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Pulmonary involvement in systemic lupus erythematosus

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SUMMARY Several series have suggested that pulmonary function abnormalities are common in systemic lupus erythematosus. However, only isolated studies have attempted to relate these abnormalities to immunological aspects of the disease. In the present study respiratory symptoms, pulmonary function tests, and immunological data were reviewed in 22 patients with systemic lupus erythematosus. Seventeen subjects had either clinical evidence or abnormalities of lung function suggestive of pulmonary involvement. A restrictive ventilatory defect or reduction in pulmonary diffusing capacity for carbon monoxide was demonstrated in 14 of the patients only 4 of whom were dyspnoeic. There was no correlation between pulmonary involvement, co-existent renal lupus, and immunological abnormality.

The lungs and pleura are commonly involved in systemic lupus erythematosus (SLE) (Winslow *et al.*, 1958; Huang *et al.*, 1965; Laitinen *et al.*, 1973). Previous studies have suggested that pulmonary function abnormalities may be common in SLE in the absence of radiological abnormalities (Huang *et al.*, 1965; Gold and Jennings, 1966). There have, however, only been isolated studies on the clinical features, pulmonary function changes and immunological aspects in patients with SLE (Holgate *et al.*, 1976). In the present study we have assessed respiratory symptoms, pulmonary function, DNA antibody, and serum complement levels in 22 patients with SLE and examined the relationship of pulmonary involvement to immunological activity.

Patients and methods

PATIENTS

Twenty-two subjects, 17 women and 5 men, were investigated. All satisfied the preliminary criteria of the American Rheumatism Association for a diagnosis of SLE (Cohen *et al.*, 1971). The mean age was 33 (range 14 to 69 years). Eleven patients had biopsy evidence of renal involvement. The extra renal clinical SLE disease activity excluding pulmonary manifestations, was graded from 0 to +++. Zero represented no evidence of disease activity, + evidence of disease activity without major organ involvement or fever, ++ evidence of major organ involvement, and +++ fever greater than 38 °C and major organ involvement. Seventeen patients were receiving corticosteroids at the time of assessment in a daily dose of 10 to 15 mg.

PULMONARY FUNCTION TESTS

Static and dynamic lung volumes were measured using a standard vitalograph spirometer. Pulmonary diffusing capacity (transfer factor) measurement was carried out according to the method of Ogilvie *et al.* (1957). The measured transfer factor values were corrected for changes in haemoglobin concentration and alveolar volume. The correction for alteration in haemoglobin concentration was made using the correction formula of Cotes *et al.* (1972). In normalisation of the transfer factor for change in alveolar volume it has been assumed that a change in lung volume of 1 litre gives a change in transfer factor of 0·867 mmol/kPa (Cotes and Hall, 1970). The vital capacity and transfer factor were considered to be reduced if less than 80% of mean predicted.

ANTI-DNA ANTIBODIES

Anti-native DNA antibodies were measured by the Farr assay and with C^{14}-labelled *E. coli* native DNA (Radiochemical Centre, Amersham) as antigen (Hughes, 1971). The results were expressed as DNA binding capacity and the normal range is 0–30%.

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COMPLEMENT C3 AND C4

Serum C3 and C4 levels were measured by a radial immunodiffusion method, the normal range for C3 being 61–232 mg/dl and for C4 31–55 mg/dl.

ANTINUCLEAR FACTOR

This was measured using an indirect immunofluorescent technique and rat liver as substance (Beck, 1961).

RHEUMATOID FACTOR

This was measured using the R3 titration test of Denver laboratories.

Results

Table 1 summarises the respiratory symptoms and the chest radiographs in the 22 patients. Eleven patients gave a history of previous episodes of pleuritic pain. Chest radiographs showed obliteration of a costophrenic angle in 2 patients, a segmental atelectatic lesion in 1 patient, and diffuse reticular shadowing consistent with interstitial fibrosis in 1 patient.

