Case Report

Calcifying Lupus Panniculitis in a Patient with Subacute Cutaneous Lupus Erythematosus: Response to Diltiazem and Chloroquine

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ABSTRACT. Lupus panniculitis has been reported to occur with a frequency of 2–3% in patients with lupus erythematosus (LE). It is most often reported in association with lesions of discoid LE. We describe a patient with subacute cutaneous LE who developed calcified nodules that were histopathologically consistent with lupus panniculitis. She was treated with a combination of chloroquine and diltiazem with a good therapeutic response. The addition of diltiazem may be beneficial in patients with calcified nodules of lupus panniculitis. (J Rheumatol 2001;28:2129–32)

Key Indexing Terms:
LUPUS ERYTHEMATOSUS
PANNICULITIS
CALCIUM CHANNEL BLOCKERS
DYSTROPHIC CALCIFICATION

Subacute cutaneous lupus erythematosus (SCLE) makes up about 10–15% of patients with lupus erythematosus (LE) and may present clinically as either nonscarring papulosquamous or annular polycyclic lesions[1]. About half the patients with SCLE fulfill criteria for systemic disease, with arthritis being the most common extracutaneous feature[1,2]. Lupus panniculitis is reported to occur with a frequency of 2–3% in patients with LE[3-5]. It is clinically characterized by subcutaneous nodules or plaques, with or without overlying epidermal changes. Lupus panniculitis has most often been reported to occur beneath a lesion of discoid LE; however, it may also present as subcutaneous nodules without overlying change. Patients with lupus panniculitis generally have a good prognosis, despite reports of systemic involvement in some patients[6-8]. Martens, *et al* reviewed the clinical and laboratory features of 40 patients with lupus panniculitis and found that 33% fulfilled the American College of Rheumatology (ACR) criteria for systemic lupus. Antinuclear antibodies (ANA) were noted to be positive in 65%, but were typically low titers[9]. Histopathologic changes in lupus panniculitis may be distinctive and include hyaline degeneration and lymphoid inflammation of the panniculus[7]. In addition, there may be calcifications of the fat. Individual elastic fibers may be calcified or large areas of calcification may involve lobules or septa[10]. Deposits may be extensive enough to be detectable on the roentgenogram. Other changes include those occurring in the skin overlying the panniculus such as epidermal atrophy, follicular plugging, hydropic degeneration of the dermal-epidermal junction, and the deposition of mucin.

CASE REPORT

A 32-year-old woman presented with a history of "skin rash" on her upper chest, upper back, neck, and anterior thighs since 1988. A skin biopsy of the photodistributed lesions in 1988 revealed a lichenoid dermatitis and the lesions on the thighs were diagnosed as morphea (localized scleroderma) by clinical and histopathologic examination. She was treated with topical corticosteroids and hydroxychloroquine but she discontinued the hydroxychloroquine after a short time. Review of systems in 1994 was unremarkable. She denied arthralgias, oral ulcerations, and fatigue.

In 1994, her examination revealed slightly scaly, erythematous plaques in a photodistribution on her arms, upper chest, back, and face (Figure 1). In addition, there were indurated plaques on her anterior thighs and buttocks that were studded with firm nodules (Figure 2). Laboratory findings revealed a positive ANA (1:320) in a homogenous pattern. Complete blood cell count, comprehensive metabolic panel, aldolase, and lipase were normal. Anti-native DNA, anti-RNP, anti-Sm, anti-SSA, anti-SSB, and alpha-1 antitrypsin were normal or negative. C3 and C4 levels were within normal limits. A roentgenogram of her thighs revealed dystrophic calcification (Figure 3).

Skin biopsy of lesions on the face and arm revealed focal follicular plugging with mild epidermal thinning and vacuolar interface changes (Figure 4). A wedge biopsy from the thigh revealed irregular hyperplasia of the epidermis with hyperkeratosis and thickening of the epidermal basement membrane zone. Mild epidermal atrophy with focal vacuolar degeneration along dermal-epidermal junction and interstitial mucin in the dermis were noted. In the subcutaneous fat, there was hyalinized necrosis and fibrosis of adipose tissue in a lobular pattern with calcification (Figure 5). These biopsies were representative of subacute cutaneous lupus erythematosus and lupus panniculitis with dystrophic calcifications.

