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Bronchiectasis in systemic sclerosis. A study using high resolution computed tomography

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ABSTRACT

Objective. *To detect noninvasively the presence of bronchiectasis in patients with systemic sclerosis (SSc), through the use of high resolution chest computed tomography (HRCT).*

Methods. *Twenty two patients with SSc, of whom 13 with diffuse and 9 with limited disease, besides a complete history, physical and routine laboratory and immunologic profile, were evaluated by pulmonary function testing and HRCT. The chi square test with Yates' correction, the Fisher's exact test, the Fisher's test (F test) and the "t" test were used for statistical analysis of the results.*

Results. *Eleven patients (50.0%) had decreased carbon monoxide diffusing lung capacity (DLCO) and, out of these, four had restrictive lung disease, based on a combined decrease of forced vital capacity (FVC) and total lung capacity (TLC). Another two patients exhibited this pattern without DLCO impairment. HRCT revealed a ground glass picture in 15 patients (68.2%), fibrosis in 9 (40.9%) (of which 5 with ground glass as well), and cylindrical bronchiectasis in 13 (59.1%). Bronchiectasis was more common in diffuse than in limited SSc, and the difference approached but did not reach the level of statistical significance. On the other hand, it was not correlated with either decreased DLCO, presence of ground glass and fibrosis, or with patients' age and disease duration.*

Conclusion. *Although the number of patients included in our study is relatively small, our data, for the first time in the literature, indicate a significant association between scleroderma and bronchiectasis. Bronchiectasis should be included in the list of pulmonary manifestations of SSc, and SSc in the list of conditions causing bronchiectasis.*

Introduction

Bronchiectasis is a rather uncommon pulmonary disease, characterized by inflammation and anatomic distortion of the bronchial walls, associated with a variety of congenital or acquired processes. High resolution computed tomography of the chest has been considered the examination of choice for the detection of bronchiectasis noninvasively, due to its high sensitivity and specificity (1). Prompted by the detection of bronchiectasis in several patients with scleroderma by this technique, actually employed for the detection of the ground glass pattern and fibrosis, we decided to apply it in all of our SSc individuals. Interestingly, bronchiectasis has not been reported in scleroderma, although it may be a feature of a number of systemic diseases (2), including rheumatoid arthritis (3).

Materials and methods

Twenty-two patients attending our rheumatology outpatient department, who fulfilled the 1980 American Rheumatism Association preliminary criteria for the classification of SSc (4), were included in the study. Seventeen were female and 5 were male. All female patients and two of the male patients had never smoked. The rest had a history of smoking less than a packet per day, but they had stopped 5 to 7 years prior to this study. Nine patients, all female, had the limited variety of the disease (40.9%). Their ages ranged between 24 and 75 years (mean ± SD 56.3 ± 5.7) and the duration of the disease between 1 and 17 years (8.2 ± 4.8).

Evaluation included a complete history and physical examination, routine laboratory (hematology, urinalysis and biochemistry), and serologic immune profile (C reactive protein,rheumatoid factor, antinuclear antibodies, antibodies to double stranded DNA and Sm, nRNP, Ro, La and Scl70 antigens and C3 and C4 complement levels). At the time of the study, chest radiograph, electrocardiogram and echocardiogram were performed as well. The main parameters used for the evaluation of the respiratory function of the patients included FEV1 (i.e. forced expiratory volume in one second), FVC, the ratio FEV1/FVC, TLC (by the helium dilution technique) and DLCO (by the single breath method). Abnormal values were considered an FVC below 80% predicted, a TLC below 80%, a DLCO below 70% and an FEV1/FVC below 70% predicted. These were based on

the suggestions of the American Thoracic Society as described by Owens *et al* (5), with the only exception being the consideration of DLCO as abnormal when it was below 70% predicted, and not below 80%, for reasons previously described (6,7). A combination of abnormal TLC and FVC was suggestive of restrictive lung disease (5-7). Finally, all patients underwent an HRCT. They were examined in the supine position at end-respiratory volume. The images were obtained with a Somatom Plus CT scanner (Siemens, Erlangen, Germany) using narrow section collimation (2 mm thick slices) at 20mm intervals from the lung apices to the lung bases. An average of 10 slices per patient was provided. The slices were reconstructed with a high-spatial-resolution algorithm. There was no need for additional prone-positioned scans in our population. The films were reviewed by a radiologist with expertise in the interpretation of this procedure, who was unaware of the diagnosis. A semiquantitative score ranging from (-) to (++) was used by us for the grading of bronchiectasis, similar to the subjective scoring system to record bronchi as normal, mildly abnormal and severely abnormal used by Diederich *et al*. (8). The presence of ground glass and fibrosis, besides any other findings, was specifically noted.

