Systemic and Discoid Lupus Erythematosus: Analysis of Pulmonary Function

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Received September 28, 1977

To determine the prevalence of pulmonary dysfunction in lupus erythematosus, 24 patients with systemic lupus erythematosus (SLE) and 5 patients with discoid lupus erythematosus (DLE) were studied. Diffusing capacity for carbon monoxide was abnormal in 17 (71 percent) SLE patients. A restrictive ventilatory defect was present in 6 (25 percent) and arterial hypoxemia in 4 of 23 (17 percent). The mean ratio of forced expiratory volume in one second to forced vital capacity (FVC) was 83 percent. To test for the presence of small airways disease, maximum expiratory flow rate at 50 percent of FVC was measured on air and on an 80 percent helium-20 percent oxygen mixture. Ten patients (5 smokers and 5 nonsmokers) with SLE were nonresponders to helium suggesting small airways disease. Pulmonary dysfunction was present in 90 percent (9/10) of SLE patients with a previous history of pleuritis and/or pneumonitis, and in 71 percent (10/14) without respiratory symptoms or history of lung disease and with a normal chest radiograph. Pulmonary function tests were normal in DLE patients except for an abnormal response to helium and/or mild arterial hypoxemia in two patients, all of whom were smokers. These data indicate that there is a high prevalence of pulmonary function abnormalities in SLE including patients without clinically evident pleuropulmonary disease.

Pleuropulmonary manifestations of systemic lupus erythematosus (SLE) have been described in previous clinical [1–7], radiologic [8–12], and post-mortem [13–19] studies. However, in only a few series [20–24] have detailed pulmonary function tests been used to assess the nature of alterations in respiratory function in SLE. A decreased diffusing capacity for carbon monoxide is the most common observed abnormality [20,21,24], and is considered the most sensitive screening test for pulmonary abnormalities in SLE [24]. A restrictive ventilatory defect has been noted in a few instances [20,22,23].

An investigation of pulmonary function in patients with discoid lupus erythematous (SLE) has not been reported previously and the possibility of lung dysfunction in such patients cannot be excluded.

The primary purpose of this study was to assess pulmonary function, including evidence of small airways disease, in patients with systemic and discoid lupus erythematosus.

PATIENTS AND METHODS

Twenty-four patients with an established diagnosis of SLE were evaluated. All had multisystemic involvement and the clinical diagnosis was confirmed in all 24 by serum factors (positive antinuclear antibody tests and positive LE preparations), and
in 19 by skin or renal biopsies. Of the 17 patients with renal biopsies, eight had a diffuse proliferative lesion (Nos. 5,8,9,10,12,21,22,23), three a membranous lesion (Nos. 3,6,13) and six a focal lesion (Nos. 7,11,14,15,19,24) documented prior to pulmonary function testing. In addition, five patients with a skin biopsy proven diagnosis of DLE, without clinical evidence of systemic involvement, were studied. Clinical history, respiratory symptoms, physical examination and chest radiographic findings were determined on the day of pulmonary function testing.

Tests of pulmonary function included maximum expiratory flow rates breathing air and then an 80 percent helium–20 percent oxygen mixture. The maximum expiratory flow volume (MEFV) curves were measured with a pneumotachygraph integrator system of Virgulto and Bouhuys [25] and a Brush 500 High Performance XY recorder (Gould Inc., Cleveland, Ohio). The pneumotachygraph was calibrated for air and helium with a flow volume calibrator [26]. The MEFV curves breathing helium were done according to the method of Dosman et al. [27]. The MEFV curves breathing air and helium were superimposed and maximal flow rates at 50 percent of vital capacity on air (MEF$_{50}$) and helium (MEF$_{50}$He) were calculated. The mean of the two most reproducible MEFV curves for air and helium was used. The flow rate response breathing helium compared to air was expressed in percent as $\Delta$ He = (MEF$_{50}$He − MEF$_{50}$)/MEF$_{50}$ × 100. Patients with $\Delta$ He less than 20 percent were considered nonresponders to breathing helium suggesting small airways disease [27,28].

