Skin manifestations of systemic disease

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Abstract
This article gives an overview of the common cutaneous manifestations which may present to the acute physician and give a pointer to an underlying general medical condition. Topics covered include autoimmune conditions such as lupus erythematosus, dermatomysositis and scleroderma, endocrine conditions such as diabetes and thyroid disease, general medical conditions such as sarcoid, pyoderma gangrenosum, and cutaneous signs of internal malignancy and flushing.

Keywords acanthosis nigricans; cutaneous lupus; dermatomyositis; erythema nodosum; flushing; genodermatosis; morphoea; necrobiosis lipoidica; paraneoplastic dermatoses; pretibial myxoedema; pyoderma gangrenosum; sarcoidosis

Lupus erythematosus

Lupus erythematosus may be subdivided on clinical and serological grounds into groups that aid management and help in prognosis.

Chronic discoid lupus erythematosus: lesions comprise well-defined, scaly plaques in which follicular plugging occurs. Chronic lesions often show atrophy or scarring, associated with hypopigmentation or hyperpigmentation (Figure 1) and permanent hair loss. The diagnosis is usually confirmed histologically; serology is usually negative. Progression to systemic disease is uncommon. See also *Medicine* 2009; **37:** 249–254.

Subacute cutaneous lupus erythematosus (SCLE) was first described in 1979[1] and affects about 10% of patients with systemic lupus erythematosus (SLE). Patients characteristically develop an erythematous, scaly eruption (which is sometimes annular) on sun-exposed sites (Figure 2). Scarring is rare. About 50% of patients fulfill the American Rheumatism Association criteria for SLE. Systemic features tend to be mild, however, and renal disease is uncommon. Diagnosis is by skin biopsy and serology. Most patients have antibodies to the extractable nuclear antigen Ro or La. Treatment is usually with topical corticosteroids, sun-screens and antimalarials. Occasionally, systemic corticosteroids are required.

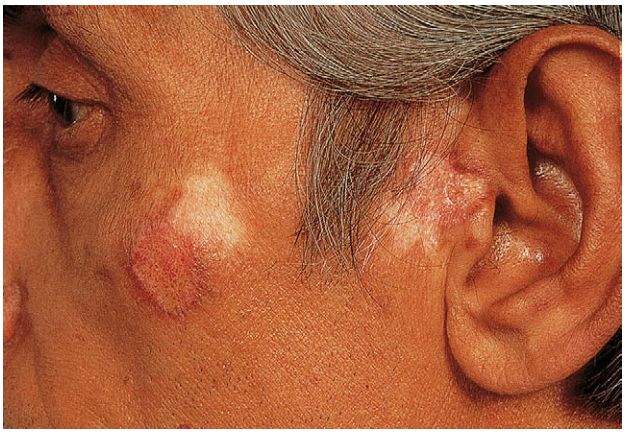

Figure 1 Discoid lupus erythematosus, showing erythematous, scaly plaques with secondary scarring and hypopigmentation.

Drug-induced lupus: this causes a mild form of lupus that seldom involves internal organs. Onset can be up to 2 years after initiation of therapy (e.g. minocycline for acne). Up to 75% of patients exhibit antihistone antibodies. Drugs implicated include anti-arrhythmics (procainamide), antibiotics (minocycline, which may cause joint pains and hepatitis), anticonvulsants (valproate, carbamazepine), antihypertensives (hydralazine, methyldopa, captopril), anti-inflammatory agents (D-penicillamine, which may cause renal disease) and lipid-lowering agents.

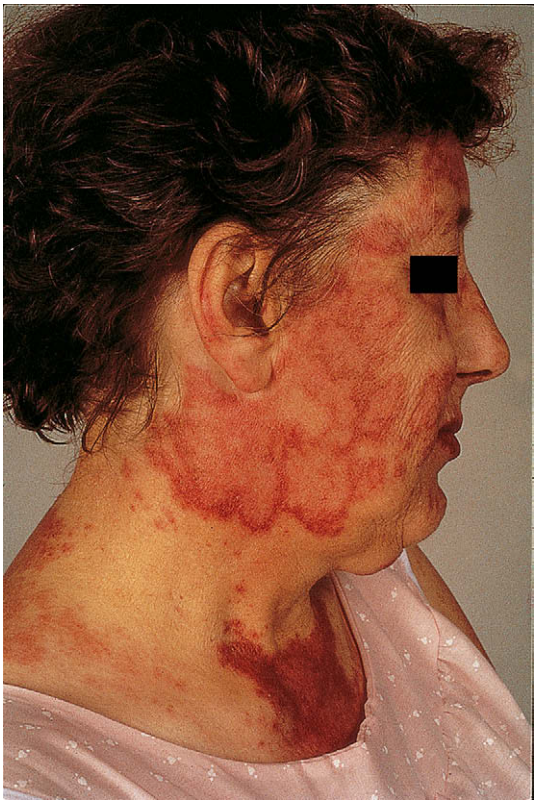

Figure 2 Subacute cutaneous lupus erythematosus, showing an erythematous, annular, scaly eruption in a 'photosensitive' distribution.

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In addition, agents such as bendrofluazide may cause an SCLE-like syndrome.

Systemic lupus erythematosus: only about 50% of patients with SLE exhibit the typical butterfly rash. Patients often have nail fold telangiectasia/infarcts, and the rash on the fingers usually affects the interphalangeal skin (Figure 3). Arthritis, arthralgia and myalgia are the most common presenting features.