One patient (Case 19) developed a left sided pneumothorax with 75% collapse of the left lung 6 months after the respiratory function tests shown in Table 2 were carried out. This complication occurred when he was recovering from a major disease exacerbation with pleuritic pain, pericarditis, myocarditis and fever, and when he was receiving 60 mg prednisolone and 10 mg of chlorambucil daily.

The respiratory function tests showed abnormalities in 16 patients (Table 2). In two of these (Cases 4 and 7), there was evidence of irreversible airways obstruction with a normal transfer factor although case 7 was a non-smoker. In the 14 other patients with abnormalities of respiratory function, 5 had reduced transfer factor alone and the remaining 9 had restrictive ventilatory defects in association with reduced transfer factor. In the latter group of 9 patients 4 were dyspnoeic but only 1 patient (case 14), had radiological evidence of interstitial fibrosis.

The immunological data are summarised in Table 3, along with the degree of system involvement. Anti-nuclear antibody was present in all sera in titres varying between 1/10 and 1/1000. Rheumatoid factor in a titre of 1/16 or greater was detected in 6 sera. Serum complement C4 levels in 21 sera tested were within the normal range in 7 and low in 14. DNA binding capacity was increased in 16 patients, the levels being highest in those with evidence of renal involvement. There were no significant differences between patients with and without reduced transfer factor with regard to presence or absence of renal disease, mean DNA binding capacity, mean C3 level, mean C4 level, or number of patients with a positive rheumatoid factor.

Discussion

Pleuritic pain was a common feature of SLE in this as in previous series. One of our patients developed a pneumothorax after a disease exacerbation with

Table 1 *Clinical and radiological features of 22 patients with SLE*

Case	*Sex*	*Respiratory symptoms*		*Cigarettes (per day)*	*Chest radiograph*
		Pleurisy	*Other*		
1	F	—	—	20	Normal
2	F	—	Dyspnoea	0	Normal
3	F	+	—	10	Normal
4	F	+	—	10	Normal
5	F	—	—	30	Normal
6	M	—	—	0	Normal
7	M	—	Wheeze	0	Obliteration costo-phrenic angle
8	F	+	—	0	Normal
9	F	—	—	0	Segmental atelectasis
10	F	+	—	15	Normal
11	F	+	Dyspnoea	10	Normal
12	M	+	—	15	Normal
13	F	—	—	0	Normal
14	M	—	Dyspnoea	20	Increased reticular markings
15	F	—	—	0	Normal
16	F	+	—	10	Normal
17	F	—	—	0	Normal
18	F	—	—	10	Normal
19	M	+	—	0	Obliteration costo-phrenic angle
20	F	+	—	0	Normal
21	F	+	—	0	Normal
22	F	+	Dyspnoea	0	Normal

pleuro-pericardial involvement and this complication has not previously been described with SLE.

This study has confirmed the frequency of pulmonary function abnormalities in the absence of radiological abnormalities in patients with SLE. Seventeen of our 22 patients had either clinical evidence or abnormalities of lung function suggestive of pulmonary involvement. The importance of correcting the transfer factor for changes in haemoglobin was emphasised in 2 patients (cases 8 and 21) who were anaemic during a disease exacerbation and whose uncorrected transfer factors expressed as percentage of mean predicted were 67% and 60% respectively, but corrected to 96% and 75%. Two patients had irreversible airway obstruction in the absence of impairment of transfer factor. The most common pulmonary function abnormality in our patients was a restrictive ventilatory defect or

