Skin Disorders in Older Adults: Manifestations of Endocrine and Metabolic Diseases

ABSTRACT: Various metabolic and endocrine diseases can produce changes in the skin. The most common cutaneous manifestations of diabetes mellitus are bullous diabeticorum, acanthosis nigricans, diabetic dermopathy, and necrobiosis lipoidica diabeticorum. In many cases, these disorders result from the deleterious effects that high glucose and insulin levels have on the vasculature. Tophi can develop in patients with chronic untreated gout. Calcinosis cutis encompasses a group of disorders in which calcium deposits form in the skin; the four major types are dystrophic, metastatic, iatrogenic, and idiopathic. Xanthomas can reflect lipid metabolism alteration associated with hyperlipidemia, or they can result from local cell dysfunction.

Key words: gout, tophus, calcinosis cutis, pretibial myxedema, hyperthyroidism, diabetes, bullous diabeticorum, bullous diabeticorum, acanthosis nigricans, diabetic dermopathy, necrobiosis lipoidica diabeticorum, xanthoma, xanthelasma

NOAH S. SCHEINFELD, MD, JD
Columbia University

A variety of metabolic and endocrine diseases have cutaneous manifestations. Diabetes affects all organs, and the skin is no exception. In many cases, the cutaneous manifestations of diabetes result from the deleterious effects that high glucose and insulin levels have on the vasculature. Other endocrine diseases, such as thyroid disease, can also cause cutaneous pathology. In this article, I will describe and illustrate these processes.

GOUT

This common disorder of uric acid metabolism can lead to recurrent episodes of joint inflammation, tissue deposition of uric acid crystals, and joint destruction if left untreated. Unlike many other rheumatic diseases, gout is highly treatable. A definitive diagnosis can be made using joint aspiration and synovial fluid analysis. Early diagnosis and treatment of gout have decreased its morbidity and mortality, as is demonstrated by the declining incidence of chronic tophaceous gout.1 How-

Figure 1 – The classic site for tophi is along the helix of the ear.
ever, tophaceous gout may occur because of misdiagnosis, poor management, or poor patient compliance.

Gout is caused by excess stores of uric acid that accumulate in tissues, including the skin and the synovium. Reducing serum uric acid levels can prevent attacks of gouty arthritis. However, urate crystals also can be found in synovial fluid in the absence of joint inflammation. Thus, the simple presence of intrasynovial urate crystals is not sufficient to cause flares of gouty arthritis.

In men, uric acid levels rise at puberty, and peak age of onset of gout is in the fourth to sixth decades. In women, uric acid levels rise at menopause, and peak age of onset is in the sixth to eighth decades. Gout is unlikely to present in premenopausal women or in men younger than 30 years unless renal insufficiency or a genetic abnormality of purine metabolism is present, such as hypoxanthine-guanine phosphoribosyltransferase deficiency or phosphoribosylpyrophosphate synthetase super-activity. Typically, tophi become clinically evident about 10 years after the first attack of gout.

Tophi represent collections of uric acid crystals in the soft tissues. They occur in more than half of untreated patients. Although the classic site is along the helix of the ear (Figure 1), they can be found in multiple locations, including the fingers and hands (Figure 2) and toes; they can also occur in the olecranon bursae and along the olecranon, where they can resemble rheumatoid nodules. The finding of a rheumatoid nodule in a patient with a negative rheumatoid factor test should prompt consideration of gout in the differential diagnosis. Keep in mind that it is unusual to find tophi in a patient who has an initial episode of gout.

CALCINOSIS CUTIS

Calcinosis cutis encompasses a group of disorders in which calcium deposits form in the skin. The four major types of calcinosis cutis are categorized according to etiology:

• Dystrophic.
• Metastatic.
• Iatrogenic.
• Idiopathic.

