), asthma (*2*) and emphysema (*3,4*). These findings, when combined with other clinical data, can be helpful in diagnosis of these diseases and occasionally even in assessment of severity.

Until now, however, no correlation has been apparent between functional and clinical manifestations of disease and the various patterns of scan abnormalities seen in patients with pulmonary emphysema. We have applied lung scanning to a group of emphysema patients with a common biochemical defect, hereditary α_1-antitrypsin deficiency. These patients display a consistent regional abnormality of pulmonary perfusion. This pattern is sufficiently characteristic that its recognition in an emphysematous patient should lead to a serologic search for antitrypsin deficiency.

The identification of patients with emphysema associated with antitrypsin deficiency is of more than academic interest. The serum protein deficiency is inherited as an autosomal recessive trait, and the homozygous state is associated with a high incidence of primary pulmonary emphysema. The heterozygous and homozygous deficiency states can be identified by simple blood testing of relatives of diseased individuals. Early identification of individuals with homozygous deficiency is feasible, and harmful environmental factors such as smoking and industrial dust exposure can be avoided. Genetic counseling is also possible. Since the pathogenetic relationship of the protein deficiency to the lung disease is unknown, specific treatment or prophylaxis is not yet possible.

SUBJECTS AND METHODS

Ten patients with the pulmonary emphysema associated with hereditary α_1-antitrypsin deficiency were studied. Clinical data and pulmonary function characteristics on seven of these individuals have been reported in detail previously (*5*). Seven of the 10 were females and three were males; their ages ranged from 32 to 69 years. Eight patients had symptoms of obstructive lung disease, and two were asymptomatic but demonstrated abnormalities of pulmonary function. As a group, the patients fell into the clinical pattern of primary emphysema as described by Reid (*6*). All demonstrated airways obstruction and hypoxia.

Vital capacities ranged from 22 to 89% of normal. The forced mid-expiratory flow rates varied from 0.11 to 1.95 liters/sec, with a mean value of 0.63 liters/sec.

Serum trypsin inhibitory capacity was assayed by the method of Eriksson (*7*). The action of trypsin upon a synthetic substrate was measured colorimetrically and standardized against soybean trypsin inhibitor. Trypsin inhibitory capacity values ranged from 0.00 to 0.39 mg of trypsin inhibited per milliliter of serum. These values were in the range reported by Eriksson (*7*) as homozygous deficiency. (Normal values for this laboratory are 1.08 ± 0.34 (2 s.d.). The α_1-globulin band on serum protein electrophoresis was nearly undetectable in all cases.

Standard posteroanterior and lateral chest roentgenograms were obtained on all patients. Each had a lung scan performed following intravenous injection of 200–225 μCi of ^{131}I-labeled macroaggregates of albumin (Albumatope-LS, E. R. Squibb & Sons). The injection was carried out with the patient breathing deeply in the sitting position. Oral premedication with 325 mg of potassium iodide was used to block ^{131}I uptake by the thyroid. Posteroanterior and anteroposterior views were scanned using a Nuclear–Chicago Pho/Dot scanner with a 3-in. crystal and a 19-hole collimator. One patient had a second scan after breathing 100% oxygen for 30 min.

RESULTS

All patients had chest roentgenographic findings of flaring of the rib cage, hyperinflation manifested by increased anteroposterior diameter and low diaphragms, and increased radiolucency over the lower 2/3 of the lung fields. The upper lung fields, in con-

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trast, showed vascular markings of greater than normal diameter, tapering gradually but extending to the lung periphery. The abnormalities were generally symmetrical. Several patients had roentgenographic evidence of right ventricular enlargement. The electrocardiogram showed a vertical axis in all five patients in whom a tracing was obtained, with some evidence of right atrial hypertrophy in those most severely affected.