Table 2 *Spirometric and gas transfer values in 22 patients with SLE*

Case	*Vital capacity (l)*				*Diffusing capacity (transfer factor; mmol/min/kPa)*		
	Observed	*Predicted*	*Mean predicted (%)*	*FEV^1% FVC*	*Observed*	*Predicted*	*Mean predicted (%)*
1	1·93	2·36–4·12	59	80	4·0	4·4– 7·8	65
2	1·98	2·28–4·04	62	97	3·8	4·4– 7·8	61
3	3·04	2·57–4·33	88	77	5·7	4·3– 7·7	98
4	4·13	2·84–4·60	110	68	5·4	4·7– 8·1	83
5	3·80	2·93–4·69	99	88	5·5	5·9– 9·3	72
6	3·56	3·06–5·13	87	100	5·7	3·9–17·1	54
7	2·61	2·94–5·14	64	56	4·9	3·5– 6·9	94
8	2·97	2·47–4·23	88	74	4·5	4·2– 7·6	75
9	3·20	2·59–4·35	92	78	6·0	5·8– 9·2	79
10	2·10	2·25–4·01	66	81	4·9	4·5– 7·9	79
11	2·08	3·66–5·42	45	92	4·5	6·8–10·1	53
12	3·80	4·82–7·02	64	94	7·1	7·4–10·8	78
13	4·13	2·94–4·70	108	77	6·9	5·9– 9·2	90
14	2·77	4·74–6·94	47	89	5·2	8·9–12·3	48
15	2·87	2·67–4·43	80	75	6·3	5·4– 8·8	88
16	3·27	2·63–4·39	93	72	4·2	5·4– 8·8	59
17	3·33	1·80–3·56	124	74	5·9	3·8– 7·2	107
18	3·20	2·73–4·49	88	90	8·3	5·4– 7·2	117
19	5·94	4·74–6·94	101	77	6·0	8·5–11·9	59
20	4·42	3·46–5·22	101	79	5·3	7·4–10·8	57
21	3·15	2·99–4·75	81	76	7·6	6·0– 9·3	99
22	1·82	2·94–4·42	49	94	5·1	6·0– 8·6	71

Table 3 *Immunological data of the 22 patients included in this study*

Case	*Sex*	*Renal involvement*	*Extra-renal activity**	*DNA binding (%)*	*C3 (mg/dl)*	*C4 (mg/dl)*	*ANF*	*R3*
Normal range				*0–30*	*61–232*	*31–55*		
1+	F	–	+	50	110	42	1000	256
2†	F	–	+	9	147	47	1000	1024
3	F	–	0	84	92	29	1000	Neg
4†	F	–	+	34	100	22	1000	Neg
5†	F	–	0	64	160	38	1000	Neg
6†	M	–	+	40	106	15	1000	Neg
7†	M	–	+	20	80	12	1000	512
8†	F	–	+	76	120	21	1000	Neg
9†	F	–	+	12	137	34	10	16
10†	F	–	–	0	–	–	1000	128
11†	F	–	+	69	72	10	256	Neg
12†	M	+	+	58	130	36	1000	Neg
13	F	+	0	94	162	20	256	Neg
14†	M	+	+	56	96	17	1000	Neg
15	F	+	+	97	73	3	1000	Neg
16†	F	+	+	80	98	29	1000	Neg
17	F	+	–	9	147	47	256	128
18	F	+	0	40	90	18	1000	Neg
19†	M	+	+++	90	100	60	250	Neg
20†	F	+	+	99	40	18	1000	Neg
21†	F	+	+	99	40	18	1000	Neg
22†	F	+	++	91	97	29	1000	Neg

*Extra-renal activity graded 0, +, ++, or +++).
†Patients with respiratory symptoms or abnormalities of pulmonary function.

impairment of transfer factor and this is in keeping with the findings of others (Edmonds *et al.*, 1975).

It has been suggested previously that patients with predominantly pulmonary involvement in SLE, had a low incidence of renal disease (Holgate *et al.*, 1976). In the group of patients investigated here no significant difference was found in the incidence of pleuro-pulmonary disease between those with and without renal involvement.

One of our patients (case 5), had no other clinical evidence of disease activity at the time of investigation, but had a raised DNA binding capacity and antinuclear antibodies in her serum. We would agree with others (Edmonds *et al.*, 1975) that pulmonary function tests appear valuable in demonstrating clinically latent abnormalities in patients without radiological evidence of lupus. Further follow up is required to determine whether lupus patients with asymptomatic abnormalities of pulmonary function are more likely to become symptomatic with future exacerbations of their disease and whether abnormalities of diffusing capacity improved on treatment of the disease process with corticosteroids or immunosuppressives. Our experience to date, based on the treatment of patients with symptomatic pulmonary disease suggests that this is not the case.

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