Skin signs of connective tissue disease

The skin can act as a very visible organ for the diagnosis and monitoring of connective tissue disease. A careful examination of the skin and mucous membranes may demonstrate specific or nonspecific signs, which aid in the diagnosis of these disorders and therefore the early institution of appropriate therapy.

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In medical school the association of a malar rash with lupus erythematosus is one of those signs learnt almost by rote. There are, however, a multitude of other skin signs of connective tissue diseases that may be helpful in making the diagnosis or in following the course of one of these disorders. Some are specific for particular entities, others merely indicative of the possible presence of a connective tissue disease. The major diseases covered in this article will be systemic lupus erythematosus, scleroderma, dermatomyositis and rheumatoid arthritis (their clinical features are summarised in the Table). Others will be mentioned where signs are particularly helpful.

A common pathophysiological thread in the connective tissue diseases is the targeting of the vascular system and its extreme reactivity, leading to a plethora of signs from mat telangiectasia to necrotic vasculitis. It should be remembered, however, that the severity of skin signs is not necessarily proportional to the extent of visceral involvement: severe disease is sometimes accompanied only by fleeting, subtle or very localised skin disease.

This article will cover those signs useful in the clinic for either suggesting a diagnosis or charting the progress of these diseases. Rather than producing an exhaustive list for each entity, I will take a regional anatomical approach that can easily be correlated with examination findings.

Head and neck signs

The face in general

There are often a number of helpful signs on the face in various connective tissue diseases (Figure 1).

Photosensitivity, common in lupus erythematosus, may present with erythema of exposed

IN SUMMARY

- **A multitude of skin signs may be helpful in making the diagnosis or following the course of a connective tissue disease.**
- **On the scalp and face, look for alopecia, scaling plaques, telangiectasia, erythema, oedema, nodules, photosensitivity and loss of expression.**
- **Signs on the trunk include induration, oedema, erythema and photosensitivity.**
- **Signs on the limbs include nodules, livedo, ulceration and punched-out lesions.**
- **Signs of connective tissue diseases are notably seen on the hands and feet. Look for nail changes, lesions on the fingertips, nodules, erythema, oedema, hyperkeratotic plaques and shiny skin.**
- **The severity of skin signs is not necessarily proportional to the extent of visceral involvement: severe disease is sometimes accompanied only by fleeting, subtle or very localised skin disease.**

Table. Clinical features of four connective tissue diseases

Systemic lupus erythematosus (SLE)

- Photosensitivity, malar rash
- Livedo, vasculitis
- Discoid lupus erythematosus (DLE) – 2% of these patients may have SLE
- Arthritis
- Antinuclear antibody, anti-DNA (anti-Ro and anti-La in subacute cutaneous lupus eryhthematosus [SCLE])

Scleroderma

- Raynaud's phenomenon
- Sclerodactyly
- Telangiectasia
- Sclerosis of skin
- Anti-SCL-70, antinuclear antibody, anticentromere antibody

Dermatomyositis

- Photosensitivity
- Heliotrope rash
- Muscle weakness
- Paronychia
- Associated internal malignancy
- Antinuclear antibody
- Elevated creatine kinase

Rheumatoid arthritis

- Joint deformities
- Rheumatoid nodules
- Vasculitis, pyoderma gangrenosum
- Bywaters' lesions
- Rheumatoid factor, antinuclear antibody

areas but demonstrates sparing of protected sites such as eyelids and under the chin. The classic 'butterfly rash' of systemic lupus erythematosus appears over the malar area and may be papular or just a macular erythema. A more generalised oedema of the face may be seen in systemic lupus erythematosus. Tumid lupus erythematosus, a subtype of discoid lupus erythematosus, is characterised by a boggy or firm erythematous plaque reminiscent of fixed urticaria, and it may be tender or occasionally ulcerating.

