# Skin manifestations of systemic disease

Ruth C Lamb

## Abstract

Skin changes can be the first sign of an underlying medical condition, and thus the skin can act as a window to a patient's general health and guide practitioners to identifying a diagnosis. Other patients may already have a pre-existing diagnosis and go on to develop skin changes as part of multisystem disease.

**Keywords** Acquired perforating disorders; calciphylaxis; dermatomyositis; erythema nodosum; pyoderma gangrenosum; sarcoidosis; systemic lupus erythematosus; systemic sclerosis

## Key points

- Changes in the skin can be the first sign of an underlying medical condition
- Some patients will have a known multisystem disease with skin changes
- Complete examination of the skin, mucous membranes, hair and nails, including paraneoplastic eruptions, can provide vital clues to an as yet undiagnosed condition

## Introduction

Dermatoses can form part of a multisystem disease. Other skin changes, for example paraneoplastic eruptions, have an association with an internal disease and thus act to aid diagnosis of an as yet undiagnosed condition. Therefore the importance of full examination of the skin, nails and mucosal surfaces cannot be underestimated in ensuring that diagnostic clues are not missed. In addition, medications given for the treatment of other diseases can produce skin changes.

Here, the skin manifestations of systemic disease are reviewed by system, focusing on dermatological clinical features, differential diagnoses, investigations and possible treatments. Skin problems associated with infection or resulting from medications, and genodermatoses, are not reviewed.

## Skin problems in rheumatology

Many autoimmune systemic conditions, for example lupus erythematosus (LE), dermatomyositis (DM) and scleroderma, have skin manifestations. Other rheumatological conditions, such as rheumatoid arthritis (nodules), cutaneous vasculitis, panniculitis and pyoderma gangrenosum (PG), also demonstrate skin changes.

### Lupus erythematosus

LE is a group of chronic inflammatory conditions with skin involvement. Systemic LE (SLE) affects several systems including renal, neuropsychiatric, haematological and musculoskeletal. It usually occurs in female patients aged 15–45, with an incidence of around 6.5 per 100,000 per year in the UK depending on the sex and racial group studied. The disease is characterized by remissions and relapses. Diagnostic criteria help diagnosis.[1] The aetiology is not fully understood, but clinical features may result from antibody production and resulting immune complexes.

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**Skin clinical features**: skin manifestations are variable in SLE; most common is a facial eruption known as a malar or 'butterfly rash' presenting as erythema over the cheeks and nasal bridge after exposure to sun. Generalized photosensitivity, mucosal ulcers and non-scarring and scarring alopecia also occur.

**Other subtypes of LE:** other subtypes exist and can occur as a manifestation of SLE or in isolation. They can be divided into subacute cutaneous LE (SCLE) and chronic cutaneous LE. Of patients with SCLE, 15% develop SLE. Chronic cutaneous LE includes discoid LE (DLE; Figure 1) which is associated with scarring in the skin. SLE develops in less than 5% of individuals with DLE.

**Investigations:** skin biopsy is needed to confirm the diagnosis. Cutaneous LE subtypes share some histopathological features including hyperkeratosis, basement membrane thickening and a superficial and perivascular inflammatory infiltrate. Direct immunofluorescence may show the 'lupus band', and baseline blood tests including antinuclear antibody (ANA) can be useful.

**Differential diagnoses:** these reflect the LE subtype. The facial rash in SLE can be mistaken for acne rosacea, seborrhoeic dermatitis, erysipelas or DM. Psoriasis and eczema should be considered with SCL, and granuloma faciale, sarcoidosis and cutaneous infections including tuberculosis with DLE.

**Treatment:** management of SLE can require systemic immunosuppression. Photoprotection is the mainstay of management for skin manifestations of all LE subtypes. Topical corticosteroids or calcineurin inhibitors can be useful.

### Dermatomyositis

DM is an idiopathic inflammatory myopathy characterized by skin changes and proximal muscle weakness. Its incidence is estimated at 2 per 100,000 annually, and it is twice as common in female patients. Cutaneous changes can precede muscle changes but are seen in around 60% of patients presenting with muscle symptoms. The pathogenesis is incompletely understood, but it is known that myofibres and capillaries are injured by an unknown mechanism.