She was treated with oral chloroquine phosphate 500 mg per day and daily application of a broad-spectrum sunscreen (SPF 30). The photodis-

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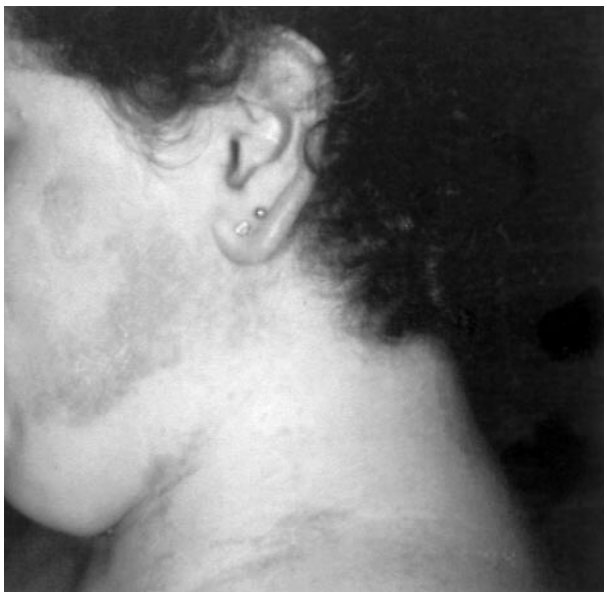

Figure 1. Photodistributed erythematosus plaques on the lateral face.

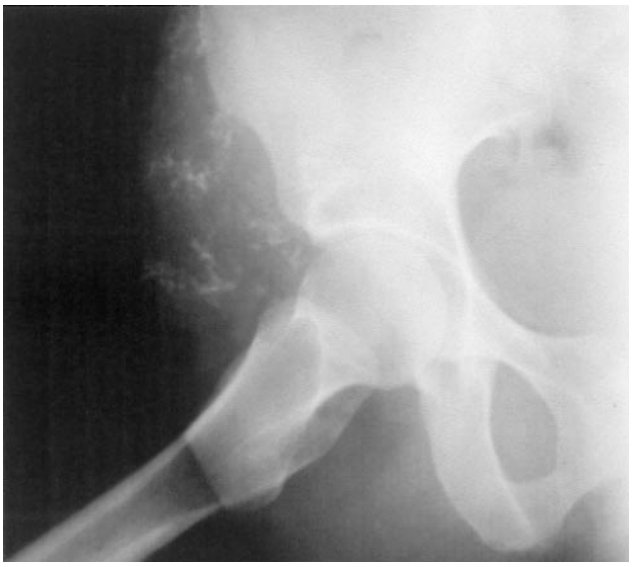

Figure 3. Soft tissue calcification in the area of the subcutaneous nodules.

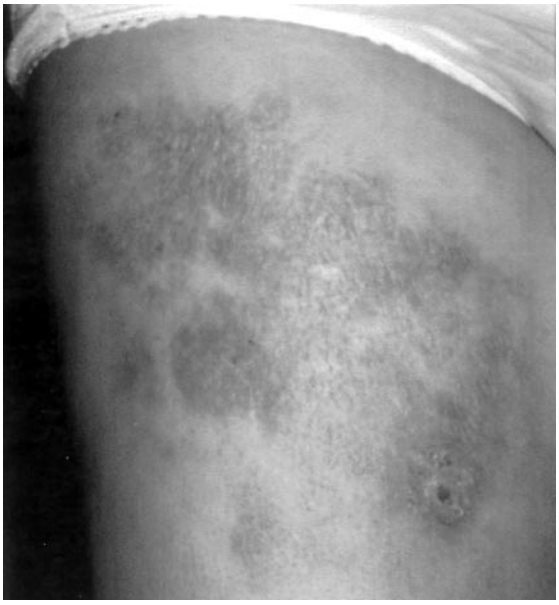

Figure 2. Indurated violaceous plaques with nodules over the anterior thigh.

tributed lesions of SCLE became quiescent about 2 months after starting therapy (Figure 6). The subcutaneous nodules showed little change and diltiazem 240 mg twice daily was added to her regimen. After 10 months of treatment, the calcinotic nodules broke into several smaller nodules and improved considerably. She has continued to have improvement of the calcinosis and continues oral diltiazem 240 mg twice daily. Her chloroquine dosage has been tapered to 500 mg per week.