Dermatomyositis

Dermatomyositis usually presents with an eruption affecting the face, neck, shoulders, elbows, forearms and hands. This rash tends to be exacerbated by sunlight and is therefore an example of a photo-aggravated disorder. Pathognomonic features are a violaceous periorbital eruption and scaly papules over the knuckles (Gottron's papules) (Figure 4). Weakness of the proximal muscles is found in most cases. Diagnosis depends on skin biopsy, muscle enzymes, muscle biopsy and electromyography. Patients with myositis may exhibit anti-synthetase antibodies (e.g. the Jo-1 antibody), which are also closely linked with interstitial lung disease, arthritis, Raynaud's phenomenon and hyperkeratotic pigmentation of the hands (mechanic's hands).[2]

Management is usually with systemic corticosteroids, sometimes in conjunction with second-line agents such as methotrexate, azathioprine, chlorambucil, cyclophosphamide or ciclosporin. A cautious approach to sun exposure should be recommended.

Note that occult malignancy may be found in 15–25% of patients with adult-onset dermatomyositis. This is thought to be less likely if anti-synthetase antibodies are present. Conversely, a novel antibody anti-P155 has recently been described which may be a marker of malignancy associated dermatomyositis.[3]

Scleroderma

Scleroderma may be subdivided, on the basis of the organs involved, into morphoea (localized to the skin) and systemic sclerosis. An autoimmune aetiology is supported by the frequent presence of autoantibodies. Previous studies investigating the link between infection with *Borrelia burgdorferi* and morphoea have produced conflicting results.

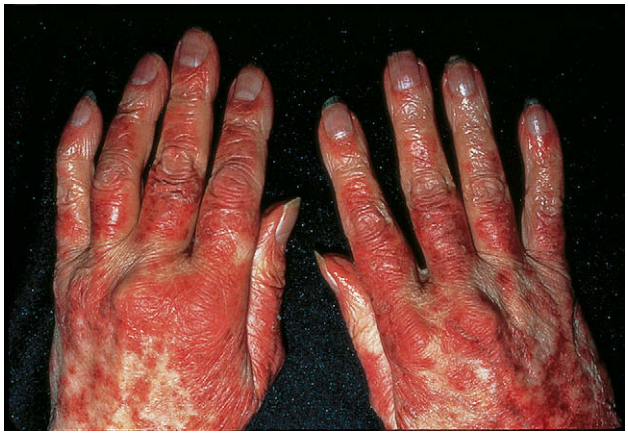

Figure 3 Erythematous, scaly eruption involving the interphalangeal skin in lupus erythematosus. Note the associated nail fold erythema.

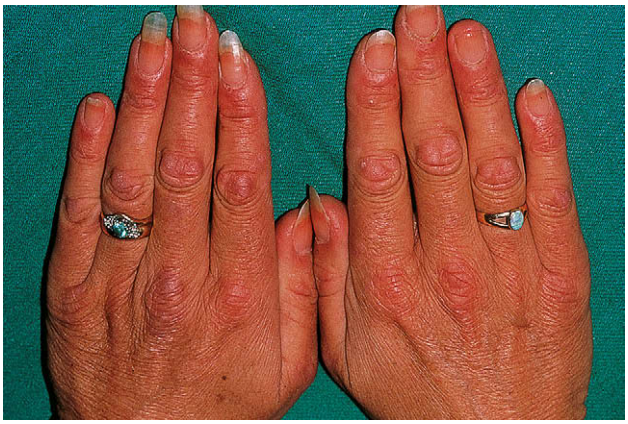

Figure 4 Erythematous papules over the knuckles in dermatomyositis (Gottron's papules).

Systemic sclerosis is a rare connective tissue disease characterized by Raynaud's phenomenon and fibrosis. The diffuse form has a poorer prognosis with systemic involvement potentially affecting the kidneys, lungs, heart, gastrointestinal tract, muscles, joints and nervous systmen.

Morphoea

- Localized morphoea can affect individuals of any age and has a female:male ratio of 3:1. Typically, patients present with a purple/mauve indurated area of skin. Older lesions become waxy centrally with a lilac-coloured edge. Lesions may become hyperpigmented as they resolve, and this can sometimes be the presenting feature.
- Linear morphoea is uncommon. Lesions are usually unilateral on the limbs. They are usually cutaneous, but underlying muscle and bone may be involved.
- Frontoparietal morphoea (*en coup de sabre*) usually presents as an indurated area on the forehead that may spread onto the scalp or the face. In some patients, this is associated with facial hemiatrophy.
- Generalized morphoea is a rare condition in which patients exhibit induration of the trunk and proximal limbs. Sclerosis of the fingers and Raynaud's syndrome are uncommon. Serology (antinuclear antibodies and Scl-70) is usually negative.

Management of morphoea is difficult. Topical corticosteroids or calcipotriol sometimes help localized lesions. Systemic corticosteroids in conjunction with methotrexate is now the preferred systemic treatment[4] but penicillamine, ciclosporin, ultraviolet A, interferon, antimalarials and calcitriol have been reported to help.

Sarcoidosis

Of patients with systemic disease, 20–30% have skin lesions, but cutaneous sarcoid may present without evidence of systemic involvement. The extent of the cutaneous lesions does not correlate with the extent of the systemic disease. Cutaneous lesions can present in many forms but the classical lesions have a violaceous, brownish hue, and although not specific for sarcoid, may exhibit 'apple jelly nodules' (granulomata) on compression with a glass slide (diascopy).

The most typical presentations include the following.

Erythema nodosum: this is most commonly associated with 'benign' sarcoid (bilateral hilar lymphadenopathy and a tendency