Subacute Cutaneous Lupus Erythematosus: Report of a Patient Who Subsequently Developed a Meningioma and Whose Skin Lesions Were Treated With Isotretinoin

Trent T. Richardson, MD, San Antonio, Texas
Philip R. Cohen, MD, Houston, Texas

GOAL

To examine the emergence of malignancies in patients diagnosed with subacute cutaneous lupus erythematosus.

OBJECTIVES

1. To discuss the possible etiology and clinical presentation of subacute cutaneous lupus erythematosus.
2. To outline a brief history of case studies in which patients with lupus erythematosus–like symptoms were associated with hematologic malignancies.
3. To present treatment options for the management of subacute cutaneous lupus erythematosus.

CME Test on page 190

This article has been reviewed by Michael Fisher, MD, Professor of Dermatology, Albert Einstein College of Medicine, in August 2000.

Cancer has been reported in patients with systemic lupus erythematosus (SLE). A possible association of the development of hematologic malignancies in patients with SLE has been suggested. In some patients, subacute cutaneous lupus erythematosus, a distinct subset of lupus erythematosus, has appeared, resolved, or both as a solid tumor-related paraneoplastic syndrome. A woman in whom a meningioma was diagnosed 44 years following the onset of subacute cutaneous lupus erythematosus is described; her skin lesions improved after starting isotretinoin therapy. The relationship between lupus erythematosus and neoplasia is summarized and the management of subacute cutaneous lupus erythematosus with retinoids is reviewed.

Dr. Richardson is a fourth-year medical student in the Department of Internal Medicine, University of Nevada, Las Vegas, Nevada. Dr. Cohen is Associate Professor with the Departments of Dermatology and Pathology, University of Texas–Houston Medical School, Houston, Texas, and the Department of Medical Specialties, Section of Dermatology, University of Texas MD Anderson Cancer Center, Houston, Texas.

Subacute cutaneous lupus erythematosus is a distinct subset of lupus erythematosus.[1] We describe a woman with subacute cutaneous lupus erythematosus who subsequently developed a meningioma and had cutaneous lesions that improved after treatment with isotretinoin. The association of lupus erythematosus and malignancy and the treatment

FIGURE 1. Distant (A) and closer (B) views of erythematous scaling plaques of subacute cutaneous lupus erythematosus on the upper back.

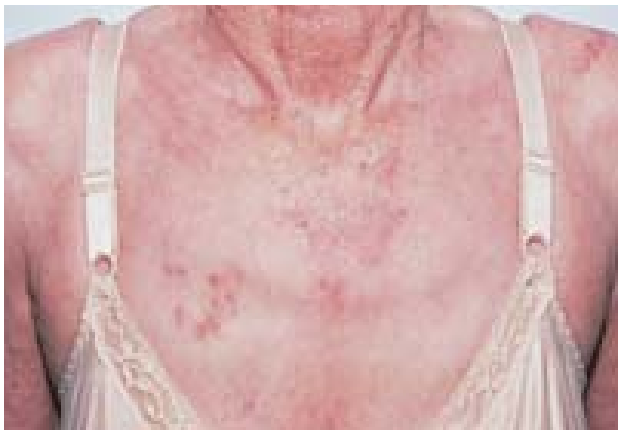

FIGURE 2. Photodistributed red patches and plaques of subacute cutaneous lupus erythematosus on the central chest.

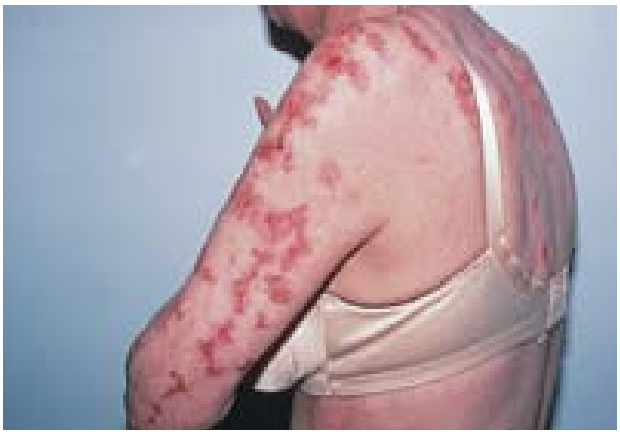

FIGURE 3. Subacute cutaneous lupus erythematosus skin lesions on the left shoulder and arm.

of subacute cutaneous lupus erythematosus with retinoids are discussed.