DISCUSSION

Subcutaneous nodules associated with lupus erythematosus were first reported by Kaposi in 1883[11]. Epidermal involvement suggestive of LE is observed in roughly 70% of patients. Some authorities utilize the terms lupus erythematosus panniculitis and lupus profundus synonymously, whereas others use lupus panniculitis to designate the patient without overlying changes of cutaneous LE. A minority of patients with lupus panniculitis fulfill 4 or more American College of Rheumatology criteria for systemic lupus, and even in those with evidence of systemic disease, the systemic involvement tends to be mild[4,7,9].

Calcification of lesions of lupus panniculitis is not uncommon and frequently occurs within older lesions[12,13]. Pain is a predominant feature when calcifications are present.

Management of patients with lupus panniculitis is similar to that for discoid LE and includes antimalarials[5,9,14-16], systemic or intralesional corticosteroids, and in resistant cases azathioprine[17] and cyclophosphamide[18]. There have also been reports of success with thalidomide[19] and dapsone[20,21]. Adjuvant treatments include topical care and prevention of injury. Successful management of cutanenous calcinosis has been reported with numerous agents including probenecid[22], low dose warfarin[23,24], intralesional corticosteroids[25], and colchicine[26]. In addition, there have been patients whose lesions have seemingly spontaneously resolved with time[27]. Calcinosis associated with dermatomyositis and systemic sclerosis has been reported to respond to longterm administration of diltiazem in several open label small case series[28-31]. However, one study failed to show an effect of diltiazem in the treatment of systemic sclerosis[32]. It has been shown that the use of diltiazem in Duchenne muscular dystrophy leads to a decrease in muscular calcification[33].

The mechanism by which diltiazem causes regression of calcinosis is not entirely clear, but it has been hypothesized that the effects occur by inhibition of the influx of calcium

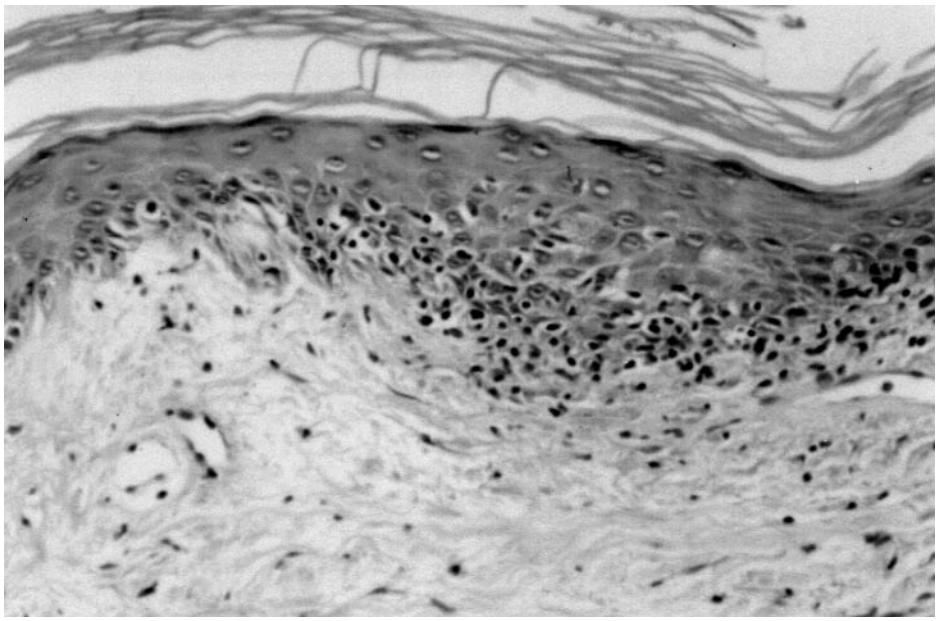

Figure 4. Biopsy of a facial lesion revealed mild epidermal thinning with vacuolar interface changes (H&E, original magnification ×100).

