

Verrucous Systemic Lupus Erythematosus

Ljubka Miteva¹, Valentina Broshtilova¹, Robert A. Schwartz²

¹Department of Dermatology and Venereology, Medical University, Sofia, Bulgaria;

²New Jersey Medical School, Newark, New Jersey, USA

Corresponding author:

Ljubka Miteva MD, PhD
Department of Dermatology and Venereology
Medical University
1 G. Sofiisky Str.
1431 Sofia
Bulgaria
lubka_miteva@abv.bg

Received: March 20, 2009

Accepted: October 3, 2009

SUMMARY Few patients with systemic lupus erythematosus have features of verrucous (hypertrophic) lupus erythematosus. A 29-year-old Caucasian woman with a 7-year history of systemic lupus erythematosus developed painful verrucous plaques on the nose. Erythematous, raised, indurated, hyperkeratotic plaques localized on the dorsa of the distal parts of the toes and over the interphalangeal joints of her fingers were also noted. A large, dull-red, indurated plaque with rolled borders on the bridge of the nose was most characteristic. Rapid therapeutic effect was obtained by systemic corticosteroid regimen. This verrucous variant of lupus erythematosus, sometimes clinically resembling actinic keratosis, keratoacanthoma and squamous cell carcinoma, is reviewed.

KEY WORDS: hypertrophic, systemic lupus erythematosus, squamous cell carcinoma

INTRODUCTION

Verrucous or hypertrophic lupus erythematosus is an unusual subset of chronic cutaneous lupus erythematosus (LE) (1-7). Although rare in systemic LE, about 2% of all patients with chronic cutaneous LE show typical hyperkeratotic plaques (2). The marked hyperkeratosis in hypertrophic LE is considered an exaggerated proliferative response to chronic antigen stimulation (3). Often the terms verrucous LE, hyperkeratotic LE, keratotic LE, and hypertrophic discoid LE are used as synonyms (4). These plaques may resemble actinic keratosis, keratoacanthoma or cutaneous squamous cell carcinoma (5-11), a critical distinction, especially since cutaneous LE itself may predispose the development of cutaneous squamous cell carcinoma, particularly within a chronic LE plaque.

CASE REPORT

A 29-year-old Caucasian woman developed systemic LE with symptoms of photosensitivity, an erythematous butterfly rash on the face, symmetric polyarthritis of the small joints of the hands, and positive antinuclear factor at the age of 22. She was treated with maintenance therapy of 4 mg/d methylprednisolone; her general condition remained normal. Three months earlier verrucous painful plaques appeared on her nose, fingers and toes. On physical examination she had normal vital signs. Butterfly erythema was present over the malar area and bridge of her nose. Erythematous, raised, indurated, hyperkeratotic plaques were localized on the dorsa of the distal parts of the toes (Fig. 1) and over the interphalangeal joints of her fingers. The most characteristic was a large,



Figure 1. Verrucous systemic lupus erythematosus with erythematous, raised, indurated, hyperkeratotic plaques localized on the dorsa of the distal parts of the toes.

dull-red, indurated plaque with rolled borders on the bridge of the nose (Fig. 2). Multiple erosions and ulcerations appeared on her buccal mucosa, tongue and palate (Fig. 3).

Laboratory examinations revealed an elevated sedimentation rate (45 mm/h), while the rest of the hematology and chemistry parameters as well as urinalysis were within the normal ranges. Antinuclear antibodies (ANA) were positive at a titer of 1:640 with a speckled pattern (indirect immunofluorescence on HEp-2 substrate). Serum immunoglobulins and complement C3 and C4 levels were normal; however, anti-Ro/SS-A antibodies were positive. A biopsy specimen taken from the face showed marked acanthosis, compact orthokeratotic hyperkeratosis, perifollicular inflammation, follicular plugging, vacuolar interface change, acrosyringal inflammation, and a thickened linear band of fibrin deposits in the basement membrane zone and around hair follicles, where it formed massive globular aggregates. The extensive edema of the upper dermis was associated with dilated vessels surrounded by marked fibrin deposits (Fig. 4). An interstitial moderate inflammatory mononuclear cell infiltrate of lymphocytes and plasma cells was seen in the superficial dermis and deep dermis. Direct immunofluorescence performed on sun-protected non-lesional skin showed fibrillar and stippled deposits of immunoglobulin M at the dermoepidermal junction. On the basis of

