

SYSTEMIC LUPUS ERYTHEMATOSUS WITH MULTIPLE MYELOMA

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Abstract. A 44-year-old white man presented with an erythematous-squamous rash in the supra-orbital and pre-auricular regions of the face. The diagnosis systemic lupus erythematosus was confirmed by histopathology, immunofluorescence (circulating antinuclear antibodies and a positive lupus band test), and by immunoelectron microscopy. Further examinations disclosed a multiple myeloma of the IgG type without cutaneous involvement. The coexistence of these two disorders has not been reported previously.

Key words: Systemic lupus erythematosus; Multiple myeloma; Coexistence

Cutaneous lesions in multiple myeloma (MM) are rare. They may occur as specific infiltrations—either as primary cutaneous extramedullary plasmacytoma (6) or as cutaneous extension of an underlying bone involvement (9). On the other hand, various non-specific cutaneous lesions have been reported in association with MM (2).

In this paper we describe a patient who presented with typical criteria of both, systemic lupus erythematosus (SLE) and MM. The diagnosis SLE was confirmed by histopathology, immunofluorescence and immunoelectron microscopy.

CASE REPORT

In April 1977, a 44-year-old white man was admitted to our dermatological department with a 2-month history of a slowly spreading, erythematous-squamous rash in the supra-orbital and pre-auricular regions of the face. In addition he complained about arthralgia of the knees and elbows. There was no evidence of Raynaud symptoms or phototoxicity.

The tentative diagnosis SLE was confirmed by a positive Lupus Band Test (LBT) and the presence of circulating antinuclear antibodies=ANA (Titre 1/80). Additional laboratory studies revealed ESR 150 mm/hr (Westergren), erythrocytes 3 130 000/mm³, hemoglobin level 9.6 g/100 ml, WBC count 2 500/mm³, with a normal differential. The bone marrow smear showed an increased number of abnormal plasma cells and was diagnostic for plasmacytoma. The total serum protein level was elevated (13.4 g/100 ml). Serum electrophoresis exhibited an in-

creased gammaglobulin (55.9%); decreased albumin (28.9%) and alpha 1 (1.6%) and beta (5.7%) fractions, respectively, were found. The alpha 2 fraction was within normal limits. Immunoelectrophoresis revealed a paraprotein band of the lambda type in the gammaglobulin fraction. The results of quantitative determinations of the serum proteins and complement fractions performed by radial immunodiffusion are listed in Table I.

By indirect immunofluorescence, using monkey oesophagus and rat liver as substrates, circulating ANA with homogeneous and peripheral patterns were found (Titre 1/80). Antibodies (AB) to double-stranded native deoxyribonucleic acid (DNA), performing Crithidia luciliae system (11) could not be demonstrated. Cryoglobulins were present in the serum of the patient. Blood T and B cell counts showed no abnormalities. HLA-A3, W25, B5, B12, CW₁, VW₃ were demonstrated.

An X-ray skeletal survey revealed osteolytic marrow changes in the ulna and radius of both sides (Fig. 1B), the scapula, the clavicle, the pelvis and the cranium (Fig. 1A). There was no evidence of depositions of amyloid. Urinalysis revealed 3+ protein; Bence Jones protein was absent.

The following laboratory tests were negative or within normal limits: VDRL, TPHA, thrombocyte count, clotting time, fasting blood sugar, SGOT, SGPT, alkaline phosphatase, LDH, serum bilirubin, serum electrolytes, serum iron, cholesterol, triglycerides, uric acid, blood urea nitrogen, serum creatinine, creatinine clearance, acid phosphatase, rheuma factor, C-reactive protein, Waaler-Rose test, Latex test, LE-cell preparations, chest X-ray and electrocardiogram.

Histopathologic examination of the skin from the erythematous pre-auricular area showed hyperkeratosis, atrophy of the epidermis and moderate signs of hydropic degeneration of the basal cell layer. The upper part of the dermis was edematous, and fibrinoid deposits occurred around collagen bundles and small blood vessels. A small number of lymphocytes surrounded the blood vessels. Increased numbers of plasma cells or abnormal plasma cells could not be detected.