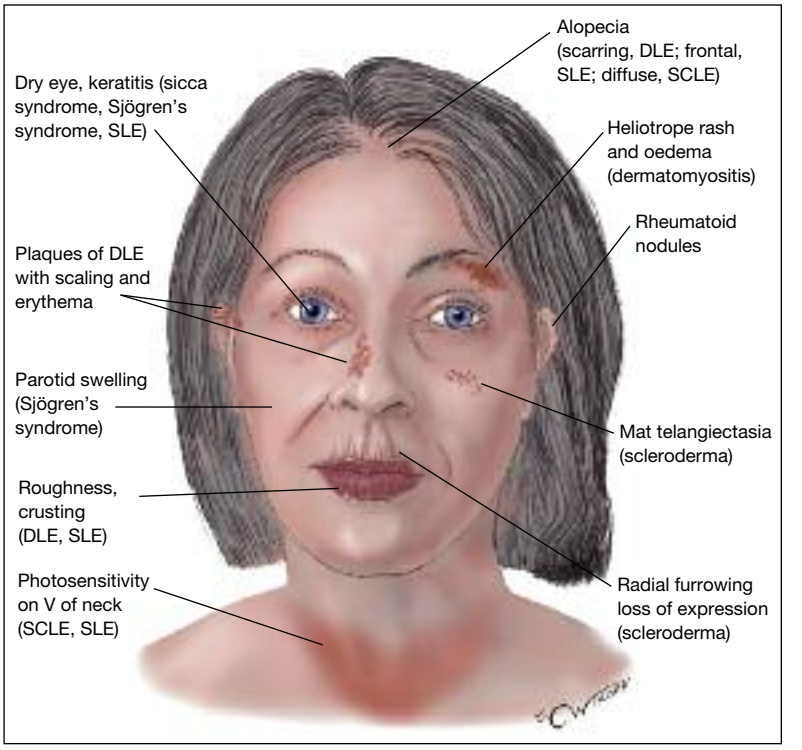

Figure 1. Skin signs of connective tissue diseases on the head and neck.

Sometimes systemic lupus erythematosus simulates rosacea, with papules, flushing and erythema; however, there are no pustules as are seen in true rosacea.

Plaques of discoid lupus erythematosus – characterised by redness, scaling atrophy, follicular plugging (giving a sandpapery texture to the involved skin) and scarring – may be found on the nose, forehead, ears and cheeks (Figure 2). Atrophy is best assessed by pinching the skin between the fingers (whereupon it develops fine wrinkling over the surface) or by looking for a loss of usual surface markings.

Pigmentation may occur in both lupus erythematosus and scleroderma, sometimes so gross as to suggest Addison's disease. Pigmentation frequently accompanies plaques of discoid lupus erythematosus. Antimalarials can cause a bluish-black pigmentation. Depigmentation may occur with both discoid lupus erythematosus and scleroderma.

Mat telangiectasia, where erythema is found in somewhat angular patterns associated with tiny arborising vessels, is typical of scleroderma and is most often found on the cheeks and nose.

Loss of facial expression, due to sclerosis of

the skin, may be apparent in scleroderma. A beaked appearance of the nose is seen in well established scleroderma, and the patient may have a reduced ability to open the mouth because of binding down of the adjacent facial skin. Associated radial furrowing produces a somewhat characteristic pursed-lip appearance (Figure 3). Trigeminal neuropathy and other cranial nerve involvement can occur in scleroderma, rarely leading to visible signs.

The ears may be a site for the development of rheumatoid nodules, which usually occur with more severe disease and occasionally develop before rheumatoid arthritis by some years. Discoid lupus erythematosus of the ears leads to considerable scarring and atrophy and may be associated with unusual pits in the concha, which also occur in systemic lupus erythematosus.

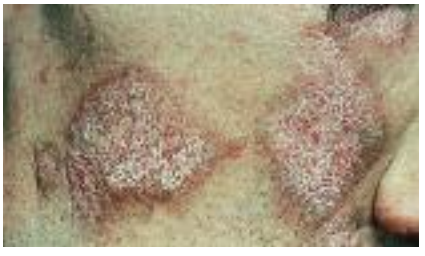

Figure 2. Plaques of discoid lupus erythematosus on the cheek.

