RELATIONSHIP OF SYSTEMIC LUPUS ERYTHEMATOSUS TO RHEUMATOID ARTHRITIS, DISCOID LUPUS ERYTHEMATOSUS, AND SJÖGREN'S SYNDROME

A CLINICAL STUDY

BY

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Because of the frequent presence of polyarthritis and the rheumatoid factor in cases of systemic lupus erythematosus (S.L.E.) and that of the L.E.-cell phenomenon and visceral lesions in cases of rheumatoid arthritis, it was thought that it would be profitable to study the correlation between the two diseases.

The dissemination of discoid lupus erythematosus, especially after exposure to strong sunlight, and its accompanying visceral manifestations have been known for a long time (Kaposi, 1872). There are also some data on the relationship between Sjögren's syndrome and S.L.E. in the recent literature (Heaton, 1959). However, the correlation of rheu-

matoid arthritis, discoid lupus erythematosus, Sjögren's syndrome, and S.L.E. has not been satisfactorily demonstrated, and we have therefore carried out more intensive systemic clinical, and laboratory investigations of the four conditions in 274 cases (Table).

Clinical and Laboratory Investigations

(1) Rheumatoid Arthritis*

In about 50 per cent. of a series of 160 classical cases of rheumatoid arthritis (R.A.) we found a

* Diagnosed by the criteria described by the American Rheumatism Association (Ropes, Bennett, Cobb, Jacox, and Jessar, 1957).

TABLE
COMBINATION OF SYMPTOMS AND INTERVAL BETWEEN TIMES OF ONSET IN 274 CASES

Basic Disease	Combination	Time of Onset of 2nd Disease					Total Combined or Alone	Total Cases
		Same Time	2-5 yrs later	6-10 yrs later	11-15 yrs later	16-20+ yrs later		
S.L.E.	With R.A. . . .	11	4	2			15	36
	With Sj		1				3	
	With Disc L.E. . .	6	2				8	
	Alone	—	—	—	—	—	10	
R.A.	With L.E. cells . .		2	4	2	2	10	160
	With Sj		1	2	2	3	8	
	With Disc L.E. . .		1	1	1*		3	
	Alone	—	—	—	—	—	139	
Discoid L.E.	With R.A. . . .		1		1		2	50
	With S.L.E. . . .		2				2	
	With Sj				1		1	
	Alone	—	—	—	—	—	45	
Sjögren's Syndrome	With R.A. . . .	3	1		1		5	28
	With S.L.E. . . .	1	2				3	
	Alone	—	—	—	—	—	20	
Total	Combined						60	274
	Alone						214	

protein anomaly, dysproteinaemia. Serum electrophoresis showed increased gamma-globulin, positive thymol turbidity, positive Kürten reaction, and in some cases a positive Sia-reaction and cryoglobulin. In the other arthritic patients with exactly similar clinical symptoms there was no such alteration in the serum proteins.

Ten of these arthritic patients with dysproteinaemia had L.E. cells which were indistinguishable from the S.L.E. cases (they are shown in the Table in the R.A. group).

The same protein anomaly was found in nearly every one of a series of 36 patients with S.L.E., and fifteen* of these 36 patients (41·7 per cent.) showed a classical polyarthritis of the rheumatoid type; in four of the latter the polyarthritis had developed 2 to 5 years after the manifestation of the typical clinical and laboratory features of S.L.E.

In this way we have 36 S.L.E. patients and ten arthritics with L.E. cells, making a total of 46 with L.E. cells. Of this group of 46 cases the ten arthritics and fifteen of the S.L.E. patients had polyarthritis, a total of 25 out of 46 (54·3 per cent.).

(2) Discoid Lupus Erythematosus†

Eight of the series of 36 patients with S.L.E. also showed the typical lesions of discoid lupus erythematosus. In six the onset was simultaneous and in two the skin lesions appeared 2·5 years after the onset of S.L.E.

In two patients the skin eruptions appeared first and the signs and symptoms of S.L.E. followed 2·5 years later.

In three arthritics the discoid skin lesions appeared 2 to 15 years after the onset of the polyarthritis,‡ and in two patients the skin eruptions appeared first and the polyarthritis developed 2·15 years later.

(3) Sjögren's Syndrome§

The combination of joint and eye lesions with hypofunction of the lacrimal, nasal, and salivary glands has been termed the sicca syndrome and Sjögren's syndrome. Sjögren (1933) described nineteen such patients, some with associated polyarthritis and parotid swelling, as well as microscopic changes in the conjunctiva, cornea, and lacrimal and

salivary glands, and these symptoms have frequently been observed in conjunction with rheumatoid arthritis. A relationship between this syndrome and the other diseases that primarily affect the connective tissue has been suggested but rarely documented.

In the course of our investigations we found that the symptoms of Sjögren's syndrome (Sj) were observed simultaneously with those of R.A. in three cases and with those of S.L.E. in one case. These are shown in the Table under the heading of Sjögren's Syndrome.

In eight arthritics Sj developed 2·25 years after the onset of polyarthritis, in three S.L.E. patients 2·10 years after the onset of S.L.E., and in one Discoid L.E. patient 13 years after the skin eruptions.

However, in four cases Sj appeared first, and was followed after 2·15 years by R.A. in two patients and after 2·5 years by S.L.E. in two patients.