Direct immunofluorescence. Biopsy specimens were taken from involved, erythematous (pre-auricular), and uninvolved sun-exposed skin of the extensor surface of the fore arm. Tissue was processed for direct immunofluorescence according to established methods (1). For characteristics of antisera, see reference (4). The lupus band test was positive. Fine granular deposits of IgM, IgG and C₃ were detected in a band-like distribution along the basement membrane zone (Fig. 2) and less con-

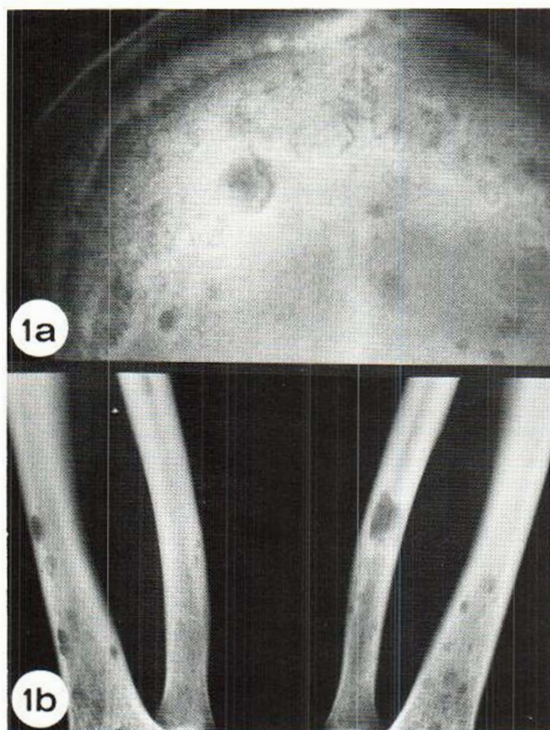


Fig. 1. Osteolytic bone marrow changes in (a) the frontal bone and (b) the ulna and the radius.

spicuous around the dermal blood vessels. IgA was negative. Fluorescence was found predominantly in the involved skin, but was present also in the uninvolved skin, though weaker in intensity.

Immunoelectronmicroscopy. A shave biopsy was obtained with a razor blade from an erythematous area of the pre-auricular skin. Chopped 50 μ m sections of the unfixed tissue were processed for the ultrastructural demonstration of in vivo bound Ig, performed by the horseradish peroxidase anti-horseradish (HRP-anti HRP) technique, as previously described (3).

Electron-dense deposits representing the HRP-reaction product were present throughout the basement membrane zone (Fig. 3A). Small irregular aggregates were found directly below the basal lamina between the anchoring fibrils and a few small deposits also between the collagen fibres in the uppermost dermis. The electron density of the basal lamina itself was slightly increased but its typical amorphous structure was preserved. The lamina lucida and the cytomembrane of the basal keratinocytes were almost completely free of deposits; only occasionally did small aggregates of reaction product occur within the lamina lucida. Control sections were completely free of reaction product (Fig. 3B).

Treatment. When the diagnosis SLE and simultaneous MM had been established, the patient received a therapeutic regimen of 4 mg 6-Methylprednisolone (Urbason, Hoechst-Austria) and 50 mg Cyclophosphamide (Endoxan, Laevosan-Linz) daily. This treatment resulted in a

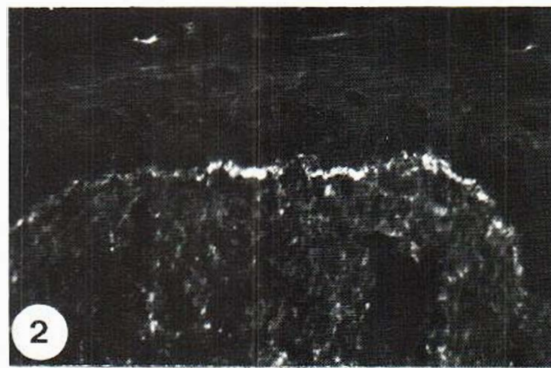


Fig. 2. Perilesional, pre-auricular skin, direct immunofluorescence, anti-human IgG conjugate, positive lupus band test, represented by fine granular fluorescent deposits along the basement membrane zone and around the dermal blood vessels.

complete disappearance of the skin lesions with 6 weeks and the ANA became negative at this time.

DISCUSSION

The patient presented with two distinct diseases, SLE and MM. The diagnosis of SLE was based on: 1) facial erythema, 2) arthralgia in knees and elbows, 3) typical histopathological findings, 4) positive LBT in direct immunofluorescence, 5) circulating ANA, 6) C₄ deficiency (5) and 7) characteristic ultrastructural findings in immunoelectron microscopy (10). The diagnosis MM-IgG type was based on the following criteria: 1) Multiple focal osteolytic bone marrow changes, 2) a paraprotein band of the gammaglobulin fraction by serum protein electrophoresis, 3) elevated IgG by immunoelectrophoresis and by radial immunodiffusion, 4) increased numbers of plasma cells in bone marrow

Table 1. Radial immunodiffusion

	Patient's serum (mg/100 ml)	Normal limits (mg/100 ml)
Immunoglobulin (Ig)		
IgG	6 930	1 000–1 500
IgA	50	170–250
IgM	35	100–150
Complement fraction (C)		
C ₃	125.0	90–130
C ₄	0	20–50
C ₅	15.0	8.1–25.2