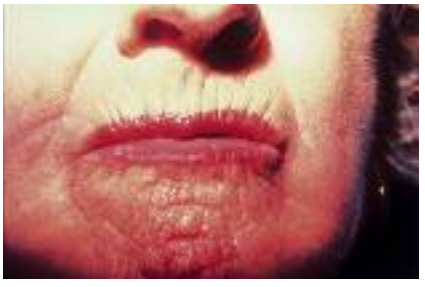

Figure 3. Perioral furrowing in scleroderma.

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Figure 4. Heliotrope rash in dermatomyositis.

Parotid swelling may be noted in Sjögren's syndrome. Features of iatrogenic Cushing's syndrome may be evident with typical steroid facies.

Eyes and periorbital areas

Discoid lupus erythematosus may affect the lower eyelids, with scarring leading to the loss of lashes in about 6% of cases.

Eyebrows may be sparse in lupus erythematosus and associated with erythema.

A conjunctivitis with velvety oedema, which may be aggravated by light exposure or trauma, can occur in systemic lupus erythematosus. Keratitis has been described in systemic lupus erythematosus: some studies have shown corneal staining with fluorescein in more than 80% of patients with the disease. Retinal and subconjunctival haemorrhages also occur.

In dermatomyositis, a characteristic purplish hue may suffuse the upper eyelids. Known as a heliotrope rash (Figure 4), it can be subtle or dramatic. Occasionally a similar picture is seen in lupus erythematosus. Even in the absence of a heliotrope rash, there may be significant oedema of the eyelids in dermatomyositis.

A sicca syndrome is common in scleroderma, and Sjögren's syndrome may coexist with other connective tissue diseases.

Mouth and teeth

Lips are not an uncommon site for discoid lupus erythematosus, and in systemic lupus erythematosus there may be roughness, crusting or redness. Inside the mouth, areas of superficial ulceration can occur – although these may well be a part of the interface dermatitis seen in systemic lupus erythematosus, rather than being secondary to vasculitis as is sometimes thought.

Widening of the periodontal membrane occurs in approximately one-third of patients with scleroderma because of fibrosis of the membrane; it generally affects multiple teeth. If only an isolated tooth is affected, it is more likely to be caused by localised periapical infection. As mentioned before, the aperture of the mouth may be reduced in a patient with scleroderma.

In dermatomyositis, involvement of the tongue produces difficulty in swallowing and speech.

Gingival disease is not uncommon in rheumatoid arthritis.

Dental caries are a significant problem in Sjögren's and other sicca syndromes because of loss of normally functioning saliva.

Scalp

Alopecia occurs in lupus erythematosus, dermatomyositis and scleroderma. In lupus erythematosus it may be scarring or nonscarring. Scarring alopecia is associated with plaques of discoid lupus erythematosus in many cases. Although discoid lupus erythematosus usually occurs as an isolated finding, in approximately 2% of affected patients systemic lupus erythematosus may coexist or develop subsequently. Scarring alopecia can therefore be a feature of systemic lupus erythematosus along with other skin signs of that disease.

Diffuse, nonscarring alopecia is marked in subacute cutaneous lupus erythematosus, where it coexists with photosensitivity and an arciform or psoriasiform rash on the trunk. 'Lupus hair' refers to short, broken-off hair, usually on the frontal margin with an unruly appearance.

Frontoparietal lesions of localised scleroderma (morphoea) produce a linear, depressed groove with associated alopecia – the 'sabre cut' appearance – which occasionally extends to involve the mouth, chin and neck. This is not associated with systemic disease.

Treatment of connective tissue diseases with antimalarials may produce an odd blonding of the hair.

Neck

In lupus erythematosus, photosensitivity may be evident with erythema of the V of the neck. In subacute cutaneous lupus erythematosus, a psoriasis-like eruption may be apparent on the back of the neck and upper back.

