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Lupoid Features in a Case of Leprosy[1, 2]

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A serologic overlap has been described between leprosy and diseases with autoimmune phenomena, in particular the connective tissue diseases. Indeed a wide spectrum of autoimmune-like factors has been found in leprosy, including the rheumatoid factors ([7]), thyroglobulin antibodies ([3]), and cold precipitable proteins ([20]), as well as positive Coombs tests and false positives in serologic tests for syphilis and typhoid fever ([23]).

The detection of L.E. cells and antinuclear factors ([5]) provides additional evidence of autoimmune-like reactions in leprosy. In addition, clinical similarities between leprosy and the connective tissue diseases have been emphasized ([5, 20]).

In the light of such findings it seemed interesting to us to describe a case of lepromatous leprosy, which, in addition to the more frequent serologic alterations, showed conspicuous clinical features similar to those of systemic lupus erythematosus. This case seems particularly fitting to illustrate the intricate etiopathogenetic and clinical problems associated with the extensive serologic and clinical overlap between leprosy and a group of diseases with autiimmune phenomena.

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CASE REPORT

The patient was a 42-year-old woman (S.S.), whose mother's brother died from leprosy at the Hansenian Colony, Gioia del Colle, Bari. A high incidence of leprosy is recorded in the patient's town.

The patient was in good health until the age of 14, when she began to complain of joint pains, mostly involving wrists, elbows, and knees. Mild remittent fever was present. Initially these symptoms occurred sporadically; later they became more frequent, and cutaneous manifestations, chiefly erythematomacular, with circumscribed infiltrations and nodules, appeared on the face, hands, and legs.

At the age of 27, after bacteriologic examination of a nasal smear, a diagnosis of leprosy was made, and the patient was hospitalized at the Hansenian Colony in Gioia del Colle. Eight months later she was discharged from the Colony, her condition being much improved. Some months later (1950), however, she was readmitted because of relapse with symptoms. After that she was hospitalized uninterruptedly at the Colony. She was treated with sulfone derivatives, calcium, and vitamins. Her skin changes were of the macular type after onset of the disease.

The patient's disease state remained practically stationary for 13 years, until April 1963. At that time continuous fever (38°-39°C) appeared, with diffuse myalgias and severe joint pains, particularly involving the elbows and shoulders. At the same time erythematous manifestations rapidly became more distinct, spreading on the nose and cheeks in a typical butterfly-like

pattern. Later on, the erythema involved the whole face, neck, and sternal area.

Such symptoms were quite sensitive to high dosage treatment with corticosteroids, mostly given as prednisone. Indeed, while the cutaneous manifestations became much less evident, the muscle and joint involvement greatly improved under such treatment. The withdrawal or even the lowering of the prednisone dosage to a level below 25 mgm. per day was sufficient to exacerbate the cutaneous manifestations as well as the arthromyalgias and the fever. In fact the patient was under continuous treatment with corticosteroids after April 1963, the steroids being administered in dosages varying from 30 to 100 mgm. of prednisone daily, or equivalent dosages of other corticosteroids, by different routes (oral, intramuscular, or intravenous).

The patient's skin lesions were sensitive to sunlight. She avoided exposure to sunlight in the Colony's park so as not to exacerbate her symptoms.

At this time physical examination revealed a pale, undernourished woman. There was total alopecia of the eyebrows; the hair was scanty and brittle. A diffuse red-purple erythema spread in a butterfly-like pattern over her cheeks and nose; it involved also the forehead and the lateral aspects of the neck, showing scattered telangiectasias and slight edema. The latter changes were most conspicuous in the lower eyelids.

Erythemato-purpuric macules occurred also in the sternal area and dorsal surface of the fingers and hands, involving the thenar and hypothenar eminences and palmar surface of the terminal phalanges. In such areas the purpuric changes were more marked. Erythemato-desquamative cheilitis was observed at the inferior lip. There was moderate enlargement of the spleen and liver.

Despite the intensive therapy, fatigue, anorexia, and hyperpyrexia remained unaltered, and the patient's general condition deteriorated progressively. At the beginning of January 1965 she experienced crisis with dyspnea and tachycardia. On 19 February she died of cardiac failure. Necropsy was not allowed.

LABORATORY EXAMINATIONS

Laboratory examinations were carried out during the entire length of the hospitalization period. The red blood cell count was 3,570,000 in May 1960, 3,400,000 in July 1962, and 3,440,000 in March 1963. Hemoglobin on the same dates ranged from 10 to 9 gm. per 100 ml. White blood cells ranged from 4,600 to 4,800.

