

Cutaneous Manifestations of Internal Disease



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Presented at Queen's University's "A Day in Dermatology," May 2006.

There are many internal diseases that present with cutaneous manifestations. This article will focus on those associated with:

- diabetes mellitus,
- renal disease,
- inflammatory bowel disease and
- lupus erythematosus.

These cutaneous signs may precede, occur concurrently, or follow the onset of the internal condition.

One of the commonly recognized conditions seen with diabetes mellitus is necrobiosis lipoidica diabetorum (Figure 1). This is manifested by atrophic yellow-orange patches with red borders often on the shins. Some of the lesions may ulcerate and heal, leaving atrophic scars. This condition has been associated with diabetic retinopathy and nephropathy.¹ The treatment options include use of topical or intralesional corticosteroids around the wound edges, pentoxifylline and local management of ulcers if present.

Another associated condition with diabetes mellitus is relapsing, generalized, eruptive granuloma annulare (Figure 2). These are characterized by flesh-coloured, pink, violaceous or reddish-brown papules, some grouped in an arciform pattern (Figure 3), on the trunk and extensor limbs.² The lesions are mostly asymptomatic and may spontaneously resolve. In the differential necrobiosis lipoidica, cutaneous sarcoidosis, lichen planus and rheumatoid nodules may be



Figure 1. Necrobiosis lipoidica diabetorum.

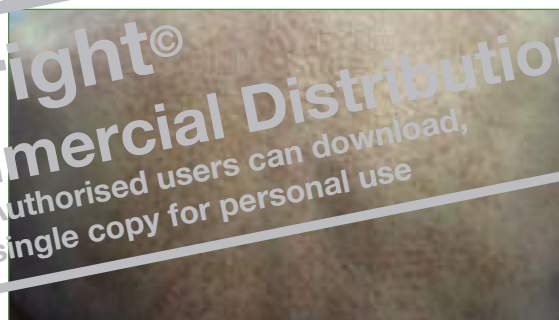


Figure 2. Generalized granuloma annulare.



Figure 3. Localized granuloma annulare.

Table 1

Cutaneous manifestations of diabetes mellitus

- Diabetic bullae
- Neuropathic ulcers
- Eruptive xanthomas (Figure 4)
- Acanthosis nigricans (Figure 5)
- Scleredema
- Partial lipodystrophy
- Acral erythema
- Hemochromatosis
- Carotenemia
- Infections:
 - Erythrasma (*Corynebacterium minutissimum*)
 - Furuncle/carbuncle
 - Candidiasis

considered. The treatment options include:

- observation alone,
- topical/intralesional corticosteroids,
- cryotherapy and
- psoralen UVA treatment.

The most common cutaneous manifestation of diabetes is diabetic dermopathy. This is characterized by small, oval, reddish-brown, atrophic macules and patches most often found on the lower limbs, possibly as a result of trauma and decreased skin perfusion.³ The importance of recognizing this condition is to help detect the early presence of renal and retinal microangiopathy.

Other miscellaneous conditions associated with diabetes mellitus are listed in Table 1.

Renal disease has been associated with pruritus and on occasions with a condition termed calciphylaxis. Calciphylaxis is characterized by progressive, painful, cutaneous necrosis found on the lateral and posterior calves. There is small and medium vessel calcification and is often seen in the setting of end-stage renal disease, diabetes mellitus and

Table 2

Etiologic factors of erythema nodosum

Infections

- Group A β -hemolytic *streptococcal* infection
- TB
- Histoplasmosis
- Coccidioidomycosis
- Yersinia

Medications

- Sulfonamides
- OCs

Miscellaneous

- Sarcoidosis
- Ulcerative colitis
- Behcet's syndrome

Idiopathic in 40% of cases

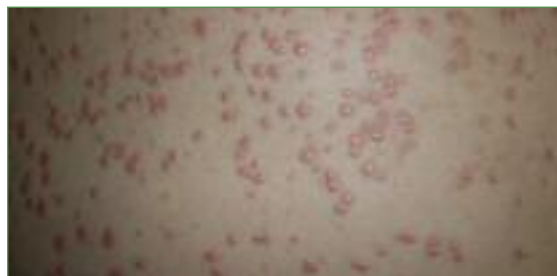


Figure 4. Eruptive xanthomas on back.



Figure 5. Acanthosis nigricans in axilla.



Figure 6. Erythema nodosum on shin.



Figure 7. Discoid lupus erythematosus.



Figure 8. Subacute cutaneous lupus erythematosus.



Figure 9. Systemic lupus erythematosus.

hyperparathyroidism. Secondary complications include infection and sepsis. The differential includes cutaneous vasculitis, necrobiosis lipoidica, pyoderma gangrenosum and warfarin/heparin necrosis. An elevated calcium phosphate product is found. The management includes treatment of the renal failure, partial parathyroidectomy, debridement of necrotic tissue and treatment of any underlying infection. Mortality is high.⁴

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Erythema nodosum, considered a hypersensitivity response, is characterized by painful, tender nodules on the lower legs (Figure 6). The common trigger factors are shown in Table 2, including infection with group A β -hemolytic *streptococcus*, medications, such as sulfonamides and OCs and miscellaneous conditions, such as sarcoidosis and inflammatory bowel disease.⁵ The lesions are idiopathic in 40% of cases. The duration of lesions is between days to weeks. The diagnosis is made clinically. A throat swab, stool culture and chest x-ray are recommended as part of the investigations. Management would include:

- bed rest,
- compression bandages,
- use of NSAIDs and
- rarely, prednisone.