Induration and thickening occurs in scleroderma. This may be evident only when the head is extended with the chin elevated, at which time thickened, taut ridges appear on the sides of the neck. This differs from normal ageing changes of the neck skin, where such ridges are soft.

Buffalo hump formation may be evident in patients with severe connective tissue diseases who have been given high dose or prolonged corticosteroid treatment.

Trunk signs

Blotchy, reticulated telangiectasia may occur over the trunk in systemic lupus erythematosus. Rarely, panniculitis occurs in systemic lupus erythematosus, with deep, tender nodules forming which may ulcerate.

The scaly, psoriasiform or arcuate annular rashes of subacute cutaneous lupus erythematosus are predominantly found on the trunk. Often there is accompanying marked photosensitivity.

Bullous lupus erythematosus occurs in the setting of active systemic disease, and these patients are often very unwell. Blisters occur over the upper trunk and sometimes face and neck. Lesions more typical of systemic lupus erythematosus are usually present elsewhere, although they may be subtle.

Firm induration, especially of the upper trunk, is seen in scleroderma. The chest wall may become so tight as to restrict adequate ventilation. Calcification may occur around the iliac crests.

Calcinosis is seen in dermatomyositis, particularly in the childhood variant where it seems to be associated with a good, long term prognosis. It is generally a late manifestation. There may also be extrusion of calcium through the skin.

Oedema and erythema of the trunk are found in dermatomyositis. Hyperpigmentation can occur in later stages.

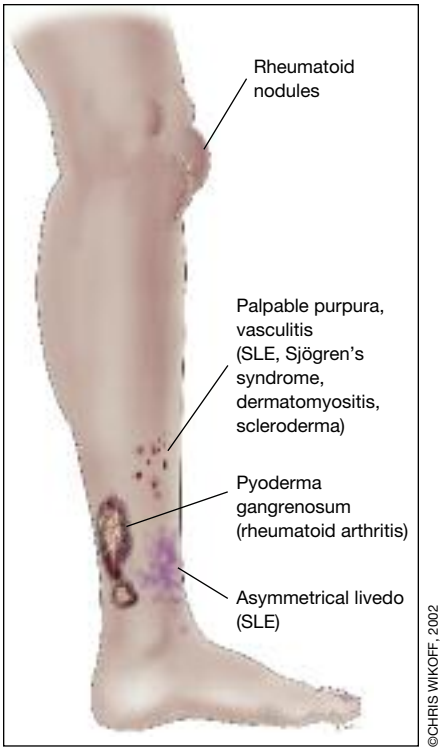

Figure 5. Skin signs of connective tissue diseases on the lower limb.

Limb signs

Figure 5 illustrates some of the signs of connective tissue diseases that can be seen on the lower limb.

A reticulate erythema called livedo (Figure 6) occurs in systemic lupus erythematosus, dermatomyositis and scleroderma. It is caused by changes affecting the superficial vessels, resulting in mottling similar to that seen in cold exposure. However, it tends to be fixed, is often asymmetrical and may be associated with ulceration, especially in the presence of anticardiolipin antibody. It is most often seen in systemic lupus erythematosus, where it may coexist with lupus vasculitis of the central nervous system.

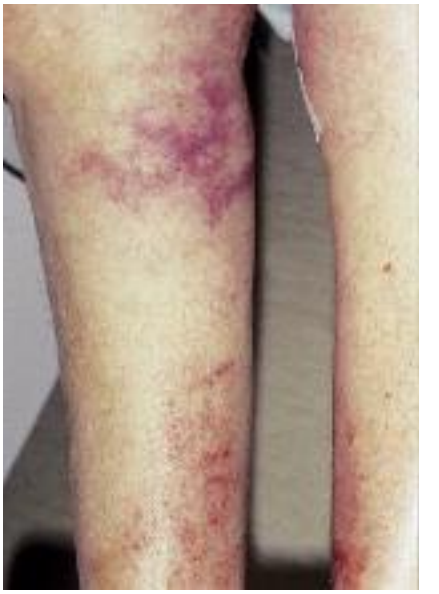

Figure 6. Livedo and vasculitis on the legs.