Repeated urinalysis gave normal results, with specific gravity ranging from 1.015 to 1.030. Some urobilinuria was observed in two urine samples. Blood urea nitrogen ranged from 20 to 27 mgm. per 100 ml. until March 1963.

Gallbladder stones were demonstrated by x-ray examination.

Destructive lesions of leprous type were observed in the feet on x-ray examination in December 1960. The distal phalanx of the fourth toe of the left foot was amputated in July 1964. A sinus, with a moderate amount of discharge, remained on the lateral aspect of the left big toe.

In the months following the onset of the persisting arthromyalgias with fever, i.e., April 1963, marked changes were observed in various blood and urine examinations. The erythrocyte sedimentation rate was moderately elevated (17 mm. in one hour and 50 mm. in two hours, in the Westergren method) in December 1963, and much more (100 mm. in one hour, and 135 mm. in two hours) in October 1964.

There was anemia. The red blood cell count was 2,640,000 in April 1964, and 2,580,000 in October 1964. Hemoglobin measured 7 (April 1964) and 6.5 (October 1964) gm. per 100 ml. The white blood cell count was 4,200 in April 1964 and 4,800 in October 1964, with 70 neutrophils, 25 lymphocytes and 5 monocytes in the differential count.

Marked proteinuria was found (1.5 gm. per liter in October 1964) with an abnormal urinary sediment (a few red cells, many white blood cells and hyaline and granular casts). Blood urea nitrogen then measured 40 mgm. per 100 ml.

Zinc sulfate and thymol turbidity and cadmium sulfate flocculation tests were strongly positive. Serum protein electrophoresis showed marked hypergamma-

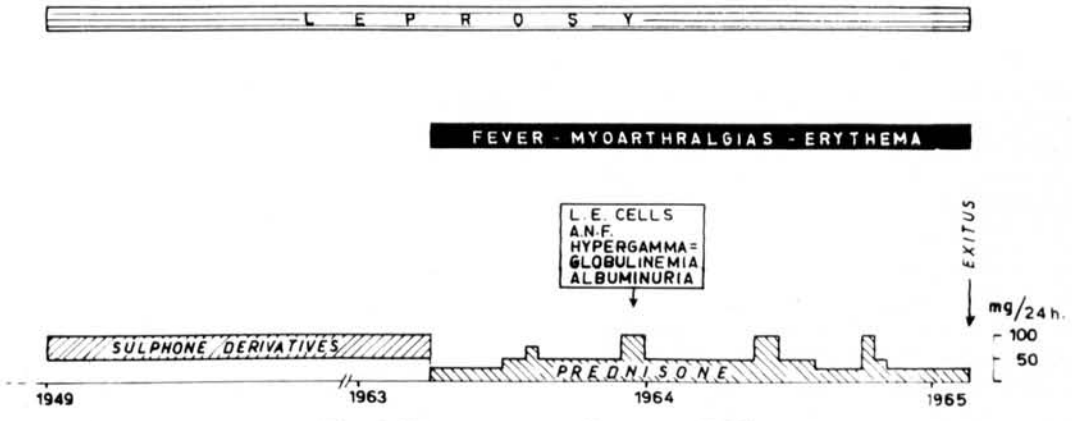

FIG. 1. Disease course of patient. (S.S.)

globulinemia with hypoalbuminemia. The following figures were recorded: albumin, 31.3; alpha$_1$ globulin 5.5; alpha$_2$ globulin, 9.9; beta globulin, 11.5; and gammaglobulin, 42.5 per cent. The total protein was 9.55 gm. per cent. The albumin-globulin ratio was 0.45.

Serologic tests for the rheumatoid factors. The R.A. test (Hyland Laboratories, Los Angeles) and sensitized sheep cell agglutination (S.S.C.A.) tests, as described by Heller *et al.* [13], were performed. Both tests were completely negative in June 1962. Later (April 1963) they became slightly positive: R.A. test 1/20; S.S.C.A. 1/14.

Antinuclear factors. The indirect technic was employed according to the description by Weir *et al.* [26]. The L.E. cell test was performed as described by Zinkham and Conley [27]. Many typical L.E. cells were detected at first testing (December 1963) (Fig. 1). Antinuclear factors were also present (1/32).

Immunoelectrophoresis. Immunoelectrophoretic analysis of the patient's serum was performed by the method of Grabar and Burtin [11], modified as a micromethod according to Scheidegger [25]. Polyvalent horse (No. 2510)[4] and goat (No. 1226)[5] antisera against normal human serum, and strictly specific antibeta$_{1A/C}$ rabbit antiserum (No. 2503)[4] were used. Increases in IgG, IgA, and, to less extent, IgM immunoglobulins were detected (Fig. 2). In contrast albumin and beta$_{1A/C}$ globulin values were remarkably decreased (Fig. 3).

