Diabetic dermopathy
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Diabetic dermopathy is a skin condition often seen in diabetes. It appears as round to oval atrophic hyperpigmented lesions on the pretibial areas of the lower extremities. The lesions are usually bilateral and have an asymmetrical distribution. Histologically, lesions show edema of the papillary dermis, thickened superficial blood vessels, extravasation of erythrocytes, and a mild lymphocytic infiltrate. The extravasated erythrocytes leave hemosiderin deposits, which provide the brownish hyperpigmentation. The lesions of diabetic dermopathy resolve spontaneously, leaving scars behind.

Diabetic Thick Skin
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Physicians have noticed that patients with DM tend to have thicker skin than those without. This has been confirmed using ultrasound.[27] Diabetic thick skin has been separated into three main categories: 1) scleroderma-like changes of the hand associated with stiff joints and limited mobility; 2) measurable skin thickness that is clinically insignificant; and 3) scleredema diabeticorum. Thickening of the dorsum of the hands may occur in a third of patients with diabetes.[7] Other signs of increased skin thickening include pebbled or rough skin, known as Huntley's papules, over the interphalangeal joints, particularly the knuckles. Waxy skin and stiff joints have been correlated with increasing age and duration of diabetes, more so for Type 1 DM, rather than the glycemic value.[4,28]

The term **scleredema** describes a clinical picture of thickening of the skin and nonpitting induration of which there are two types. The first, scleredema of Buschke, can occur at any age and is usually subsequent to a viral or streptococcal infection. The posterior neck and upper part of the back are frequently affected. Scleredema diabeticorum has the same distribution as scleredema of Buschke, but the skin thickening extends to the upper extremities, including the hands.

Histologically, large disorganized collagen bundles in a thickened dermis are separated by clear spaces with small amounts of acid mucopolysaccharides. Diabetic scleredema may be difficult to distinguish clinically from scleroderma. Hanna and Friesen reveal that diabetic thick skin has distinct light and electron microscopic features from those seen in scleroderma.[29] Unlike scleroderma, diabetic thick skin seldom has collagen fibers below 60nm, and bimodality of fibers was not observed.[29]

Some studies have mentioned an increased synthesis of type 3 collagen (small fibers) in scleroderma, resulting in a bimodal distribution of collagen size.[29-32]

Another study mentioned an increase in hyaluronic acid in diabetic scleredema with a predominance of dermatan sulfate in scleroderma.[29,33]

The pathogenesis of diabetic thick skin has not been clearly defined. Potential explanations include the hydration of collagen secondary to polyol accumulation[4,34] and nonenzymatic glycosylation of collagen.[4,35]
There is no treatment for this condition although strict glycemic control may be beneficial.

**Diabetic Bullae**

Diabetic bullae are usually confined to the hands and feet. The blisters occur spontaneously, and most are nonscarring. Patients tend to have adequate circulation in the affected extremities but have signs of diabetic peripheral neuropathy. There are three types of diabetic bullae. The most common type is sterile and fluid-containing and heals without scarring. Histology shows intraepidermal cleavage without acantholysis.[7] The second type is hemorrhagic and heals with scarring. Histology depicts cleavage below the dermoepidermal junction with destruction of anchoring fibrils.[7,37] The third type involves mostly multiple nonscarring bullae on sun-exposed, tanned skin. Histology reveals cleavage at the lamina lucida.[37,38] One study mentioned an association with long-term Type 2 DM[39] with peripheral neuropathy, and another study mentioned a connection with chronic Type 1 DM.[4]

The pathogenesis of these lesions has not been clearly elaborated. Therapy of diabetic bullae focuses on preventing infection.

**Yellow Skin**

Yellow nails and skin associated with diabetes is a benign condition with no known significance. The pathological cause of yellow skin remains in controversy. The change may be due to either elevated levels of carotene or nonenzymatic glycosylation of dermal collagen.[4] One glycosylation end product, 2-(2-furoyl)-4(5)-(2-furanyl)-1H-imidazole, has a yellow hue, which could provide the characteristic color of yellow skin.[3,16]

The yellow color is best appreciated at the distal hallux of the nails, palms, and soles. There is no current treatment for this condition.
Diabetic Ulcers

Diabetic patients form the single largest group of nontraumatic amputations in the United States.[40] For the majority of diabetic patients, the initial condition that leads eventually to amputation begins with a skin ulcer (Figure 5). Diabetic foot ulcers are separated into two categories: ischemic and neuropathic ulcers. [40] Peripheral neuropathy plays a central role in nearly four-fifths of diabetic patients. The most common neuropathy is a mixed distal motor and sensory neuropathy. [4,41] In the majority of cases, ulceration occurs as a consequence of the loss of protective sensation. The combination of motor and sensory neuropathy along with mechanical factors plays a role in the pathogenesis of neuropathic ulcers. [4,42]

Clinical signs of paresthesias with loss of temperature and pain sensation along with disturbances in sweating are prevalent in neuropathic diabetic ulcers. The pathogenesis of ischemic ulcers involves diabetic atherosclerotic disease. The ischemic patient will present with disproportionately excruciating pain associated with a superficial ulcer, while the neuropathic patient is unaware of a large, deep ulcer. The ischemic patients will often elicit a history of intermittent claudication, foot pain on leg elevation, and pain relieved with resting.

Prevention of foot ulcers is critical. Clinicians should routinely examine the feet of diabetic patients. A nylon monofilament test provides a method of early determination for the loss of peripheral sensation and identifies patients at risk for ulceration. Education in foot care, proper footwear, avoidance of burns and trauma, and close medical follow up are steps needed for the prevention of diabetic ulcers. [40] Glycemic control will diminish the progression of peripheral neuropathy, a key factor in the development of ulcers. Smoking cessation must be emphasized. Patient compliance along with physician intervention are the mainstays of the prevention strategy of diabetic ulcers.