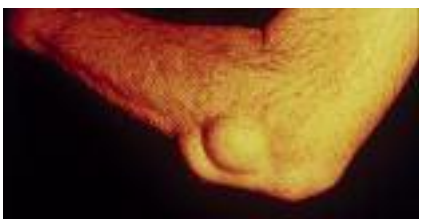

Figure 7. Rheumatoid nodules over the ulnar border of the forearm.

Subcutaneous nodules of systemic lupus erythematosus can be found over the wrists and knees and may be difficult to differentiate from rheumatoid nodules. Rheumatoid nodules, however, occur most commonly in rheumatoid arthritis over the ulnar border of the forearm (Figure 7) and tend to be associated with more severe disease. They can cause erosion into the underlying bone.

In systemic lupus erythematosus, ulceration of the lower leg may occur from frank vasculitis, usually of small vessels and at times associated with a palpable purpura. Vasculitis may also manifest as punched out lesions (Figure 8), and biopsy is useful to identify vasculitis as the cause in these lesions.

continued

Calcinosis in dermatomyositis may result in joint contracture, as can also be seen in scleroderma.

In dermatomyositis, there may be striking erythema of the extensor surfaces of the limbs. Occasionally there is also tenderness to palpation of the proximal muscle girdles.

Pyoderma gangrenosum, with a typical bluish, undermined edge and a sloughy base, may be a sign of active rheumatoid arthritis (Figure 9) and to a lesser extent other connective tissue diseases. These ulcers often expand rapidly, do not respond to antibiotics, and are very painful. New lesions, sometimes pustular, may occur at sites of skin trauma.

Ulceration occurs in rheumatoid arthritis owing to other factors including stasis and venous insufficiency, vasculitis, neuropathy and arterial disease, both occlusive and arteritic. There is some suggestion it is more common in Felty's syndrome (rheumatoid arthritis, splenomegaly and leucopaenia). Sometimes ulceration is related to underlying rheumatoid nodules.

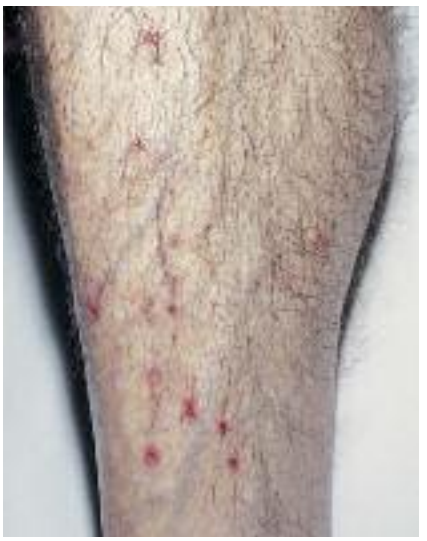

Figure 8. Punched out lesions of vasculitis in the leg.

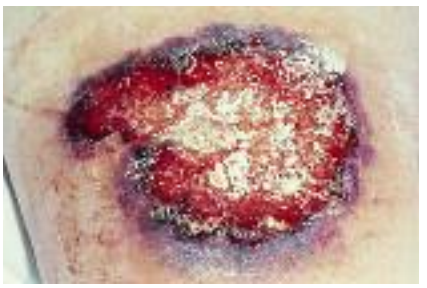

Figure 9. Pyoderma gangrenosum in rheumatoid arthritis.

Hands and feet signs

Perhaps more than any other site, the clinical findings of connective tissue diseases are notably demonstrated on the hands (Figure 10) and feet.