Lung volumes were determined by the nitrogen washout method. Diffusing capacity for carbon monoxide (DLCO) was measured by the single breath method of Ogilvie et al. [29] and results were corrected for anemia using the equation of Dinakara et al. [30]. Arterial blood gas determinations were done in the sitting position breathing ambient air.

All patients had posterior-anterior and lateral chest radiographs on the day of pulmonary function testing. Renal function (blood urea nitrogen and serum creatinine) also was determined in all patients on the day of the study.

RESULTS

Patients with SLE were classified as follows:

Group 1: Patients with respiratory symptoms; history of pleuropulmonary disease and/or an abnormal chest radiograph (10 patients).

Group 2: Patients without respiratory symptoms, history of pleuropulmonary disease or chest radiographic abnormalities (14 patients).

Table 1 summarizes the clinical features of Group 1 patients. Two of these Group 1 patients (Nos. 2 and 4) and five Group 2 patients (Nos. 11,14,17,18, and 21) were smokers (Table 2). All five DLE patients were smokers and none had respiratory symptoms, a history of pleuropulmonary disease or an abnormal chest radiograph. Table 2 shows that patients with SLE ranged in age from 15 to 59 years and with DLE from 33 to 60 years. One Group 1 patient was a male; all other patients with SLE and DLE were females. In none of the 24 SLE patients was the blood urea nitrogen greater than 20 mg/100 ml or serum creatinine greater than 1.5 mg/100 ml when pulmonary function was determined. All but three patients with SLE (Nos. 2,7,20) were receiving corticosteroids at the time of the study. Nine patients (Nos. 5,6,9,10,12,13,14,17,23) were receiving azathioprine in addition to corticosteroids. All DLE patients were receiving only topical corticosteroid therapy.

Table 2 shows pulmonary function results for SLE and DLE patients. Measure-
PULMONARY FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

iment of diffusing capacity was abnormal, less than 70 percent of predicted [31], in 17 of 24 patients with SLE. In these 17 mean DLCO was 55 percent of predicted (range 36–69 percent). Nine of 10 patients (90 percent) in Group 1 had an abnormal DLCO. An abnormal DLCO was also present in 8 of 14 (57 percent) Group 2 patients who had no clinical or chest radiographic manifestations of lung involvement.

Forced vital capacity and lung volumes suggested a restrictive pattern of ventilation in 6 of the 24 SLE patients (Nos. 2,3,5,9,19 and 23), and each of these 6 also had a low diffusing capacity. Four of the 6 patients had an FVC less than 80 percent of predicted [32] and four had a total lung capacity (TLC) less than 80 percent of predicted [33].

The ratio of FEV1 to FVC was 70 percent or greater in all 24 patients, mean 83 percent. Ten patients (5 smokers and 5 nonsmokers) were nonresponders to breathing helium, (Δ He < 20 percent) suggesting peripheral airway obstruction. Five nonresponders to helium were from Group 1 and five from Group 2. Four of the 10 patients with a Δ helium less than 20 percent also had flow rates breathing air at 50 percent of vital capacity (Vmax50) that were abnormal, less than 80 percent of predicted [32]. The other six nonresponders to helium had a normal Vmax50.

Arterial oxygen tension (PaO2) was mildly abnormal [34] in 4 of 23 patients (Nos. 5,9,11 and 12). The mean PaO2 of these four patients was 83 mmHg (range 80–86 mmHg). Two patients with hypoxemia were from Group 1 and two from Group 2. The values for arterial carbon dioxide tension (PaCO2) were below 36 mmHg in 18 of 23 patients.