A few rare types have been variably classified as dystrophic or idiopathic. These include calcinosis cutis circumscripta, calcinosis cutis universalis, tumoral calcinosis, and transplant-associated calcinosis cutis.

Dystrophic calcinosis cutis usually occurs in a specific area of tissue damage, although it may be generalized, as can occur in patients with dermatomyositis. In metastatic calcinosis cutis, calcium deposition is frequently generalized. Large deposits are typically found around large joints, such as knees, elbows, and
shoulders, in a symmetrical distribution. Visceral organ deposition of calcium in the lung, kidneys, blood vessels, and stomach actually occurs more frequently than deposition within the skin or muscle. In iatrogenic calcinosis cutis, calcification generally is located at the site of an invasive procedure, although diffuse deposition may occur. In idiopathic calcinosis cutis, calcification usually centers in one general area.

In all cases of calcinosis cutis, insoluble compounds of calcium precipitate in the skin. These calcium salts consist primarily of hydroxyapatite crystals or amorphous calcium phosphate. The etiology of calcinosis cutis remains to be defined; it is sometimes related to a serum calcium/phosphate product that exceeds 40, 50, or 60 depending on the source reviewed. Dermatomyositis and CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome are associated with calcinosis cutis.

The clinical presentation of calcinosis cutis can vary according to the diagnosis and underlying process. The most common manifestation consists of isolated white yellow papules (Figure 3). However, calcinosis cutis can appear as multiple, firm, whitish dermal papules, plaques, nodules, or subcutaneous nodules. Distribution and pattern are based on the underlying disease. The papules of calcinosis cutis may extrude a yellow-white, gritty substance. The papules usually do not bother patients, but they can be painful or restrict joint mobility.

Treatment is directed toward management of the underlying disease. The papules or nodules can be surgically removed if they are symptomatic.

PRETIBAL MYXEDEMA

Pretibial myxedema is related to hyperthyroidism. The peak age of incidence is about 60 years of age.

The early manifestations of pretibial myxedema are bilateral, firm, nonpitting, asymmetrical yellow, pink to purple-brown plaques or nodules (Figure 4). The plaques are usually a darker color than the surrounding skin. The ostia of the hair follicles often prominently appear, giving the skin a peau d’orange texture. There can be areas of non-pitting edema in the legs that accompany pretibial myxedema. In severe cases, also referred to as elephantiasic pretibial myxedema, plaques may coalesce to give the entire leg a swollen and warty appearance. Overlying hyperhidrosis or hypertrichosis may be noticed in severe cases. Plaques of pretibial myxedema usually manifest on the lateral or anterior aspect of the legs, but they may occur on the thighs, the shoulders, the hands, the forehead, or any other skin surface. These plaques are often found in areas of recent or prior trauma or skin graft donor sites.

Pretibial myxedema must be distinguished from the generalized myxedema that results from hypothyroid-
ism. Pretibial myxedema occurs in the skin and is associated with other physical findings of hyperthyroidism, such as proptosis; in fact, nearly all patients with pretibial myxedema have thyroid ophthalmopathy.

Thyroid acropachy occurs in 1% of patients with Grave’s disease. Thyroid acropachy manifests with clubbing of the fingers and the toes, periosteal proliferation of the shafts of the phalanges and other distal long bones, and swelling of the soft tissues overlying affected bony structures. Ophthalmopathy precedes pretibial myxedema, which precedes acropachy.

Pretibial myxedema is difficult to treat. Even if the underlying thyroid disorder is effectively treated, pretibial myxedema does not necessarily resolve.

**ACANTHOSIS NIGRICANS**

Acanthosis nigricans is characterized by a diffuse, velvety thickening and hyperpigmentation of the skin, most frequently on the neck and axillae (Figure 5) and occasionally on the groins, umbilicus, hands, areolae, and submammary areas. It represents an increase in papillation of the dermis and epidermis, not a deposition of pigmentation. Acanthosis nigricans is not exclusive to persons with diabetes; it can occur in those who are obese or who take medications such as nicotinic acid and corticosteroids. It is rarely associated with stomach carcinoma, in which case it can occur in locations such as the palms (so-called tripe palms) (Figure 6).