DISCUSSION

For a long time the clinical pattern of our patient was typical for a diagnosis of lepromatous leprosy, which occurred in the patient's family and environment as well. After years of hospitalization and stationary disease a new symptom complex was superimposed on the clinical pattern of lepromatous leprosy. Many of the patient's clinical and laboratory findings were similar to those commonly observed in systemic lupus erythematosus, as described in the case series of different authors [18]. In fact febrile episodes, arthromyalgias, renal involvement with marked proteinuria, and the finding of L.E. cells in suitable preparations occurred in this patient.

In particular, several aspects of the skin manifestations were indistinguishable from those of systemic lupus erythematosus, viz., their erythemato-purpuric character and sensitivity to sunlight exposure, the distribution in a butterfly-like pattern on the face, and the simultaneous involvement of most of the skin areas that are usually the site of the manifestations of systemic lupus erythematosus.

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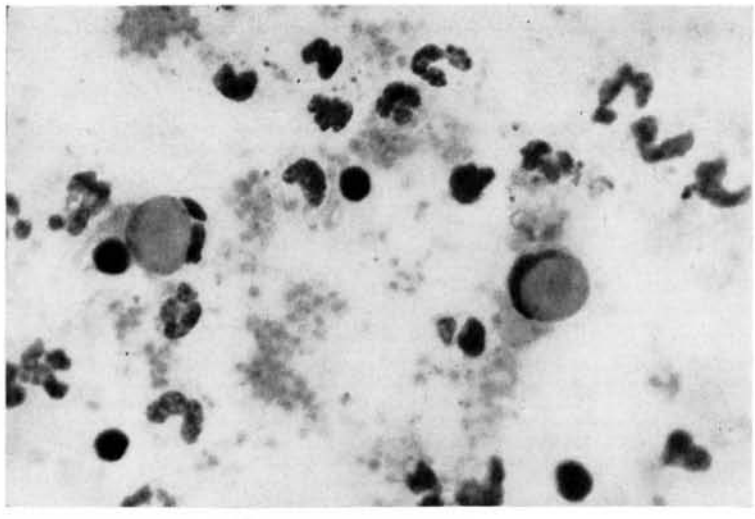

FIG. 2. L. E. cell in the peripheral blood of the patient. (S.S.)

In addition, the aspects and course of the cutaneous manifestations were different from those of lepra reactions, although the polymorphism of such lesions is well known. Actually skin changes of the reactional type ([9]) were never observed in our patient, such as erythema nodosum or manifestations of erythema multiforme, or subcutaneous nodules with a tendency to ulcerate.

On the other hand the immunoelectrophoretic pattern of the patient's serum showed an interesting feature, namely a considerable decrease of the $beta_{1A/C}$ globulin fraction, a finding that has been described as characteristic of systemic lupus erythematosus ([24]). Indeed it was not found, or at any rate never definitely, in 47 sera of leprous patients (40 of the lepromatous and seven of the borderline type). It should be remarked that seven of these patients exhibited typical lepra reactions, a diagnosis that was debatable in our case at the time of our study, and that a number of them showed L.E. cells and antinuclear factors.

On the basis of findings described, it seems to us that this case represents an

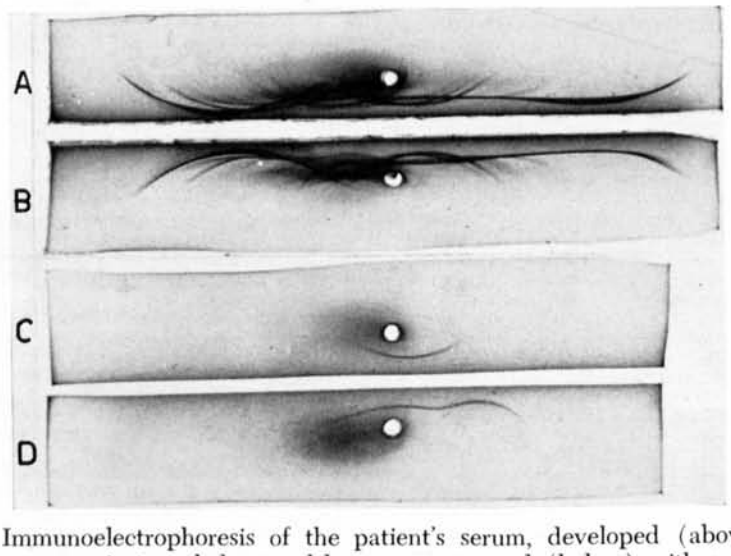

FIG. 3. Immunoelectrophoresis of the patient's serum, developed (above) with a horse antiserum against pooled normal human serum, and (below) with a rabbit antiserum anti-$beta_{1C}$. **A** and **C:** patient's serum. **B** and **D:** normal human serum. Note the increase of IgG and IgA immunoglobulins, and the marked decrease of the $beta_{1C}$ fraction.

instance of leprosy with clinical and serologic overlap with systemic lupus erythematosus.