Among the 10 Group 1 patients a reduced diffusing capacity was the most common pulmonary function abnormality (9), followed by a lack of response to breathing helium (Δ He < 20 percent) (5), a restrictive ventilatory defect (4) and arterial hypoxemia (2). For the 14 Group 2 patients without any other evidence of pleuropulmonary disease a decreased DLCO was present in 8, an abnormal response to breathing helium in 5, arterial hypoxemia in 2 and a restrictive pattern of ventilation in 2.

| Pt. No. | History of Pleuropulmonary Disease | Respiratory Symptoms at Time of Testing | Chest Radiograph at Time of Study | Previous Chest Radiographic Abnormalities |
|---------|-----------------------------------|--------------------------------------|----------------------------------|----------------------------------------|
| 1       | Pleuritis                          | None                                 | Normal                           | Obliteration of costophrenic angle     |
| 2       | Pleuritis                          | Mild Dyspnea                         | Normal                           | Pleural Effusion                       |
| 3       | Chronic Interstitial Pneumonitis   | Mild Dyspnea                         | Diffuse Interstitial lung infiltrate | Diffuse Interstitial lung infiltrate |
| 4       | Acute Lupus Pneumonitis with Pleuritis | Mild Dyspnea     | Normal                           | Lung Infiltrate and Pleural Effusion |
| 5       | Pleuritis                          | Mild Dyspnea                         | Normal                           | Pleural Effusion                       |
| 6       | Pleuritis                          | Mild Dyspnea                         | Tenting of both hemidiaphragms   | Tenting of both hemidiaphragms         |
| 7       | Pleuritis                          | None                                 | Normal                           | Obliteration of costophrenic angle     |
| 8       | Acute Lupus Pneumonitis            | None                                 | Normal                           | Lung Infiltrate and Pleural Effusion   |
| 9       | Aspiration Pneumonia               | Mild-Moderate Dyspnea                | Normal                           | Lobar Consolidation                    |
| 10      | Pleuritis                          | None                                 | Normal                           | Pleural Effusion                       |
TABLE 2
Results of Pulmonary Function Tests in Patients with SLE and DLE*