Pyoderma gangrenosum is characterized by the onset of a violaceous nodule or hemorrhagic pustule which progresses to an ulcer with overhanging edges and undermined borders. The ulcer base may be purulent and hemorrhagic with a necrotic eschar. Healing occurs with a cribriform scar. The lesions are usually seen on the lower extremities and associated with inflammatory bowel disease, rheumatoid arthritis and acute myelogenous leukemia. Pathergy, the occurrence of new lesions at sites of trauma, such as from a needle stick or biopsy, may be present.⁵ The diagnosis is usually made clinically. Management consists of ulcer dressings, intralesional/oral corticosteroids and rarely the use of other systemic agents, such as minocycline, cyclosporine, azathioprine, mycophenolate mofetil, etanercept,⁶ infliximab and dapsone.

Lupus erythematosus may be divided into three categories:

- Discoid
- Subacute Cutaneous
- Systemic

Discoid lupus (Figure 7) is characterized by round to oval, slightly indurated, sharply



Table 3

Non-specific eruptions of lupus erythematosus

- Photosensitivity
- Raynaud's phenomenon
- Alopecia
- Aphthosis
- Cutaneous infarcts
- Livedo vasculitis
- Neonatal lupus
- Lupus panniculitis

demarcated, violaceous plaques with hyperkeratosis and central atrophy, found on sun-exposed areas.⁵ The lesions progress to atrophic scars and post-inflammatory hypopigmentation. In

the differential actinic keratosis, psoriasis and tinea faciei may be considered. Less than 10% of patients have systemic manifestations. The diagnosis is made both on clinical grounds and biopsy for histology and immunofluorescence. The management consists of sun screens, topical/intralesional corticosteroids and occasionally antimalarial agents.

Subacute cutaneous lupus erythematosus (Figure 8) presents with psoriasiform or annular lesions mostly on the upper trunk and arms. There may be associated arthralgias, serositis and renal disease.⁷ The differential includes psoriasis, seborrheic dermatitis, tinea corporis and dermatomyositis. Blood work shows positive anti-Ro antibody associated with neonatal congenital heart block and neonatal lupus.

Systemic lupus classically presents with a malar rash in a “butterfly distribution” (Figure 9).

Table 4

Miscellaneous conditions with skin signs⁴

Cutaneous manifestation	Internal disease
Clubbing	Chronic lung disease, pulmonary neoplasms
Icterus	Bile duct obstruction
Erythroderma	Drug reactions, lymphoma, leukemia
Pruritus	Lymphoma, leukemia
Acanthosis nigricans	GI tract adenocarcinoma
Acquired ichthyosis	Lymphoma
Erythema gyratum repens	Carcinoma of breast, lung, bladder
Sweet's syndrome	Viral infection, acute myelogenous leukemia
Necrolytic migratory erythema	Glucagonoma
Paget's disease	Intraductal carcinoma of the breast
Extramammary Paget's disease	Genitourinary or rectal adenocarcinoma
Carcinoma <i>en cuirasse</i> and carcinoma <i>erysipeloides</i>	Metastatic breast carcinoma
Sister Mary Joseph's nodule	Colonic, ovarian, pancreatic, breast carcinoma
Hypertrichosis lanuginosa acquisita	Anorexia nervosa, pulmonary neoplasms

There may be associated fever, arthritis, renal, pulmonary, cardiac manifestations and seizures. The cutaneous lesions may be erythematous, papular, urticarial or discoid and are mostly found on sun-exposed areas. A positive lupus band test is found on biopsy from both sun-exposed and non-exposed skin. Antinuclear antibody is positive in > 90% of cases. There may be hematologic abnormalities including leukopenia, anemia, thrombocytopenia and low levels of complement. Management consists of:

- bed rest,
- avoidance of sun exposure,
- prednisone and
- antimalarial agents, such as hydroxychloroquine.

Occasionally, other immunosuppressive agents, such as azathioprine and cyclophosphamide are used.

Nonspecific manifestations of lupus erythematosus are listed in Table 3.

There are a number of other internal diseases that present with rarer cutaneous signs (Table 4).⁸

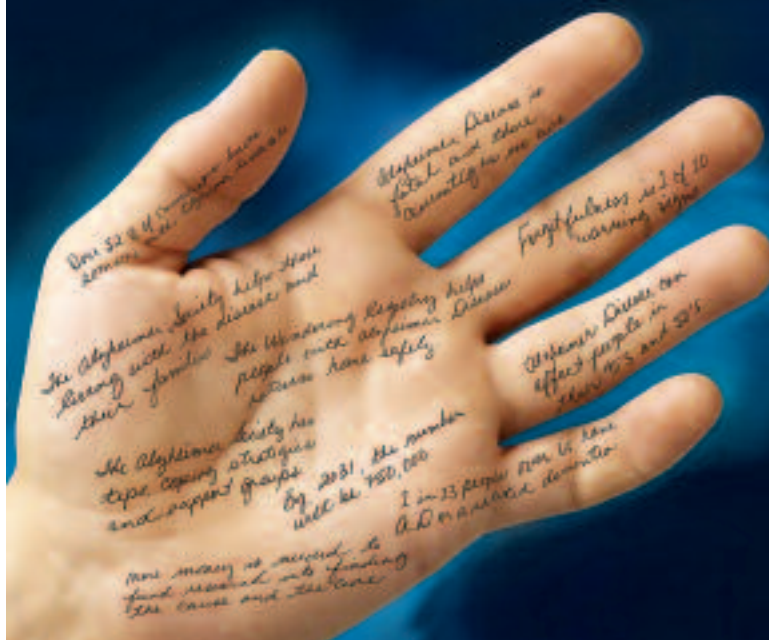
This article has briefly summarized some of the commonly recognized cutaneous diseases seen as a manifestation of internal disease. It is important to know and identify these cutaneous signs which may help in diagnosing the internal condition at an early stage.

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