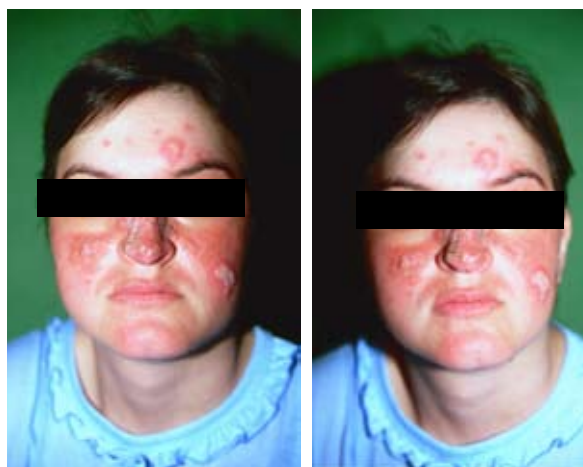


Figure 2. Verrucous systemic lupus erythematosus: note a large, dull-red, indurated plaque with rolled borders on the bridge of the nose.

these clinical, histologic, and immunopathologic data, the previous diagnosis of systemic LE was confirmed. The cutaneous manifestations were classified as hypertrophic LE. The patient was treated with 40 mg/d methylprednisolone gradually tapered to maintenance therapy of 8 mg/d. Resolution of the skin lesions was noted at the 2-month follow up visit.

DISCUSSION

Verrucous (hypertrophic) LE, LE tumidus, chilblain LE, and LE profundus are uncommon subtypes of chronic cutaneous LE (5). The former was originally described by Bechet (8) in 1942 as lupus hypertrophicus et profundus. This form consists of dull-red, raised, indurated plaques covered by keratotic, multilayered, horny, white or yellow scales. The arms, legs, upper back, and



Figure 3. Systemic lupus erythematosus with multiple erosions and ulcerations on the buccal mucosa, tongue and palate

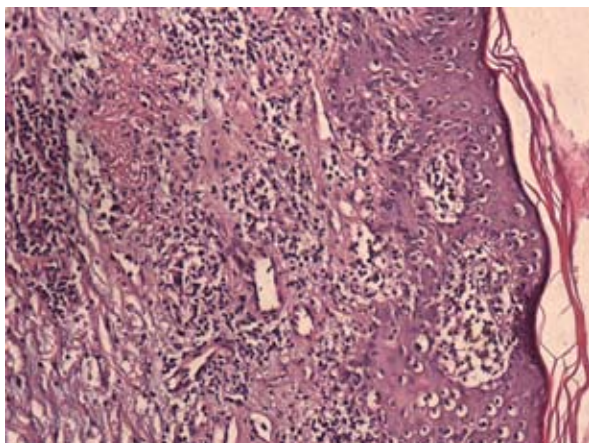


Figure 4. Facial plaque, histologic view, showing diffuse hyperkeratosis, marked acanthosis, thickened linear band of fibrin deposits in the basement membrane zone and around hair follicles, and a mild perifollicular and perivascular infiltrate of lymphocytes and plasma cells (hematoxylin-eosin; original magnification X 400).

the face are the most often affected body parts. When the palms and soles are involved, hypertrophic lupus produces localized or partially diffuse keratoderma (6).

Clinically, hypertrophic LE is most often evident as hyperkeratotic and verrucous plaques clinically resembling keratoacanthomas, lupus vulgaris, or hypertrophic lichen planus (3,12). Sometimes the hyperkeratosis may be hard to differentiate histologically from pseudocarcinomatous hyperplasia, actinic keratosis, keratoacanthoma, and squamous cell carcinoma, which need to be considered on differential diagnosis, especially in the scarred refractory cases of chronic cutaneous LE (13). Therefore, the histologic verification showing marked acanthosis, compact orthokeratotic hyperkeratosis, perifollicular inflammation, follicular plugging, vacuolar interface change, and acrosyringeal inflammation is important. Our case showed these typical features.

Only a few patients have been described with systemic LE showing characteristic hyperkeratotic plaques (14,15). Cardinali *et al.* (14) described a patient with a long history of systemic LE that developed erythemo-indurated cutaneous plaques with oral ulcerations and ocular involvement. Only one of the clinical plaques, localized on the first finger of the right hand, had the characteristic large dull-red indurated plaque with keratotic central plug and adherent scales. Histologically, it was consistent with the hypertrophic variant of LE.

Remarkably, our patient showed the typical discoid LE hyperkeratotic plaques involving the face, fingers and toes, but in the clinical, laboratory and immunopathologic constellation of systemic LE.

Pock *et al.* (15) describe a woman with symmetric livid plaques on the fingers and toes in the clinical setting of discoid chilblain LE. Left untreated, in the following 5 years, the patient developed yellowish hyperkeratotic plaques and gradually developed systemic symptoms of LE with mild leukopenia, C3 and C4 hypocomplementemia, and positive ANA. The skin biopsy specimen revealed hyperkeratosis and hypergranulosis, hydropic degeneration of basal keratinocytes, massive hyaline degeneration of collagen in the perivascular area, and mild superficial and deep dermal perivascular lymphocytic infiltrate. Thus, the combination of extensive hyperkeratosis and hyalinization was considered a feature of longstanding, untreated chilblain LE. In contrast, our patient developed hyperkeratotic plaques in the course of pre-existing and treated systemic LE as a clinical and immune relapse of the disease.