| Pt. No. | Age | Sex | Smoking (pkg. yrs.) | FVC L. | FEV₁ L. | FEV₁/FVC (%) | RV L. | TLC L. | \( \dot{V} \) Max₂₀ L. | \( \Delta \)He (%) | DLCO ml/min/mmHg | PaO₂ (mmHg) | PaCO₂ (mmHg) | pH |
|---------|-----|-----|---------------------|--------|---------|--------------|-------|-------|----------------|---------------|----------------|-------------|--------------|-----|
| **SLE Patients** |
| **Group 1** |
| 1 | 43 | F | None | 2.59 (89) | 1.96 (80) | 76 | 2.21 (144) | 4.56 (99) | 1.90 (57) | 26 | 13 (49) | 89 | 32 | 7.42 |
| 2 | 30 | F | 30 | 2.38 (76) | 1.88 (70) | 76 | 1.48 (106) | 4.75 (102) | 1.88 (52) | 17 | 12 (48) | 88 | 35 | 7.40 |
| 3 | 18 | F | None | 2.63 (72) | 2.32 (78) | 89 | 0.98 (70) | 3.24 (64) | 3.10 (80) | 61 | 14 (38) | 89 | 28 | 7.44 |
| 4 | 28 | F | 12 | 3.31 (102) | 3.03 (107) | 92 | 1.42 (98) | 5.41 (110) | 4.00 (106) | 18 | 13 (51) | 83 | 36 | 7.42 |
| 5 | 20 | F | None | 2.56 (83) | 2.28 (83) | 89 | 0.83 (72) | 3.02 (70) | 4.09 (107) | 11 | 16 (52) | 82 | 32 | 7.49 |
| 6 | 33 | F | None | 3.68 (100) | 2.82 (91) | 77 | 2.28 (116) | 5.94 (99) | 2.92 (75) | 4 | 24 (68) | 87 | 39 | 7.43 |
| 7 | 48 | F | None | 3.52 (117) | 2.87 (115) | 82 | 1.40 (79) | 4.95 (98) | 3.89 (118) | 32 | 16 (57) | 94 | 36 | 7.43 |
| 8 | 19 | M | None | 4.20 (87) | 3.70 (89) | 88 | 1.19 (83) | 5.49 (87) | 4.53 (101) | — | 26 (84) | 98 | 34 | 7.42 |
| 9 | 15 | F | None | 2.62 (77) | 2.26 (72) | 86 | 1.25 (76) | 4.35 (76) | 2.82 (67) | 18 | 14 (36) | 86 | 33 | 7.47 |
| 10 | 17 | F | None | 3.54 (105) | 3.01 (97) | 85 | 1.07 (70) | 4.57 (85) | 3.68 (90) | 25 | 23 (62) | 90 | 34 | 7.41 |
| **Mean ± SD** | | | | 3.10 ± 0.62 | 2.61 ± 0.57 | 84 ± 6 | 1.41 ± 0.48 | 4.63 ± 0.93 | 3.28 ± 0.91 | 24 ± 16 | 17 ± 5 | 89 ± 5 | 34 ± 3 | 7.43 ± 0.03 |
| **Group 2** |
| 11 | 29 | F | 10 | 3.65 (103) | 3.18 (104) | 87 | 1.16 (66) | 4.75 (84) | 3.60 (92) | 15 | 18 (61) | 80 | 39 | 7.40 |
| 12 | 29 | F | None | 3.29 (108) | 2.59 (101) | 79 | 1.11 (94) | 4.21 (100) | 3.55 (99) | 21 | 25 (87) | 82 | 38 | 7.43 |
| 13 | 16 | F | None | 3.27 (105) | 2.87 (100) | 88 | — — | — — | 3.35 (85) | 31 | 16 (45) | 90 | 34 | 7.41 |
| 14 | 23 | F | 6 | 3.07 (94) | 2.44 (85) | 80 | 1.07 (79) | 4.07 (85) | 3.13 (81) | 38 | 19 (73) | 86 | 33 | 7.42 |
| 15 | 59 | F | None | 3.34 (109) | 2.52 (103) | 75 | 2.18 (106) | 5.54 (102) | 2.44 (77) | 12 | 21 (78) | 86 | 34 | 7.44 |
| 16 | 30 | F | None | 3.40 (108) | 2.63 (97) | 77 | 1.23 (88) | 4.63 (99) | 2.61 (71) | 30 | 18 (58) | 92 | 32 | 7.46 |
| 17 | 47 | F | 30 | 3.48 (120) | 2.44 (101) | 70 | 1.31 (80) | 4.42 (93) | 2.77 (84) | 0 | 15 (69) | 85 | 31 | 7.54 |
| 18 | 48 | F | 20 | 2.78 (88) | 2.35 (90) | 84 | 2.30 (123) | 5.50 (104) | 3.50 (103) | — | 24 (83) | 82 | 33 | 7.45 |
| 19 | 22 | F | None | 2.80 (78) | 2.65 (85) | 95 | 1.13 (71) | 4.56 (84) | 4.20 (104) | 19 | 19 (53) | 95 | 33 | 7.42 |
| 20 | 28 | F | None | 3.73 (112) | 3.15 (109) | 84 | — — | — — | 4.10 (110) | 23 | 26 (78) | 83 | 32 | 7.44 |
| 21 | 29 | F | 10 | 3.24 (107) | 2.91 (89) | 90 | 1.23 (95) | 4.38 (99) | 4.32 (119) | 14 | 19 (64) | 86 | 30 | 7.48 |
| 22 | 21 | F | None | 3.41 (92) | 3.16 (95) | 93 | 3.00 (188) | 6.10 (112) | 5.00 (123) | 22 | 23 (62) | — — | — — | 7.47 |
| 23 | 22 | F | None | 3.56 (89) | 2.88 (92) | 81 | 1.48 (75) | 4.99 (78) | 3.62 (85) | 38 | 21 (61) | 86 | 31 | 7.47 |
| 24 | 17 | F | None | 3.35 (114) | 2.75 (102) | 82 | 1.12 (95) | 4.25 (94) | 3.20 (89) | — | 21 (80) | 92 | 30 | 7.46 |
| **Mean ± SD** | | | | 3.31 ± 0.28 | 2.75 ± 0.28 | 83 ± 7 | 1.53 ± 0.62 | 4.78 ± 0.63 | 3.53 ± 0.71 | 22 ± 11 | 20 ± 3 | 87 ± 5 | 33 ± 3 | 7.45 ± 0.04 |
TABLE 2—Continued