**Skin clinical manifestations:** patients are often photosensitive. Characteristic findings include Gottron's papules (violaceous




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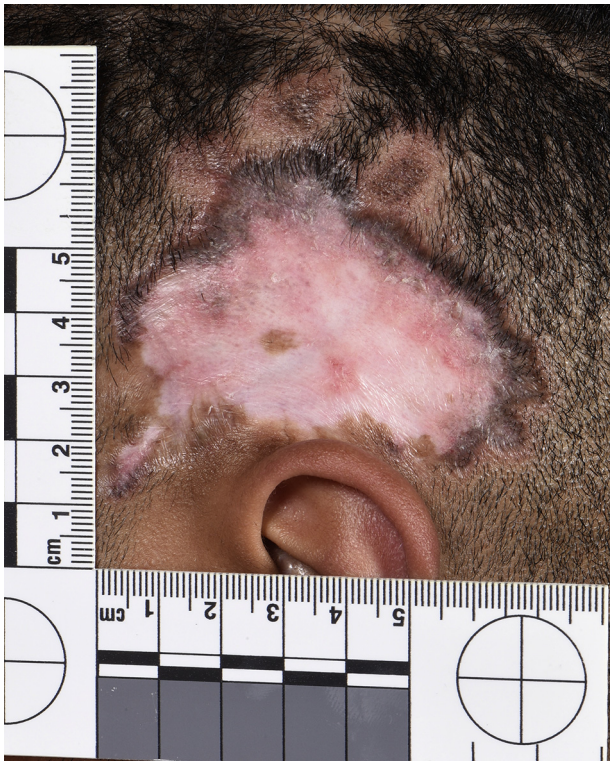

**Figure 1** Chronic discoid lupus erythematosus left scalp.

papules on the dorsal metacarpo- and intercarpo-phalangeal joints), a heliotrope eruption (erythematous eruption on the upper eyelids) and the 'shawl sign' (poikiloderma and pigmentary change in photoexposed sites, e.g. upper back, V of the neck). Nail fold changes include periungual erythema, ragged cuticles, haemorrhagic infarcts and abnormal capillaries at the proximal nail fold. Cutaneous calcium deposits may be seen in juvenile DM.

**Investigations:** skin biopsy and serology including ANA and extractable nuclear antigen (ENA) can be useful. Myositis-specific autoantibodies such as antisynthetase antibodies including anti-Jo 1 may be detected. Diagnosis of muscle disease is by imaging, electromyography, muscle biopsy and blood tests including creatinine kinase and inflammatory markers. Adults with DM can have up to a sevenfold increased risk of malignancy, so adult patients should undergo targeted investigation to exclude this.[2]

**Differential diagnoses**: these include other inflammatory skin conditions such as LE, psoriasis and eczema.

**Management:** this depends on the degree of muscle involvement. Skin disease can be managed with topical corticosteroids or systemic medications such as hydroxycholoroquine or methotrexate.

### Scleroderma and systemic sclerosis (SSc)

'Scleroderma' describes thickened skin. It can be localized to a limited area of skin (morphoea) or be part of a systemic condition with internal organ involvement, known as SSc. SSc is further characterized as diffuse or limited cutaneous SSc. The incidence of SSc is 0.6–122 per 100,000 per year. Pathogenesis involves immune activation, vascular damage and increased collagen deposition.

**Clinical features:** systemic symptoms including Raynaud's phenomenon, arthralgia, myalgia, fatigue, breathlessness and weight loss can occur in SSc. Gastrointestinal, cardiac, renal and lung involvement can also be seen. Skin changes typically affect the digits, hands and face, and include changes in pigment, sclerodactyly, ulceration and telangiectasia. Calcium deposits can be seen later in the disease. Localized scleroderma (morphoea), not associated with internal organ involvement, can be subdivided by extent (generalized, localized) and clinical appearance (e.g. en coup de Sabre), which appears in a linear formation affecting the scalp or face.

**Investigations:** diagnosis is made on the basis of suggestive symptoms or clinical findings. Bloods should be checked for ANA/ENA, including antitopoisomerase (anti Scl-70) and/or anti-RNA polymerase III antibody.

**Differential diagnosis of SSc:** this includes other scleroderma-like disorders such as morphoea, scleromyxoedema and scleroedema. Alternative diagnoses to consider in morphoea alone include erythema chronicum migrans.

**Treatment:** SSc can require systemic immunosuppression and agents to promote systemic vasodilatation. Morphoea can be treated with topical corticosteroids or ultraviolet light treatment, usually UVA.

## Skin problems in gastroenterology

Several hepatic and bowel disorders, such as pruritus resulting from deranged liver function or primary biliary cirrhosis, can affect the skin non-specifically. Dermatitis herpetiformis, associated with gluten-sensitive enteropathy, is characterized by skin changes in addition to bowel manifestations. Inflammatory bowel disease (IBD) is associated with skin changes in approximately 15% of patients; these include erythema nodosum (EN), mucosal surface changes such as episcleritis, PG and psoriasis. Some cutaneous manifestations, for example EN and episcleritis, mirror bowel disease activity, but others, such as PG, can occur independently of this. Additionally, patients with IBD can be affected by cutaneous problems surrounding their stoma site such as PG, or by irritant dermatitis from stoma bags or bowel contents.

### Erythema nodosum

EN occurs in around 10% of individuals with IBD. It is also associated with other systemic conditions including sarcoidosis, infections such as tuberculosis or streptococcal infections and drugs such as the oral contraceptive pill. An episode can last from 3 weeks but rarely up to 6 months. Pathogenesis is not fully understood, but EN may be a delayed hypersensitivity reaction after exposure to unknown antigens.




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