The vast majority of cases of acanthosis nigricans are associated with diabetes or obesity. If a case does not fit the usual pattern or distribution, consider other possible causes such as an underlying neoplasm.

The only adverse affects of acanthosis nigricans seem to be cosmetic. Treatment is generally directed at...
correction of the underlying cause, but retinoic acid, topical calcipotriene, and salicylic acid have been reported to be helpful in some patients.9

**DIABETIC DERMOPATHY**

Diabetic dermopathy, also known as shin spots, occurs in up to 40% of persons with diabetes.10 Shin spots are the most common cutaneous manifestation of diabetes mellitus. The exact cause of diabetic dermopathy is unknown. It may serve as a clinical sign of an increased likelihood of internal complications in patients with diabetes, such as retinopathy, nephropathy, and neuropathy.11

Diabetic dermopathy is characterized by round to oval circumscribed, atrophic, slightly depressed, hyperpigmented lesions that occur on the anterior aspect of the lower legs and are generally bilateral and asymmetric (Figure 7). The lesions are usually asymptomatic. They recur in crops and spontaneously resolve, eventually healing with scar formation.

Histological characteristics of diabetic dermopathy are edema of the epidermis and papillary dermis, extravasated erythrocytes, and a mild lymphohistiocytic infiltrate. Older lesions have thick-walled capillaries in the upper dermis, occasional extravasated erythrocytes, and a positive Perl stain for iron.

There is currently no standard of treatment for diabetic dermopathy. Moreover, controversy exists as to whether diabetic dermopathy is a true entity or a variant of stasis dermatitis.12

**NECROBIOsis LIPOIDICA DIABETICORUM**

Necrobiosis lipoidica diabeticorum (NLD) typically manifests as atrophic, asymptomatic, yellow, red, or brown patches on the legs that can progress to yellow, depressed atrophic plaques (Figure 8). NLD can also occur on other areas of the body. This disease involves collagen degeneration with a granulomatous response, thickening of blood vessel walls, and fat deposition.

The age of onset of NLD ranges from infancy to the 80s; it tends to develop at an earlier age in patients with diabetes. Fifty percent of patients with NLD have diabetes, but only 0.3% of patients with diabetes have NLD.13

The first line of treatment consists of glycemic control and use of a topical corticosteroid or tacrolimus. If this strategy is not effective, consider stronger immunosuppressive or immunomodulatory therapy.14-16

**XANTHOMA**

Xanthomas are characterized by accumulations of lipid-laden macrophages. Cutaneous xanthomas associ-
ated with hyperlipidemia can be classified as xanthelasma palpebrarum, which occurs over the eyelids (Figure 9); tuberous xanthoma, which occurs over joints (Figure 10); tendinous xanthoma, which occurs over tendons; eruptive xanthoma, which can occur anywhere on the body as yellow or red nodules (Figure 11); plane xanthoma; and generalized plane xanthoma. Xanthoma disseminatum and verruciform xanthoma are usually not associated with hyperlipidemia.

Xanthomas can be a reflection of lipid metabolism alteration or a result of local cell dysfunction. In patients with xanthomas, primary hyperlipidemia is chiefly a diagnosis of exclusion. Appropriate blood, urine, and radiographic evaluations are needed to rule out a secondary cause of hyperlipidemia. Because lipid levels can be elevated in patients with diabetes, there is an association of xanthomas and diabetes. Xanthomas can occur in persons of any age; however, xanthelasma usually occurs in persons older than 50 years.

Treatment of xanthomas involves normalization of lipid levels. In the case of xanthelasma, trichloroacetic acid or a laser can be used to peel away or physically ablate the xanthomas.17

**REFERENCES:**