Case Report

A 68-year-old menopausal white woman was originally diagnosed with lupus erythematosus 44 years ago; subsequently, her diagnosis was revised to subacute cutaneous lupus erythematosus. She had been treated with sunscreen, various topical corticosteroids, and hydroxychloroquine (400 mg/d). She had experienced intermittent minor improvement with this regimen. However, the hydroxychloroquine had recently been discontinued because of retinal toxicity.

Her medical history was significant for a meningioma located in the right occipital area that was detected by magnetic resonance imaging during the workup of recalcitrant headaches 1.5 years ago. Other medical problems included hypertension and atypical angina.

Cutaneous examination showed annular, nonscarring, erythematous plaques with central clearing on her upper back, central chest, shoulders, and arms (Figures 1 to 3). A biopsy specimen revealed orthokeratosis in the overlying epithelium. There was mild acanthosis and marked vacuolar alteration of the basal layer; apoptotic keratinocytes (colloid bodies) were also present in the basal layer. There was a dense lymphocytic infiltrate in the papillary dermis with focal exocytosis of lymphocytes in the lower layers of the epithelium (Figure 4).

Laboratory analysis demonstrated the presence of antinuclear antibody (1:80) and anti-Ro (Sjögren's syndrome A) antibody (1:6400). Her complete blood cell count with differential and platelet counts, serum chemistries, complement (C3 and C4) levels, and urinalysis gave normal results. Antibodies to La (Sjögren's syndrome B), ribonuclear protein, and native DNA were absent. Correlation of the cutaneous lesions, pathology features, and laboratory findings were consistent with the diagnosis of subacute cutaneous lupus erythematosus.

Isotretinoin at a dose of 1 mg/kg (50 mg/d) was started. Topical corticosteroid therapy (alternating

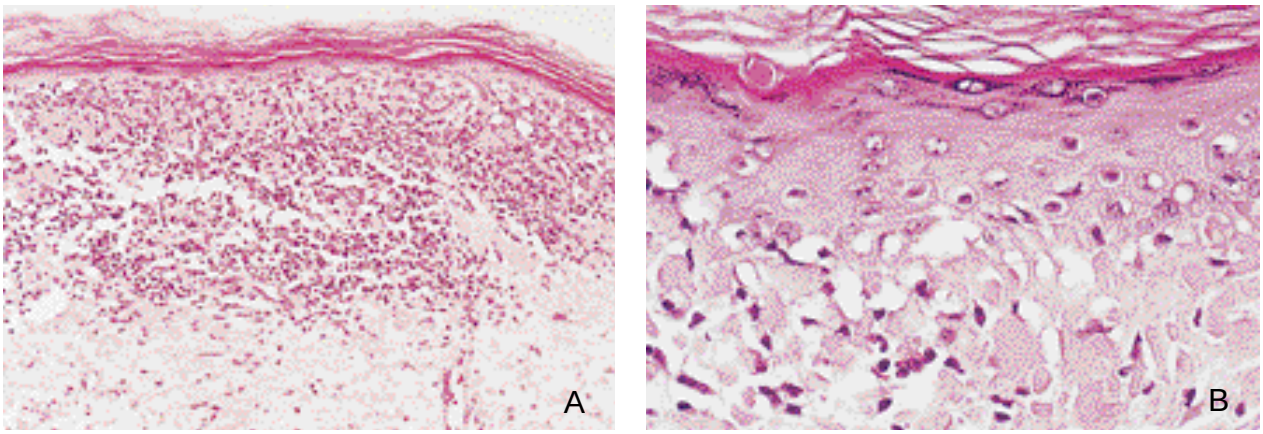

FIGURE 4. Low (A) and higher (B) magnifications of a lesional skin biopsy of subacute cutaneous lupus erythematosus. The epidermis shows orthokeratosis, mild acanthosis, basal layer vacuolar alteration, and colloid bodies. In the papillary dermis, there is a dense lymphocytic infiltrate with exocytosis of lymphocytes into the overlying epidermis (H&E; A, original magnification x50; B, original magnification x100).

clobetasol propionate 0.05% and fluocinonide 0.05% every 2 weeks) twice daily and sunscreen were continued. There was some improvement of her skin lesions within 2 weeks after initiating retinoid therapy. Her skin lesions continued to show progressive improvement on follow-up examination 1 month later.