Lung scans of all patients showed decreased perfusion in the lower lung fields, with normal or increased perfusion in the upper regions. Abnormalities were diffuse and tended to be symmetrical. The asymptomatic patients (Figs. 1,2) had scans with modest but definite decrease in lower zone perfusion. Those with moderate disease showed moderately advanced changes of a similar sort (Figs. 3,4). The severely affected patients (Figs. 5,6) had

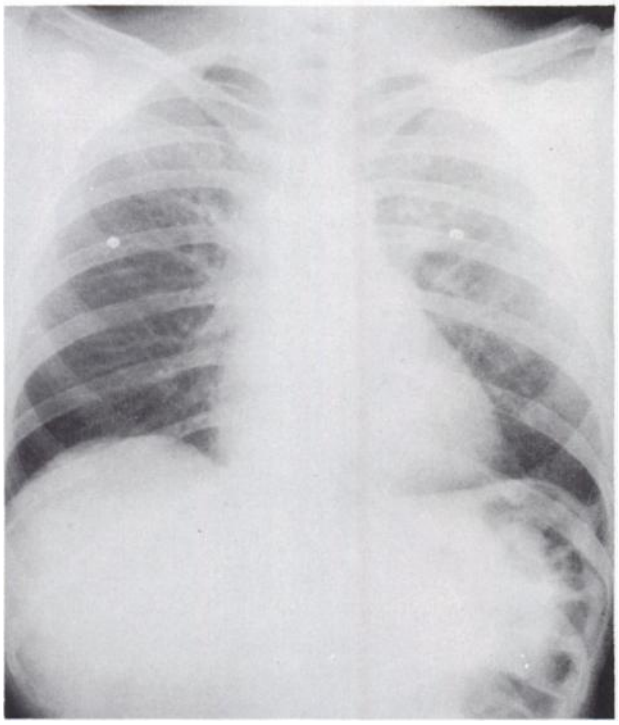

FIG. 1. Antitrypsin deficiency with mild lung disease.

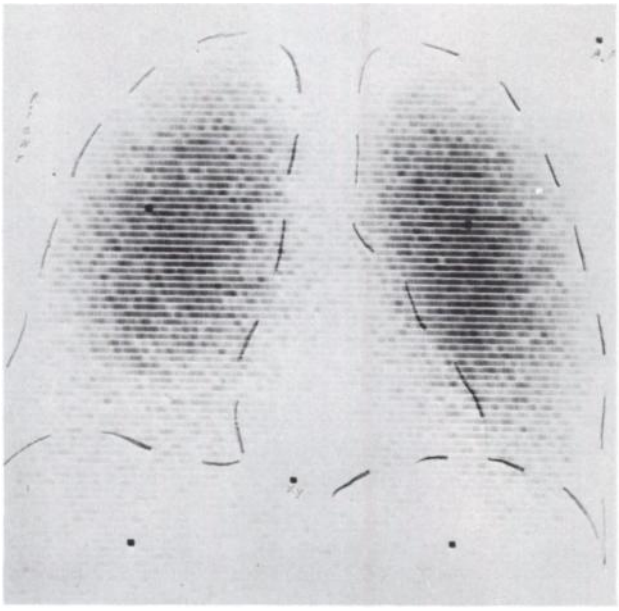

FIG. 2. Antitrypsin deficiency with mild lung disease.

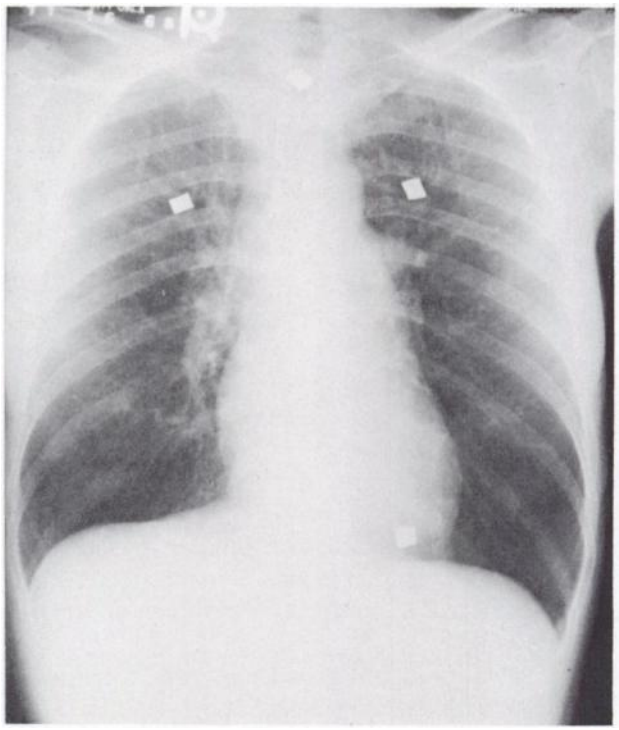

FIG. 3. Antitrypsin deficiency with moderate lung disease.