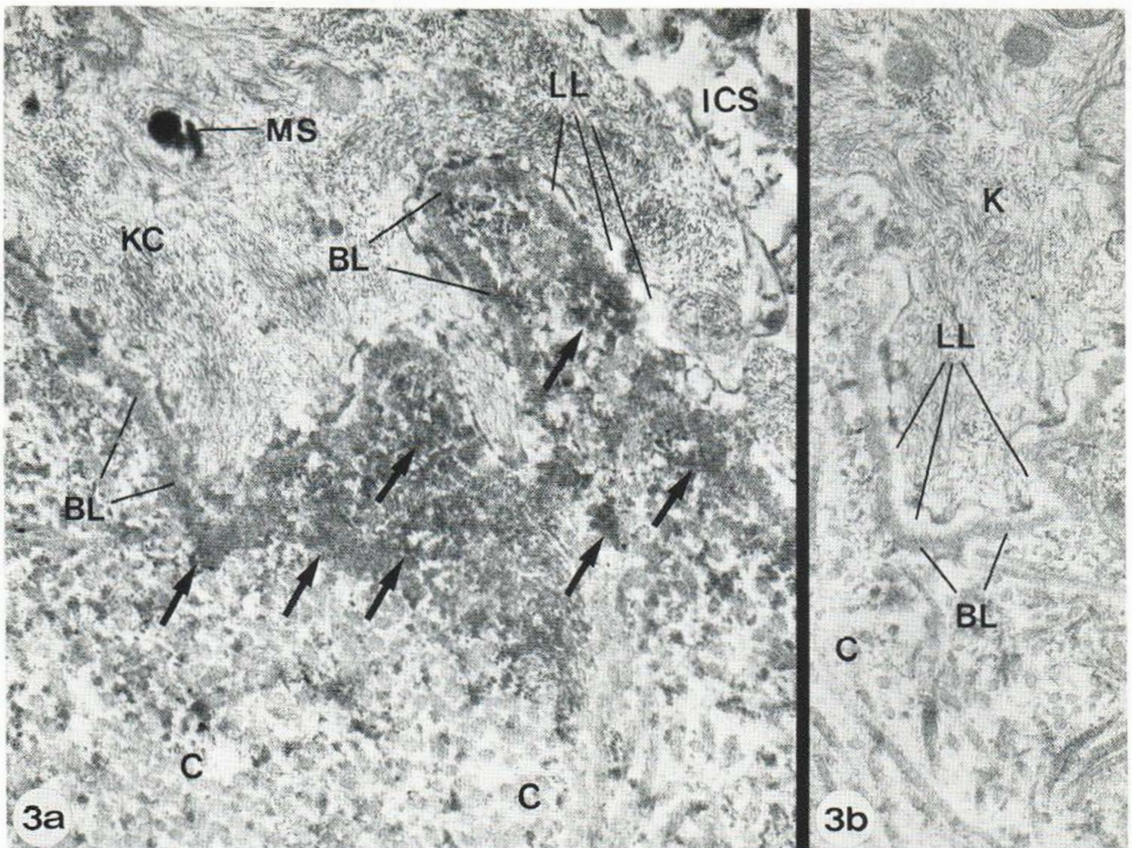


Fig. 3. Immunoelectronmicroscopy of involved skin. (a) Electron-dense reaction product (arrows) visualizing in vivo bound Ig is present in the uppermost dermis below the basal lamina (BL). The lamina lucida (LL) is almost completely free of deposits. The electron density of the

basal lamina is slightly increased. C, Collagen bundles; ICS, intercellular space; K, basal keratinocytes; MS, Melanosome. (b) Control is free of reaction product, LL, Lamina lucida; BL, basal lamina; C, collagen; K, keratinocyte.

smear, diagnostic for plasmocytoma. Proteinuria in the absence of Bence Jones protein, anemia, leukopenia, persistently and markedly elevated ESR, could not serve as differential diagnostic criteria in this case, since all these findings may occur in either, SLE and in MM.

The histopathology was fairly typical of SLE. Consequently it could be ruled out that the erythematous skin lesions simply represented myelomatous infiltrations of the skin. No plasma cells could be detected in histopathological specimens and immunofluorescence showed a positive LBT. Direct immunofluorescence investigations of specific skin lesions in MM did not produce positive results, when performed (9), and in only 50% of marrow smears from patients with MM was characteristic fluorescence of the myeloma cells found (12).

Non-specific lesions in MM appear rather as secondary vis-à-vis depositions of abnormal proteins such as amyloid or cryoglobulins, vs. anemia, leukopenia, thrombocytopenia or involvement of internal organs, e.g. kidney and lung (2). In addition, herpes zoster, fungus infections, xanthomatosis and scleroderma-like lesions have been reported (9).

To our knowledge the occurrence of SLE together with MM has not been described and recently published papers do not list MM among the neoplasias developing in SLE (7) or diseases showing positive LBT (8).

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