Comments

In 1979, Sontheimer et al[1] reported 27 patients who had serologic abnormalities and musculoskeletal complaints similar to lupus erythematosus. They also had cutaneous lesions that were recurrent, superficial, and nonscarring. However, these patients did not meet the diagnostic criteria of systemic lupus erythematosus (SLE) and did not have serious renal or central nervous system involvement. The investigators concluded that subacute cutaneous lupus erythematosus was a disease with severity intermediate between chronic cutaneous lupus erythematosus and severe SLE.[1]

Numerous case reports have described concurrent systemic lupus erythematosus and malignancy. However, an association of SLE with cancer has been controversial. Whereas some of these reports described concurrent SLE in patients with solid tumors,[2] the preponderance of papers demonstrate a possible association of SLE and hematopoietic malignancies.[3-13] The small series of studies that discusses this possible association is outlined in Table I.[14-19] Although some studies found no relationship between SLE and cancer,[14-17] others found a link with either hematopoietic malignancies[19] or with all cancers.[15,16,18]

Description of malignancy in patients with subacute cutaneous lupus erythematosus is limited to only a few case reports. In 1982, Blanc and Kienzler[20] reported a patient with lupus erythematosus gyratus repens (considered to be synonymous with annular subacute cutaneous lupus erythematosus) who developed squamous cell lung carcinoma. Subsequently, 5 additional patients with subacute cutaneous lupus erythematosus have been reported who developed cancer in either their breast (2 patients), lung, stomach, or uterus.[21-25]

In a recent report by Brenner et al,[25] a woman with paraneoplastic subacute cutaneous lupus erythematosus associated with small cell carcinoma of the lung was described; her lupus-related skin lesions appeared 3 months prior to the diagnosis of malignancy and disappeared during chemotherapy. Tumor-associated subacute cutaneous lupus erythematosus was also noted in 5 other patients; their lesions either appeared within 8 months prior to the discovery of the cancer or disappeared within hours to 6 months after initiation of tumor-directed therapy, or both.[21-25] Our patient did not fulfill McLean's[26] 2 essential criteria for a paraneoplastic dermatosis: (1) the dermatosis must occur after the development of the cancer and (2) that both the dermatosis and the cancer must follow parallel courses. Her meningioma was discovered 44 years after the diagnosis of her subacute cutaneous lupus erythematosus.

Several modalities for treating subacute cutaneous lupus erythematosus have been reviewed.[27-30] After diagnosis and examination for systemic disease, first-line therapies include sun protection and potent topical corticosteroids or intralesional corticosteroids, or both. Patients failing these initial therapies are often started on systemic antimalarials (hydroxychloroquine, quinacrine, or chloroquine), either alone or in combination. For individuals similar to our patient, in whom hydroxychloroquine was contraindicated, alternative second-line therapies include retinoids and dapsone. Third-line therapies may include

Table I.

Association of Systemic Lupus Erythematosus and Malignancy[1]

No. of Patients		Type of Study	Number and Type of Malignancy	Conclusion	Reference
In Study	Developing Cancer				
39	1	Prospective, with 225 patient-year follow-up	1 melanoma	No association (rate ratio, 1.85; CI, 0.05–10.28)	14
70	8	Small series, followed over median of 6.75 y	5 gynecologic; 1 multiple myeloma; 1 RCS; 1 skin (Bowen's)	11.4% developed malignancy; "increased incidence of malignancy may be present in SLE"	16
205	15	Prospective, followed for 2340 person-years	7 NHL; 2 breast; 2 soft tissue; 1 liver; 1 melanoma; 1 pancreas; 1 renal; 1 thyroid; 1 uterine	Increased risk of all cancers (relative risk, 2.6; 95% CI, 1.5–4.4), including increased risk of NHL (relative risk 44; 95% CI 11.9–111)	16
219	6	Prospective, followed for 10 y	3 breast; 1 colon; 1 NHL; 1 vulvar	No association (rate ratio, 1.36; 95% CI, 0.50–2.96)	17
484	18	Retrospective cohort, over 20 y	6 gynecologic; 3 lung; 2 breast; 2 RCS; 1 colon; 1 HL; 1 skin (SCCa); 1 stomach; 1 thyroid	"Exaggerated" frequency of neoplasms (3.72% developed malignancy, $P<.0005$, computed by chi-square)	18
724	24	Prospective cohort, followed for 24 y	4 breast; 4 gynecologic; 4 lung; 3 colon; 3 NHL; 2 leukemia; 2 pancreas; 1 macroglobulinemia; 1 renal	4.1-fold increased risk of hematologic cancers in SLE patients compared to general population (SIR, 1.5; 95% CI, 1.52–9.01); no increased risk of all cancers (SIR 1.08; 95% CI 0.70–1.62)	19