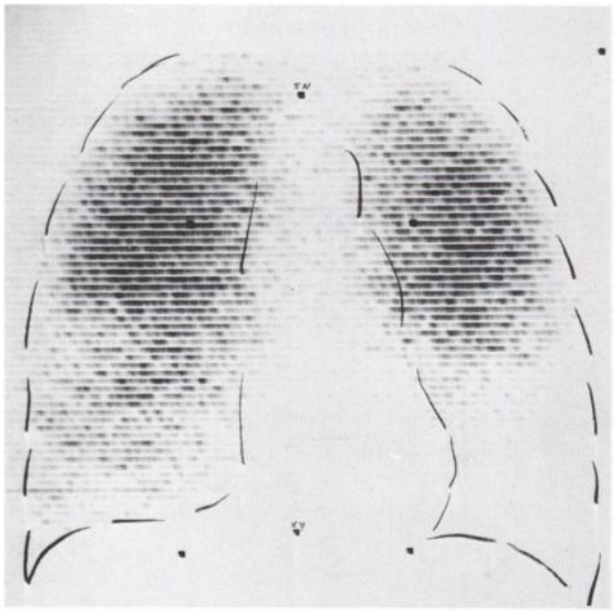

FIG. 4. Antitrypsin deficiency with moderate lung disease.

scans with little evidence of radioactivity in the lower zones. One patient in whom the scan was repeated after 100% O_2 breathing showed no change in the scan pattern following this maneuver.

Although the lung-scan pattern could be predicted from the chest radiograph abnormality in most of these patients, the scan was usually more definitive. In the patients with only mild emphysema the radiograph tended to be near normal in the face of a clearly abnormal scan.

DISCUSSION

Lopez-Majano, Tow and Wagner in 1966 (*3*) reported findings on lung scans in a group of 62 patients with emphysema and described abnormalities in 95%. They were able to classify the scans in four groups on the basis of distribution of areas of decreased perfusion: patchy, unilateral, patchy and unilateral, and normal. They were unable to correlate these patterns with clinical and functional manifestations of disease; and they described no patients with predominant upper or lower zone involvement. In a more recent review (*4*) Poulose, Reba and Wagner report more severe involvement of upper than lower zones in most patients with chronic obstructive pulmonary disease.

Regional abnormalities of pulmonary perfusion have been studied by other methods as well. Reid (*6*) has made the interesting observation of roentgenographic appearance of regional plethora in several of her patients with primary (panacinar) emphysema. She commented that this was in contrast to the usual findings in patients with chronic bronchitis. In a laminographic study of 17 patients with emphysema, Dulfano and DiRienzo (*8*), took particular note of the tendency for the normal increase in vessel size over the lower lung fields to be maintained. In only two cases was this relationship reversed.

In a description of pulmonary angiograms in patients with obstructive lung disease, Scarrow (*9*), observed a relative increase in blood flow to the upper lobes in those individuals with the clinical pattern of primary (panacinar) emphysema. Similar angiographic findings were described by Eriksson (*7*) in patients with α_1-antitrypsin deficiency and primary emphysema. No angiographic or pathologic data are available in our series, but the autopsy studies reported in the literature (*7,10,11*) reveal panacinar emphysema in subjects with antitrypsin deficiency, and our patients have the clinical pattern of primary emphysema.

Bentivoglio (*12*) used ^{133}Xe to study a series of 40 patients with emphysema and noted close correspondence between regional decreases in ventilation and perfusion. He found predominantly lower zone abnormality in one or both functions in half of the patients. It is problematic why Lopez-Majano, Tow and Wagner did not observe a similar tendency in their series studied with lung scans. Perhaps the selection of patients differed; and perhaps a patchy appearance within regions of abnormality obscured