The chi square test with Yates' correction, the Fisher's exact test and the F test (Fisher's test) were used for the statistical evaluation of the results. A "t" test was performed wherever the results of the F test showed no statistical significance.

Results

Regarding serology, all the patients had positive antinuclear antibodies in high titers, the majority of the fine speckled pattern. Four patients had antinucleolar pattern, 4 exhibited the anti-centromere pattern and another 4 patients had anti-Scl70 antibodies.

Demographic data and information regarding extent of skin involvement, serologic profile, pulmonary function and HRCT findings of our patients are seen in Table I. The extent of bronchiectasis and the degree of fibrosis were estimated on a scale from (-) to (++).

Eleven patients (50.0%) had decreased DLCO and of them, 4 had decreased FVC and TLC, compatible with restrictive lung disease. Another 2 patients had decreased FVC and TLC but normal DLCO.

High resolution computed tomography revealed a ground glass picture in 15 patients (68.2%) and fibrosis in 9 (40.9%). Five (22.7%) of these patients exhibited both patterns.

Cylindrical bronchiectasis by HRCT was detected in 13 individuals (59.1%). Its appearance varied from isolated focal lesions (Fig. 1) to very extensive and complex findings (Fig. 2). Ten of the 13 patients with diffuse scleroderma (76.9%) had bronchiectasis compared with 3 of the 9 with limited disease(33.3%). This difference approached but did not reach the level of statistical significance ($p = 0.0539$ by Fisher's exact test).

Ten of the 15 patients with ground glass (66.7%) had bronchiectasis, compared with 3 of the 7 without ground glass (42.9%). The difference was not statistically significant. Of the 9 patients with fibrosis, five (55.6%) had bronchiectasis, compared with 8 out of the 13 (61.5%) without fibrosis (p not significant). Seven of the 11 patients with decreased DLCO (63.6%) had bronchiectasis, whereas 6 of the 11 with normal DLCO (54.5%) did (p not significant). Of the 6 patients with restrictive disease, 4 (66.7%) had bronchiectasis, compared with 9 of the 16 without restrictive disease (56.3%). The difference again was not significant. Furthermore, the patients' autoantibody profile did not influence the possibility of developing bronchiectasis. Similarly, we could not find any significant statistical correlation between the presence of bronchiectasis and either age (mean ± SD 53.8 ± 15.2 years for those with bronchiectasis, 59.9 ± 16.6 for those without) or disease duration (6.8 ± 4.6 years and 10.2 ± 4.4 respectively) of our patients.

Table I. Demographic data, clinical and serologic features and HRCT findings of the study population.

Sex	Age (yrs.)	Dis. dur. (yrs.)	Diffuse/ limited	ANA profile	FCV TLC	DL_{CO}	Ground glass	Bronchi- ectasis	Fibrosis
F	75	6	Dif.	F.S.* Scl70	Yes	Yes	Yes	++	+
F	73	12	Lim.	A.C.A.**	No	Yes	No	_	_
F	75	7	Dif.	F.S. Scl70	Yes	No	Yes	_	_
F	66	13	Lim.	Nucleolar	No	No	No	_	++
M	75	5	Dif.	Nucleolar	No	No	No	_	+
F	31	10	Dif.	F.S. Scl70	No	No	Yes	+	+
F	57	6	Dif.	F.S.	No	No	Yes	++	++
F	46	17	Lim.	A.C.A.	No	Yes	Yes	_	_
F	55	15	Lim.	F.S.	No	Yes	Yes	_	+
F	42	14	Lim.	F.S.	No	No	Yes	+	_
F	64	12	Dif.	F.S.	No	Yes	No	+	+
F	24	7	Dif.	Nucleolar	Yes	No	No	_	_
F	65	5	Lim.	A.C.A.	No	Yes	Yes	_	_
F	60	11	Lim.	A.C.A.	No	No	Yes	_	+
F	63	1	Dif.	Nucleolar	Yes	Yes	Yes	+	_
F	71	2	Dif.	F.S.	No	No	Yes	+	_
F	49	6	Lim.	F.S.	No	Yes	No	+	+
M	25	5	Dif.	F.S. Scl70	Yes	Yes	Yes	+	_
F	62	6	Lim.	Homogeneous	Yes	Yes	Yes	+	_
M	43	15	Dif.	F.S.	No	Yes	No	+	_
M	65	1	Dif.	Homogeneous	No	No	Yes	++	_
M	52	14	Dif.	F.S.	No	No	Yes	+	_