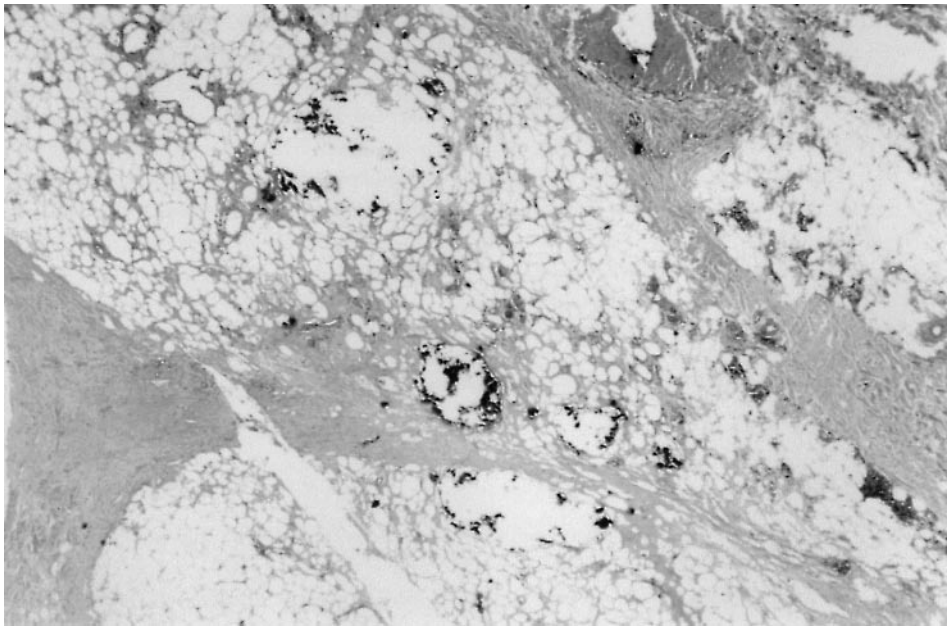

Figure 5. Lobular panniculitis with calcification (H&E, original magnification ×40).

into cells via slow ion dependent calcium channels. In patients with atherosclerosis, diltiazem has been found to inhibit calcium movement into damaged endothelial cells[34].

To our knowledge, this the first report of calcifying lupus panniculitis responding to treatment with diltiazem.

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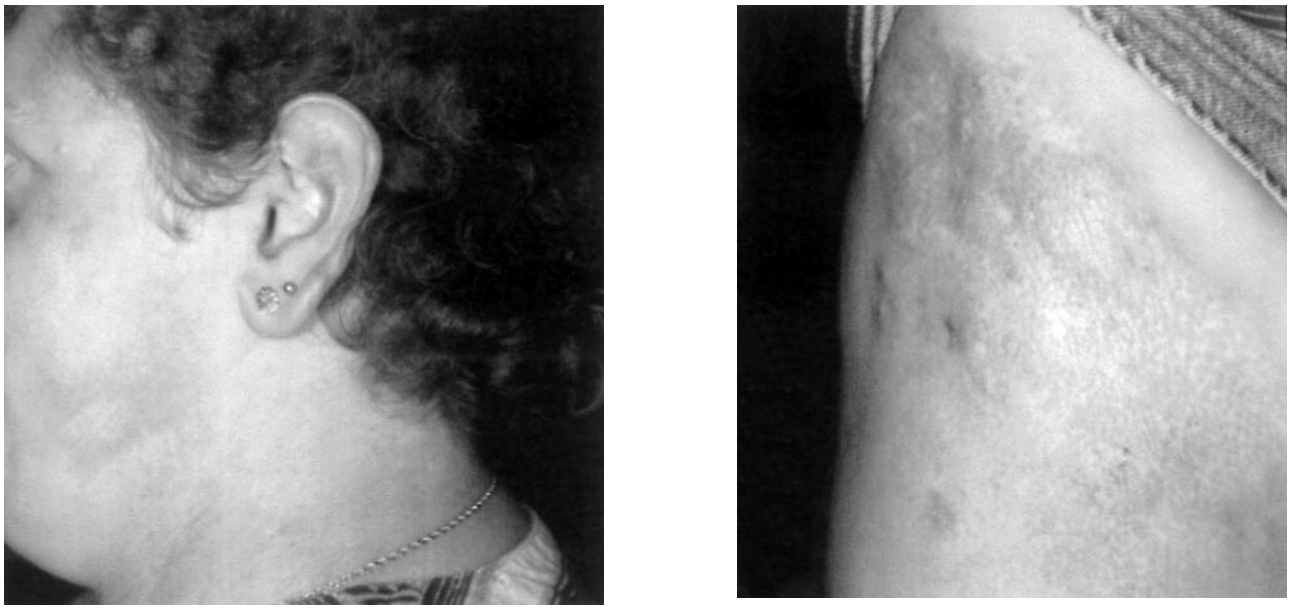

Figure 6. Face and thigh 2 months after initiation of chloroquine, with significant improvement of SCLE.

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