In systemic lupus erythematosus, signs may vary from a subtle erythema over the palms, soles and pulps of fingers (resembling that seen with liver disease) to insidious gangrene of the digit tips. Nail changes include ragged cuticles, splinter haemorrhages and dilatation of the nailfold capillaries. The latter is also seen with other connective tissue diseases to various extents. Other signs of systemic lupus erythematosus may be Raynaud's phenomenon and erythema along the shafts of the phalanges.

Lesions of discoid lupus erythematosus can also present on the hands or feet, often with a quite hyperkeratotic, papular appearance. A warty variant can appear on the palms and the soles, making walking difficult.

In scleroderma, there may be telangiectasia and calcinosis, especially in the CREST variant (calcinosis, Raynaud's, oesophageal dysmotility, sclerodactyly and telangiectasia). Pitted scars occur on the tips of the fingers (Figure 11), and sclerodactyly results in the typical smooth, shiny, bound-down skin of the digits and the dorsum of the hands and feet. Over time, the distal pulp of the fingers may atrophy, and the hand is often held in semiflexion. Nailfold capillaries are often enlarged and distorted, and they may be visible with the naked eye. Under simple oil magnification, capillary loop dropout is evident as are abnormalities of the number and nature of the loops. These changes may be seen to a lesser

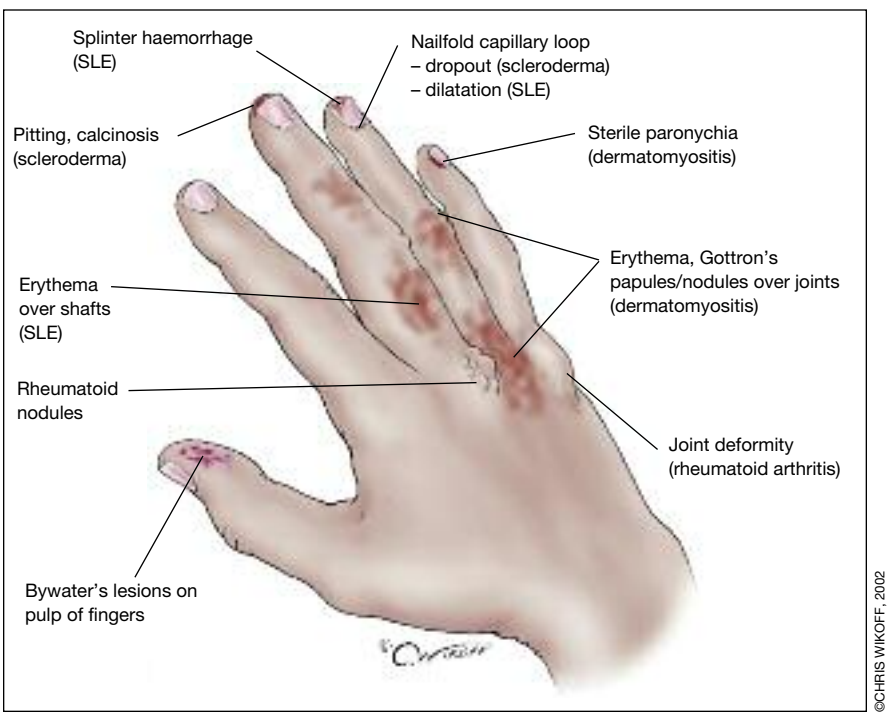

Figure 10. Skin signs of connective tissue diseases on the hand.

extent in other connective tissue diseases.

Dermatomyositis often presents with characteristic nodules called Gottron's papules over the knuckles (Figure 12). These are small, red or purple flat papules or plaques. They are seen also on the dorsa of the finger joints and sometimes over the toes, knees and elbows. A violaceous erythema without nodules can occur over the finger joints (contrasting with the erythema of systemic lupus erythematosus, which occurs over the shafts). A sterile paronychia seems to be associated with more aggressive dermatomyositis. Capillary changes of dilatation and tortuosity occur and are more marked in patients who have Raynaud's, arthritis and pulmonary involvement. Oedema of the hands may be striking in dermatomyositis.