The development of lupus-like clinical alterations seems particularly interesting in view of the marked serologic similarities (conspicuous hypergammaglobulinemia, occurrence of antinuclear factors, red cell antibodies, false positives in the Wassermann reaction) between the leprosy and systemic lupus erythematosus.

L.E. cells and antinuclear factors were present in our case; these phenomena, however, may occur in patients with lepromatous leprosy who do not show distinctive clinical features from other leprous patients without antinuclear factors. The same argument seems valid to us for a number of clinical features that may occur in cases of leprosy but are otherwise typical of systemic lupus erythematosus.

In other words all these various aspects cannot prove the diagnosis of systemic lupus erythematosus, not even in the form of an associated disease, in a leprous patient.

Because of the protean aspects of leprosy, similar problems may arise in the diagnosis between that and other diseases; indeed, as observed recently, there may be a striking resemblance between leprosy and sarcoidosis [8], which sometimes makes the distinction between the two impossible [16].

On the other hand, serologic [14] and clinical interrelationships have been described in the group of connective tissue diseases [2, 15, 17, 19, 21, 22] between the connective tissue disease and other disease states with autoimmune alterations [1, 4, 6, 12, 22], or in the group of the autoimmune diseases [10].

The special interest of the case described lies in the demonstration of such a wide overlap between the serologic and clinical features of leprosy and those of systemic lupus erythematosus. Indeed the serologic intricacy of leprosy with disease states in which circulating autoimmune factors occur, may indicate some similarities in the etiopathogenetic mechanism active in such diseases. On the basis of the case described here, and other data in the literature [5, 20], it seems attractive to suggest that in some instances such similarities in the etiopathogenetic mechanisms, besides leading to a serologic overlap, may attain the clinical level.

As emphasized elsewhere [5] the interrelationships between autoimmune diseases and leprosy seem of particular relevance to understanding of the fundamental mechanisms underlying such various diseases. Indeed diseases of known etiology with autoimmune factors, such as leprosy, may be considered as true experiments of nature, throwing some light on the obscure etiopathogenetic mechanisms of diseases with which they share a number of laboratory and clinical aspects. Reciprocally, established points in the pathogenetic and clinical aspects of the connective tissue and autoimmune diseases suggest new approaches to understanding of some features of leprosy.

Consequently, on the basis of the wide spectrum of autoimmune activities found in leprosy, a therapeutic trial with antimitotic or immunosuppressive drugs, as suggested by Matthews and Trautman [20], seems definitely worthwhile in leprous patients. Furthermore, the overlap between leprosy and systemic lupus erythematosus suggests a trial of chloroquine, which might be particularly indicated in some stages and forms of leprosy, i.e., the most active cases and the reactional phases.

SUMMARY

A case of lepromatous leprosy is described which showed a number of lupoid serologic and clinical features. This serologic and clinical overlap is discussed in the light of possible similarities in the etiopathogenetic mechanisms active in leprosy and in diseases with autoimmune phenomena.

A therapeutic trial with antimitotic drugs, or with chloroquine, is suggested, particularly for the reactional phases of leprosy.

RESUMEN

Se describe un caso de lepra lepromatosa la cual mostró un número de características

lupoides, serológicos y clínicas. Se discute esta sobreposición serológica y clínica a la luz de posibles similitudes en los mecanismos activos etiopathogeneticos en lepra y en enfermedades con el fenómeno de autoinmunidad.

Un ensayo therapeútico con drogas antimitóticas, o con cloroquina, se sugiere, particularmente en las fases reaccionales de la lepra.

RÉSUMÉ

On décrit ici un cas de lèpre lépromateuse montrant un certain nombre de caractéristiques sérologiques et cliniques lupoïdes. On a discuté de cette interférence sur le plan sérologique et clinique, à la lumière de similarités possibles dans les mécanismes étiopathogéniques intervenant dans la lèpre et dans les maladies avec phénomènes d'auto-immunité.

On suggère de procéder à un essai thérapeutique avec des médicaments anti-mitotiques, ou bien avec la chloroquine, particulièrement dans les phases réactionnelles de la lèpre.

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