| Pt. No. | Age | Sex | Smoking (pkg. yrs.) | FVC (L.) | FEV₁ (L.) | FEV₁/FVC (%) | RV (L.) | TLC (L.) | Ê Max₁₀ (L.) | ΔHe (%) | DLCO (ml/min/mmHg) | PaO₂ (mmHg) | PaCO₂ (mmHg) | pH |
|---------|-----|-----|---------------------|----------|-----------|--------------|---------|----------|--------------|---------|-------------------|------------|-------------|----|
| DLE Patients |
| 25      | 33  | F   | 15                  | 3.13 (102) | 2.24 (85) | 72           | 1.65 (114) | 4.24 (90) | 3.19 (89) | 20      | 33 (133)         | 81         | 33          | 7.44 |
| 26      | 33  | F   | 20                  | 2.88 (107) | 2.80 (122) | 97           | 1.52 (110) | 4.57 (108) | 5.89 (182) | 31      | 17 (81)          | 88         | 38          | 7.41 |
| 27      | 60  | F   | 30                  | 2.41 (84) | 2.09 (91) | 87           | 1.44 (90) | 3.85 (91) | 2.82 (93) | —       | 23 (108)         | 82         | 33          | 7.45 |
| 28      | 49  | F   | 30                  | 2.80 (92) | 2.16 (85) | 77           | 2.45 (132) | 5.45 (104) | 2.70 (81) | —       | 28 (117)         | 75         | 38          | 7.42 |
| 29      | 36  | F   | 20                  | 3.70 (106) | 2.75 (93) | 74           | 2.80 (150) | 5.56 (98) | 2.44 (63) | 3       | 22 (77)          | 78         | 30          | 7.42 |
| Mean ± SD |    |     |                     | 2.98 ± .48 | 2.41 ± .34 | 81 ± 10      | 1.97 ± .61 | 4.73 ± .75 | 3.41 ± 1.44 | 18 ± 14 | 24 ± 6           | 81 ± 5     | 34 ± 4       | 7.43 |

*FVC = forced vital capacity, FEV₁ = forced expiratory volume in 1 sec., RV = residual volume, TLC = total lung capacity, Ê Max₁₀ = maximal flow rates at 50 percent of FVC, ΔHe = percent increase in Ê Max₁₀, breathing a mixture of helium and oxygen compared to air, DLCO = diffusing capacity for carbon monoxide, PaO₂ = partial pressure of oxygen in arterial blood, PaCO₂ = partial pressure of carbon dioxide in arterial blood, L. = liters. Parentheses indicate percent predicted.
Flow rates, lung volumes and DLCO were normal in all five DLE patients (Table 2). The only abnormalities detected in these patients were an abnormal $\dot{V}_{\text{max}, 50} \Delta \text{He}$ and in patient No. 29 and mild arterial hypoxemia in two patients (Nos. 25 and 29). Both of these patients were smokers.

DISCUSSION

The results of this study indicate that pulmonary dysfunction in systemic lupus erythematosus is common. Pulmonary function abnormalities (decreased DLCO, $\Delta \text{He} < 20$ percent, arterial hypoxemia, and/or a restrictive defect) were detected in 90 percent of patients (9/10) with a history of pleuritis and/or pneumonitis (Group 1) and in 71 percent of patients (10/14) without clinically evident lung disease (Group 2). Some lung function abnormalities were noted in our group of patients with discoid lupus. However, all DLE patients were smokers which could account for these findings [27].