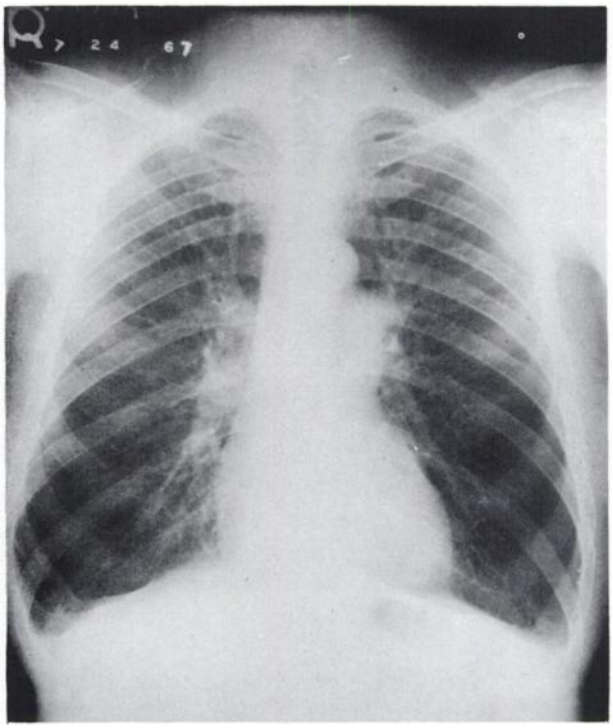

FIG. 5. Antitrypsin deficiency with severe lung disease. From *Arch. Intern. Med.* (*5*).

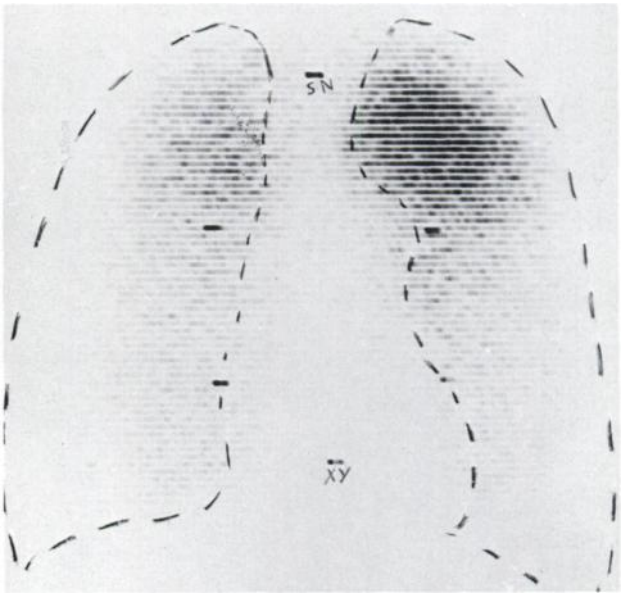

FIG. 6. Antitrypsin deficiency with severe lung disease. From *Arch. Intern. Med.* (*5*).

an overall zonal decrease in perfusion. The xenon technique, as used by Bentivoglio, would not necessarily detect small patchy areas of involvement.

At any rate, a survey of the literature on abnormal pulmonary perfusion in emphysema reveals a striking heterogeneity within groups of patients. In contrast, ten consecutive patients with emphysema associated with α_1-antitrypsin deficiency have been noted to have a bilateral decrease in lower zone perfusion. This finding is consistent with angiographic findings reported by Eriksson in patients with this disease. It has recently been confirmed by Medina at the University of Minnesota who used ^{133}Xe to study two patients with emphysema and antitrypsin deficiency. He found bilateral decrease in lower zone ventilation and perfusion (*13*). Whether this is a characteristic pattern in panacinar emphysema in general or in that associated with α_1-antitrypsin deficiency in particular remains to be seen. The precise location of the abnormality within the ramifications of the pulmonary vascular tree remains to be identified, and the extent to which functional as opposed to structural changes are involved awaits quantitation.

Since the pathophysiologic state characteristically thought to be associated with greater perfusion in upper than lower zones is postcapillary pulmonary hypertension associated with mitral stenosis or chronic congestive failure, the question of a similar state in panacinar pulmonary emphysema arises. This hypothesis seems unlikely but needs to be explored by hemodynamic studies. A related consideration is the possibility that the reduced lower lobe perfusion is due to regional vasospasm related to regional hypoxia. Our failure to produce a change in the scan of one patient with 100% O_2 breathing provides a shred of evidence that the abnormality is structural rather than functional.

SUMMARY

Ten patients with pulmonary emphysema associated with hereditary antitrypsin deficiency were studied with radioisotope lung scans. These patients were clinically similar in that they presented the syndrome of primary emphysema as opposed to chronic bronchitis. There was a wide range of severity of disease, however.

All patients studied had a bilateral decrease in perfusion to the lower lung fields. This similarity within a group of patients is in contrast to the variability in lung-scan patterns previously described in heterogeneous populations of emphysema patients. This characteristic lung-scan appearance should be helpful in identifying patients with antitrypsin deficiency.

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