CI indicates confidence interval; RCS, reticulum cell sarcoma; Bowen's, squamous cell carcinoma in situ; SLE, systemic lupus erythematosus; NHL, non-Hodgkin's lymphoma; HL, Hodgkin's lymphoma; SCCa, squamous cell carcinoma; and SIR, standard interval ratio.

thalidomide, gold, and clofazimine. Finally, systemic corticosteroids, other immunosuppressives (including azathioprine, methotrexate, and cyclophosphamide), and interferon-α have been used successfully in patients with more severe and refractory disease.

To the best of our knowledge, the first use of a systemic retinoid (etretinate) to treat subacute cutaneous lupus erythematosus was first described by Lubach and Wagner[31] in 1984. In 1985, Ruzicka et al[32] reported the treatment of 7 patients with subacute cutaneous lupus erythematosus (6 women, 1 man) with 50 mg of etretinate in divided doses each day for 6 weeks; 2 individuals showed an "excellent" response (complete clearing) and 2 individuals showed a "good" response.

Treatment of subacute cutaneous lupus erythematosus with either isotretinoin or acitretin has also been published in the English literature.[33-36] Newton et al[33] described a 43-year-old woman who was treated with 40 mg of isotretinoin twice daily for 16 weeks with excellent results (almost total disappearance of the lesions). Furner[34] also reported a 78-year-old man with subacute cutaneous lupus erythematosus whose skin lesions resolved with isotretinoin therapy. The patient's initial dose was 1 mg/kg of isotretinoin (40 mg each morning and 10 mg each evening); the dose was decreased to 20 mg and then 10 mg daily after 2 and 6 months, respectively. He was then maintained on 10 mg of isotretinoin for another 6 months. There was clearing of more than 90% of his lesions within 1 month after starting treatment; subsequently, there was complete clearing.

Several patients with subacute cutaneous lupus erythematosus have been treated with acitretin.[35,36] Ruzicka et al[35] initially reported 2 men and 4 women who were treated with 80 mg oral acitretin each day, with adjustment of their dose according to response and side effects, to a maximum of 75 mg and a minimum of 10 mg daily. Treatment was continued until remission was achieved or for up to 12 weeks. Five of the patients had an "excellent" response (complete clearing); the final patient had marked improvement (marked clearing with minor residual lesions).[35] Subsequently, Ruzicka et al[36] described 8 additional patients who were treated with 50 mg oral acitretin each day for 8 weeks. In 46% of these patients, complete clearing or marked improvement was observed.[36]

Conclusion

Several studies suggest that there is an association with SLE and cancer, particularly hematologic malignancies. Larger, multicenter cohort studies are necessary to confirm to what extent patients with SLE are at increased risk for developing malignancy. There are only a few reports of cancer patients with subacute cutaneous lupus erythematosus. However, in several of these individuals, either the onset of subacute cutaneous lupus erythematosus occurred within 6 months of the diagnosis of the associated tumor, the cutaneous lesions of subacute cutaneous lupus erythematosus resolved following tumor-directed therapy, or both. These observations raise the possibility of subacute cutaneous lupus erythematosus occurring as a cutaneous paraneoplastic syndrome in these patients. In contrast, the temporal relation between the detection of our patient's meningioma and the onset of her subacute cutaneous lupus erythematosus was not paraneoplastic.

Antimalarials can be used in the management of subacute cutaneous lupus erythematosus that is refractory to topical or intralesional corticosteroid therapy. However, in patients with subacute cutaneous lupus erythematosus for whom antimalarials are either ineffective or contraindicated, alternative agents must be considered. For these individuals with subacute cutaneous lupus erythematosus, a trial of retinoids may be warranted.

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