Verrucous (hypertrophic) LE is often treatment resistant (16). Intralesional corticosteroids generally give only transient thinning. Successful treatment of hypertrophic LE in chronic cutaneous LE has been demonstrated with etretinate (17), isotretinoin (7,18), and thalidomide (19). However, in the context of systemic LE, the hypertrophic plaques showed a favorable therapeutic response to systemic corticosteroids (14). The hyperkeratotic cutaneous plaques in our patient resolved quickly and thoroughly upon short-term systemic corticosteroid therapy.

References

1. Sontherheimer RD. The lexicon of cutaneous lupus erythematosus – a review and personal perspective on the nomenclature and classification of the cutaneous manifestations of lupus erythematosus. *Lupus* 1997;6:122-31.
2. Callen JP. Discoid lupus erythematosus – variants and clinical associations. *Clin Dermatol* 1985;3:49-57.
3. Santa Cruz DJ, Uitto J, Eisen AZ, Prioleau PG. Verrucous lupus erythematosus: ultrastructural studies on a distinct variant of discoid lupus erythematosus. *J Am Acad Dermatol* 1983;9:82-90.
4. Uitto J, Santa Cruz DJ, Eisen AZ, Leone P. Verrucous lesions in patients with discoid lupus

- erythematosus. *Br J Dermatol* 1978;98:507-20.
5. Kuhn A, Schuppe HC, Ruzicka T, Lehmann P. Rare cutaneous manifestations of lupus erythematosus. A clinical overview. *Hautarzt* 2000;51:818-25.
 6. Meurer M. Lupus erythematosus. In: Burgdorf WHC, Plewig G, Wolff HH, Landthaler M, eds. *Braun-Falco's Dermatology*, 3rd edn. Heidelberg: Springer; 2009. pp. 716-41.
 7. Rubenstein DJ, Huntley AC. Keratotic lupus erythematosus: treatment with isotretinoin. *J Am Acad Dermatol* 1986;14: 910-4.
 8. Bechet PE. Lupus erythematosus hypertrophicus et profundus. *Arch Dermatol Syphilol* 1942;45:33-9.
 9. Mulwafu WK, Fagan JJ, Jessop S. Squamous cell carcinoma in black patients with discoid lupus erythematosus. *S Afr J Surg* 2006;44:144-6.
 10. Zedek DC, Smith ET Jr, Hitchcock MG, Feldman SR, Shelton BJ, White WL. Cutaneous lupus erythematosus simulating squamous neoplasia: the clinicopathologic conundrum and histopathologic pitfalls. *J Am Acad Dermatol* 2007;56:1013-20.
 11. Ee HL, Ng PP, Tan SH, Goh CL. Squamous cell carcinoma developing in two Chinese patients with chronic discoid lupus erythematosus: the need for continued surveillance. *Clin Exp Dermatol* 2006;31:542-4.
 12. Zawirska A, Adamski Z, Stawicka E, Schwartz RA. Lupus vulgaris exfoliatus: persistent for 40 years with an associated squamous cell carcinoma. *Int J Dermatol* 2009;48:125-7.
 13. Perniciaro C, Randle HW, Perry HO. Hypertrophic discoid lupus erythematosus resembling squamous cell carcinoma. *Dermatol Surg* 1995;21:255-7.
 14. Cardinali C, Giomi B, Caproni M. Cutaneous hypertrophic lupus erythematosus in a patient with systemic involvement. *Skin Med* 2004;1:49-51.
 15. Pock L, Petrovska P, Becvar R. Verrucous form of chilblain lupus erythematosus. *J Eur Acad Dermatol Venereol* 2001;15:1009-10.
 16. Spann CR, Callen JP, Klein JB, Kulick KB. Clinical, serological and immunogenetic studies in patients with chronic discoid lupus erythematosus who have verrucous and/or hypertrophic skin lesions. *J Rheumatol* 1988;15:256-61.
 17. Grupper CH, Berretti B. Lupus erythematosus and etretinate. In: Cunliffe WJ, Miller AJ, eds. *Retinoid therapy: a review of clinical and laboratory research*. New York, NY: Springer-Verlag; 1984. pp. 73-81.
 18. Green S, Piette W. Treatment of hypertrophic lupus erythematosus with isotretinoin. *J Am Acad Dermatol* 1987;17:364-8.
 19. Georgala S, Katoulis AC, Hasapi V, Koumantaki-Mathioudaki E. Thalidomide treatment for hypertrophic lupus erythematosus. *Clin Exp Dermatol* 1998;23:141.