*Fine speckled antinuclear pattern; **Anticentromere antibodies.

Discussion

Interstitial inflammation of the lung parenchyma, which eventually progresses into fibrosis resulting in restrictive lung disease and pulmonary hypertension, is a common manifestation of SSc, contributing significantly

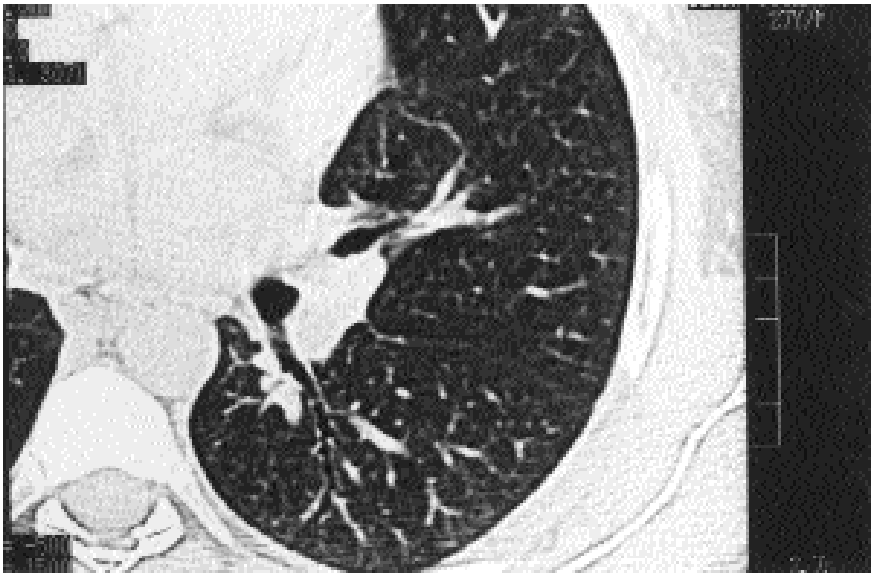

Fig. 1. HRCT, left lung:One dilated bronchus at the apical segment of the lower lobe is sectioned longitudinally. The "string of pearls" configuration and peribronchial thickening are apparent.