Treatment of diabetic ulcers becomes necessary once preventive measures have failed. Many diabetic ulcers fail to heal because patients continue to put weight on their affected lower extremities. Approximately 90 percent of ulcers can be treated by relieving weight from the ulcerated area, treatment of infections with systemic antibiotics, and arterial perfusion restoration.[43] A common mistake is the use of wet-to-dry dressings on a clean ulcer bed.[40]
The removal of the dry dressing interrupts the healing process of re-epithelialization. The preservation of a wet saline dressing maintains a moist wound environment. New adjunctive therapies, such as becaplermin gel (recombinant platelet-derived growth factor), show modest benefit in improving granulation tissue and wound repair.

The role of growth factors and cytokines in the process of wound healing is an area of ongoing investigation. Bioengineered skin equivalents, such as Apligraf® (Novartis Pharmaceutical Inc., East Hanover, New Jersey) and Dermagraft® (Smith & Nephew Inc., Largo, Florida), promote more rapid healing.

These innovative therapies are not substitute for basic management of diabetic ulcers, such as adequate offloading, treatment of infections, and debridement.

The decision to perform vascular surgery depends on the severity of the vascular impairment, the surgical risks, and rehabilitation potential. The therapeutic goal of the treatment of diabetic ulcers is the eventual healing and avoidance of amputation, thereby improving function and quality of life.

Diabetic Cutaneous Infections

Well-controlled diabetic patients are no more susceptible to infections than the normal population. Patients with uncontrolled DM and ketosis are more predisposed to severe systemic and cutaneous bacterial infections. Bacterial infections of the skin, usually caused by Staphylococcus aureus and beta-hemolytic Streptococci, include impetigo, erysipelas, cellulitis, and necrotizing fasciitis.

Obese patients with DM have a higher predisposition to erythrasma caused by Corynebacteria minutissimum.

Systemic antibiotic therapy and surgical debridement are indicated for severe infections, particularly for necrotizing fasciitis. Candida is one organism correlated with increased serum glucose levels and an early indicator of undiagnosed DM.

Commonly affected areas involve the nail folds and the web spaces of the fingers and toes. Normalization of blood glucose and use of topical and systemic antifungals are the main modalities of treatment. Patients with DM are also at risk for rhinocerebral mucormycosis, an extensive life-threatening infection beginning in the nasal passages and spreading into the orbit and cerebrum.

Treatment consists of debridement and intravenous fungal therapy, such as amphotericin B.
Malignant external otitis caused by *Pseudomonas aeruginosa* is a rare but serious infection in elderly people with diabetes. Initially, there is a purulent discharge and severe pain of the external auditory meatus, which then progresses to cellulitis and then to meningitis.\[4,7,48\]

Treatment involves surgical debridement and intravenous anti-Pseudomonal antibiotics. Patients with malignant otitis externa have high mortality rates.

**Perforating Dermatosis**

The majority of patients with adult-onset acquired perforating dermatosis have kidney failure associated with diabetes.\[50\] Itching and scratching accompany this entity, also known as Kyrie's disease or reactive perforating collagenosis. The lesions are located primarily on the extensor surfaces of the lower extremities but can occur on the face and trunk. The lesions are described as a few millimeters in diameter, papular, often with a keratotic plug. Another feature consists of the elimination of collagen and elastin throughout the affected epidermis. Histologic examination of these lesions reveals a hyperplastic epidermis surrounding a plug of degenerated material, which has elements of leukocytes, collagen, and nuclear debris.\[3,4,5\]

Acquired perforating dermatosis is difficult to treat. Retinoic acid has shown some benefit along with topical antihistamines to alleviate the pruritus.\[52\]

A Chinese study showed a reduction of pruritus with the use of transcutaneous electrical nerve stimulation.\[53\]

A German article mentioned two patients being successfully treated with allopurinol.

**Eruptive Xanthomas**

Eruptive xanthomas in the context of DM are accompanied by hyperlipidemic and hyperglycemic states. The lesions are described as waxy, yellow papules surrounded by an erythematous rim and usually occur on the extensor surfaces and popliteal region. Histologic samples depict lipid-laden histiocytes and a mixed lymphoneutrophilic infiltrate in the dermis. The main treatment option is strict control of the hyperlipidemic and hyperglycemic condition.
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associated with the DM

**Other Dermatoses**

There is some evidence of higher incidence of vitiligo in diabetic patients. Patients with vitiligo have family histories of autoimmune diseases, such as Addison's disease, Hashimoto's thyroiditis, and pernicious anemia. Vitiligo has a higher incidence among adults with diabetes; therefore, it is recommended to evaluate for diabetes among late-onset vitiligo.

One-fourth of porphyria cutanea tarda patients have diabetes.

Diabetes generally precedes the onset of porphyria, a possible result of the nonenzymatic glycosylation of the heme pathway.

Granuloma annulare is a chronic, asymptomatic dermatosis with a predilection for the dorsum of the hands, feet, and elbow. The lesions may be difficult to distinguish from necrobiosis lipoidica diabeticorum and are self limited. The generalized form may have an association with DM.

Nearly one-half of diabetic patients with psoriasis develop psoriasis before diabetes, but the association between diabetes and psoriasis has not been clearly defined.

Similarly, the association between diabetes and lichen planus, Kaposi's sarcoma, and skin tags remain controversial.