Rheumatoid nodules may occur on the dorsa of the hands as firm, subcutaneous lesions that can ulcerate with trauma. If digital necrosis occurs, it closely correlates with the presence of rheumatoid nodules and rheumatoid factor. Nailfold infarctions are the most characteristic of skin lesions in rheumatoid arthritis. They tend to be short lived and are usually painless. This is in contrast to Bywaters' lesions, which represent painful, purpuric nodular areas of leucocytoclastic vasculitis in the pulp of the fingers.

Particular signs in children

Signs of connective tissue disease in the paediatric population may resemble those in adults, but several features may differ.

In dermatomyositis in children, the association with malignancy is rare but there is a much greater incidence of calcinosis. This can result in significant loss of function, particularly when accompanied by joint contracture, and it requires aggressive drug treatment and physiotherapy. (Warfarin may be helpful.)

Benign rheumatoid nodules can occur in childhood without any association with aggressive rheumatoid arthritis.

Figure 11. Digital ischaemia in scleroderma.

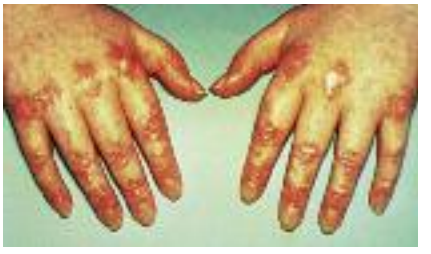

Figure 12. Gottron's papules and erythema in dermatomyositis.

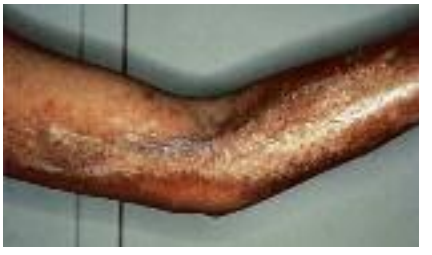

Figure 13. Linear scleroderma on the arm.

Neonatal lupus erythematosus presents with a rash composed of large annular lesions, at times triggered by sun exposure. It occurs in the children of one in 200 patients with anti-Ro antibodies, although there is no way of predicting which offspring will be affected. The most serious association is neonatal heart block and approximately one-third of mothers of babies with heart block may go on to develop systemic lupus erythematosus. Therefore, the mother of an affected baby should be tested for anti-Ro antibodies.

Although it is not associated with systemic disease, linear scleroderma produces such significant morbidity it is important to recognise it. Children with this condition present with linear areas of scleroderma-like induration on a limb (Figure 13) or less commonly the trunk. Sometimes there is preceding oedema. The condition may involve underlying muscle or bone. There is resulting growth disturbance in approximately 20% of children with the condition, and severe flexion deformities are possible.

Conclusion

The skin can act as a very visible organ for the diagnosis and monitoring of connective tissue diseases. A careful examination of the skin and mucous membranes may demonstrate specific or nonspecific signs of these diseases.

This should not be considered just as an academic exercise because early diagnosis of conditions such as dermatomyositis has life-or-death consequences. The early detection and treatment of the internal malignancy associated with 20 to 50% of cases of dermatomyositis can obviously result in a striking improvement in the patient's prognosis. Realisation of the association of neonatal lupus erythematosus and congenital heart block may prevent premature severe consequences and also highlights the risk of systemic lupus erythematosus in the mother. Appreciation of the subtle, early changes of scleroderma in the facial appearance of affected patients may lead to earlier screening and intervention for the systemic sequelae of the disease.

This is not to suggest that examination alone is sufficient for the diagnosis and monitoring of patients with connective tissue diseases. Careful history taking, investigations with appropriate serological assays and assessment of systemic involvement are all essential in the management of these patients. However, as symptoms of connective tissue diseases can be nonspecific and serology may vary with time, treatment and disease activity, there is no substitute for a clinician's observant eye for the signs of these diseases. MT