Discussion

The relationship of S.L.E., rheumatoid arthritis, discoid lupus erythematosus, and Sjögren's syndrome should be observed progressively, as one or other group of symptoms may predominate in the same patient with the passage of time, and they may occur in any combination and in any order.

We were able to demonstrate various combinations in 60 out of 274 cases (21·8 per cent.), but these figures represent a minimal frequency of concurrent symptoms limited by the regularity with which repeated examinations could be carried out. The interrelationship of other members of the collagen group of diseases—polyarteritis nodosa, scleroderma, dermatomyositis—the development of one condition into another, and their frequent combination with S.L.E. have already been accepted by most observers (Pagel and Treip, 1955).

Summary

The relationship and concurrent course of systemic lupus erythematosus, rheumatoid arthritis, discoid lupus erythematosus, and Sjögren's syndrome have been studied by clinical and laboratory investigations, the diagnosis of the four conditions being strictly controlled by various tests.

The nature and incidence of the combinations of these four conditions in individual patients largely depend on the time of the investigation, the duration of the observation period, and the frequency with which the patients can be reviewed.

* These are shown in the top row of the Table in the S.L.E. group.

† For criteria of diagnosis, see Appendix.

‡ In one remarkable case (marked * in the Table) the rheumatoid arthritis began in 1948 (diagnosis supported by the histological study of a subcutaneous rheumatic nodule); L.E. cells first appeared 10 years later (in 1958), and 2 years later (in 1960) skin eruptions were observed (Bencze, Lakatos, and Forró, 1961).

§ For criteria of diagnosis (see Appendix).

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APPENDIX

Criteria used in Diagnosis

Disc. L.E.:

(A) Results of Laboratory Investigations:

- (i) Positive L.E.-cell phenomenon;
- (ii) Raised erythrocyte sedimentation rate;
- (iii) Dysproteinaemia (lowered albumin, increased gamma-globulin, abnormal thymol turbidity);
- (iv) False positive Wassermann reaction;
- (v) Haematological changes (anaemia, leucopenia, thrombocytopenia).

(B) Clinical Symptoms:

- (i) Fever (often septic);
- (ii) Skin eruptions; erythematous rash on face; Raynaud's phenomenon; photosensitivity; urticaria;
- (iii) Joint lesions (arthralgia, polyarthritis of rheumatoid type);
- (iv) Serositis or polyserositis (pleuritis, pericarditis);
- (v) Adenomegaly, splenomegaly, hepatomegaly;
- (vi) Visceral lesions (kidney, lung, heart, central nervous system, gastro-intestinal tract, pancreas, liver).

(C) An episodic clinical process and a favourable response to treatment with steroids or chloroquine.

For a definite diagnosis we required the positive L.E.-cell phenomenon, the raised erythrocyte sedimentation rate, and at least one other abnormal laboratory test, and at least two clinical symptoms. Our patients had been systematically reviewed every 3 to 6 months since 1954 to check the *episodic clinical process* and the effects of therapy.

SJÖGREN'S SYNDROME:

(A) Hypofunction of the lacrimal, nasal, or salivary glands, manifest by dryness of the eyes, mouth, nose, larynx, or skin, sometimes scleroderma-like, with skin lesions and achylia;

(B) Parotid swelling;

(C) Arthralgia or polyarthritis of rheumatoid type;

(D) Raynaud's phenomenon;

(E) Photosensitivity.

The degree of keratoconjunctivitis sicca (inflammation of the cornea and conjunctiva in consequence of dryness) was determined by Schirmer's method of measuring the tear secretion. A filter paper, 0.5 cm. wide and 3.5 cm. long was applied to the corner of the eye, and the degree of humidity noted after 5 min. The test was considered as positive only if the strip of paper moistened was smaller than 15 mm.

For a definite diagnosis we required at least one of symptoms (B) to (E) besides the keratoconjunctivitis sicca (A).

Le rapport entre le lupus érythémateux disséminé et l'arthrite rhumatoïdale, le lupus érythémateux discoïde et le syndrome de Sjögren. Etude clinique

RÉSUMÉ

Le rapport réciproque et l'évolution concomitante du lupus érythémateux disséminé, de l'arthrite rhumatoïdale, du lupus érythémateux discoïde et du syndrome de Sjögren furent étudiés par des méthodes cliniques et de laboratoire; le diagnostic des quatre affections fut contrôlé strictement par de différents tests.

La nature et la fréquence des combinaisons de ces quatre affections chez des malades individuels dépendent pour une grande part du moment de l'examen, de la durée de la période d'observation et de la fréquence avec laquelle on peut re-examiner le malade.

Relaciones entre el lupus eritematoso diseminado, y la artritis reumatoide, el lupus eritematoso discoide y el síndrome de Sjögren.—Estudio clínico

SUMARIO

Las relaciones y el curso simultáneo del lupus eritematoso diseminado, de la artritis reumatoide, del lupus eritematoso discoide y del síndrome de Sjögren fueron investigados por métodos clínicos y de laboratorio; el diagnóstico de las cuatro afecciones fué estrictamente controlado por diferentes reacciones.

La naturaleza y la frecuencia de estas cuatro afecciones en enfermos individuales depende en gran parte del tiempo de la investigación, de la duración del periodo de observación y de la frecuencia con la cual se puede re-examinar el enfermo.