Our findings in SLE patients confirm the results of previous studies. All of the patients in Gold and Jennings' series [20] of 20 SLE patients had abnormal pulmonary function. All 20 had chest radiographic abnormalities and 18 had mild to severe dyspnea. Sixteen of 17 patients tested had a decreased DLCO, and 12 of their 20 patients appeared to have restrictive lung disease. The authors conclude that the single breath DLCO is the most sensitive indicator of the presence of lung involvement in systemic lupus. Huang et al. [21] also noted a high prevalence of pulmonary dysfunction in SLE patients and suggested that respiratory function may be abnormal even in the absence of clinical symptoms or abnormal chest radiographs. In their series, the DLCO was low in 4 of 6 asymptomatic SLE patients with normal chest radiographs.

In 2 of 20 patients with SLE, Gold and Jennings [20] noted airway obstruction indicated by a decreased $\text{FEV}_{1}/\text{FVC}$ percent and increased total airway resistance. These authors did not discuss smoking history. In Hunt et al.'s series of 17 SLE patients [22], 11 had decreased maximum mid-expiratory flow rates indicative of an obstructive ventilatory defect. Six patients were smokers and one was an ex-smoker. Ten of the patients with SLE in our series, of whom 5 were nonsmokers, did not respond to helium suggesting small airways disease [28]. Maximum mid-expiratory flow rates were normal, while breathing air, in 6 of our 10 patients who were nonresponders to helium. Dosman et al. [27] have described normal maximum mid-expiratory flow rates breathing ambient air in patients who did not respond to breathing helium indicating that the latter test may be a more sensitive indicator of peripheral airways obstruction.

The physiological abnormalities detected in this study and by others can be related to pathological changes frequently noted in the lungs of patients with SLE. Purnell et al. [19] detected interstitial pneumonitis in 29 of 54 autopsy cases of systemic lupus. Gross et al. [17] reviewed pulmonary alterations in histologic specimens from 44 patients with SLE and found interstitial pneumonitis in 41. In addition, several pulmonary vascular abnormalities have been observed in SLE. These include fibrinoid necrosis [18], vasculitis [15], and thickened arterioles and arteries [15]. The presence of interstitial pneumonitis with or without pulmonary vascular changes can account for the restrictive defect and decreased diffusing capacity observed in our patients and in other series [20–24].

Gross et al. [17] noted distal airway alterations in all of their autopsy cases including focal panacinar emphysema. These changes could explain the small airways obstruction detected in the present investigation. Furthermore, from the anatomic
studies of Baggenstoss [13] it is known that basophilic mucinous edema is often found within the peribronchial connective tissue and within the bronchus itself in SLE. This mucinous edema could result in airway obstruction.

Lee and co-workers [35] have identified a high prevalence of impaired diffusing capacity and restrictive ventilatory abnormalities among patients in renal failure of various etiologies. Although it is possible that renal disease contributed to pulmonary dysfunction in our patients, it is unlikely since none had evidence of renal insufficiency at the time of evaluation. In a recent study, Gibson et al. [24] found no higher incidence of renal dysfunction among 30 patients with SLE and pulmonary function abnormalities than in those without lung involvement.

Cytotoxic drugs, particularly bleomycin, methotrexate and busulfan, have been associated with pulmonary toxicity and abnormal pulmonary function tests [36]. Nine patients in this series were receiving a cytotoxic drug (azathioprine); however, this agent has not been established as toxic to the lungs [36]. All but three patients with SLE were receiving corticosteroids which have been used successfully to treat lupus pneumonitis [7]. Therefore, corticosteroids may have minimized the pulmonary defects noted in the present series.

Our findings of a high prevalence of occult pulmonary dysfunction in SLE suggest that all patients with this disease should undergo pulmonary function tests as part of a complete assessment of organ involvement. Chest radiographs and even respiratory questionnaires are insensitive means of detecting the presence of lung disease in SLE. Prospective, longitudinal studies are required to determine how frequently isolated pulmonary function abnormalities progress to clinically significant lung disease.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the secretarial assistance of Ms. Janet Watson. The authors also thank Drs. Stephen E. Malawista, James D. Kenney, Charles A. DiSabatino and John Hayslett for referring patients for evaluation.

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