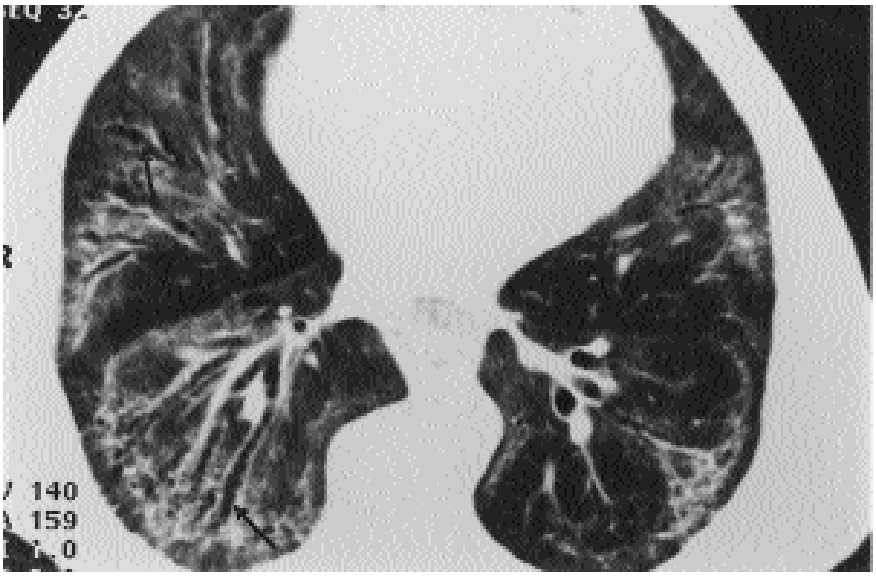

Fig. 2. HRCT scan, slice at the middle level of the lungs:middle lobe, lingula and apical segments of lower lobes are seen with diffuse ground glass infiltrates and peripheral fibrosis. Many bronchial dilatations appear in all lung fields sectioned longitudinally. They are more extensive at the right lung. Most of the bronchiectatic lesions are characterized by the "string of pearls"configuration and peribronchial thickening (**arrows**).

to the mortality of the disease. These features have been explicitly described in the literature and are considered the principal manifestations of lung involvement by scleroderma.

Stimulus for the present study was the finding of cylindrical bronchiectasis in HRCT's, performed initially in a few of our SSc patients with decreased DLCO, in order to detect ground glass (9) and possible reversible interstitial lung inflammation, potentially treatable with cyclophosphamide and steroids (10). Prompted by the above and by the fact that major internal medicine (11,12), respiratory medicine (2) and rheumatology (13,14) textbooks do not include bronchiectasis in the manifestations of scleroderma or scleroderma in the list of conditions associated with bronchiectasis, and the absence of such an association in the literature as well, we decided to check all of our SSc patients with HRCT for the presence of bronchiectasis.

Our results indeed showed that cylindrical bronchiectasis is a common feature of lungs affected by SSc. The lesions are predominantly located in the lower lobes and do not produce the classic symptoms of bronchiectasis, such as excessive expectoration or hemoptysis. The latter is not necessary though in bronchiectasis of any cause, and "dry bronchiectasis" is well documented (2).

Conditions associated with bronchiectasis (2) include bronchial obstruction and infection, primary ciliary dyskinesia, cystic fibrosis, allergic bronchopulmonary aspergillosis, immunodeficiency, alpha1-antitrypsin deficiency, bronchopulmonary sequestration, unilateral hyperlucent lung, congenital cartilage deficiency, yellow nail syndrome, ammonia burns, Ehlers-Danlos syndrome, Marfan's syndrome and rheumatoid arthritis (3). None of these was apparently present in our patients.

Of interest may be the fact that the presence of bronchiectasis was not associated with patients' age or disease duration, ground glass, fibrosis or decreased DLCO. It should be noted , however, that it was more common in the patients with ground glass and decreased DLCO compared to those without, although the differences were not statistically significant. Inflammation of the bronchial wall or peribronchial tissue is mainly responsible for the bronchiectatic process. In our individuals, as mentioned above, bronchiectasis was more common in those with ground glass and decreased DLCO which, in the absence of primary pulmonary hypertension, may reflect the degree of interstitial inflammation. The fact that a statistically significant correlation between decreased DLCO or the presence of ground glass with bronchiectasis was not found may simply be due to the small number of patients, included in this study.

The possibility of infection contributing to bronchiectasis in our patients, especially of the type of aspiration pneumonia (not uncommon in SSc), is also present. A clear cut history of such events could not be elicited from our patients, but silent aspiration pneumonia was not easy to exclude. The fact that in some of our patients with local-

ized bronchiectasis fibrosis was not detected may be in favor of possible aspiration pneumonia underlying the process. However, bronchiectasis in our individuals was not a temporary finding. The majority of them had follow up HRCT's and the process proved either stable or progressive. A more definitive answer to the question regarding the pathology underlying the development of bronchiectasis in scleroderma could perhaps be provided through the performance of autopsy studies. The need of larger SSc populations to be studied is obvious, as well.

However, our results showing such a high incidence of bronchiectasis in a relatively uncommon disease such as scleroderma, strongly suggest an association between the two. Bronchiectasis should be included in the list of pulmonary manifestations of SSc, and scleroderma should be included in the list of conditions associated with bronchiectasis. Furthermore, the clinician dealing with such patients should be aware of the possibility of bronchiectasis in a sceroderma patient presenting with a respiratory infection, which may seriously compromise his respiratory function.

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