REVIEW ARTICLE

The "SKINNY" on skin in obesity

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ABSTRACT
The rashes in obesity present a challenge to any physician in terms of clinical approach, diagnoses, and management. Obesity has become an epidemic in the United States and is on the rise in many developing nations; thus, it is essential for physicians to have a solid understanding of the manifestations of associated skin disorders and the impact of excess weight on the skin to better treat these patients. Their specific management vastly differs from that of the standard, average-sized "75-kg" individual.
Obesity is linked to a wide spectrum of skin-related diseases such as: acanthosis nigricans, adiposis dolorosa, cellulitis, hidradenitis suppurativa, hirsutism, hyperandrogenism, infections, insulin resistance and its associated syndromes, keratosis pilaris, lymphedema, plantar hyperkeratosis, psoriasis, redistribution of adipose tissue, skin tags, striae, venous insufficiency and tophi. This review focuses on a brief overview of the clinical features, skin physiology, cutaneous disorders, management and treatment strategies in the obese subject.

INTRODUCTION
Addressing the dermatoses in obese populations has emerged as an important area of consideration that must be understood. As the obese population increases and the number of obese patients in healthcare facilities also rises, the incidence of obese skin diseases is becoming more widely acknowledged. According to body mass index (BMI), overweight individuals have a BMI of 25 kg/m^2 or higher and obese individuals have a BMI or 30 kg/m^2. During 2009-2010, the reported prevalence of obesity in the United States was 35.7% and over 78 million U.S. adults were obese.[1] By 2030, the number of obese adults worldwide is projected to be 573 million, reaching an absolute number of 1.12 billion if current trends continue.[2] Due to the physiologic and metabolic changes occurring throughout the skin layers during the weight-gaining process, obese individuals are vulnerable to a spectrum of skin conditions. A variety

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of factors, such as neurologic diseases, health/hygiene issues, systemic problems, gender, ethnicity, skin subtype, culture/background, individual habits, socioeconomic status, and tobacco/alcohol consumption may contribute to the onset and sustainability of dermatologic disease in obese individuals. The diagnosis and management of the obesomatoses pose a formidable challenge to dermatologists and other physicians. Weight loss is a difficult hurdle to overcome, thus management may be tedious. Obese patients often have multiple medical problems and regimens with several medications, physical requirements, etc. Additionally, the clinical manifestations of skin disorders in obese patients differ from those of normal-weight individuals and thus do not present in a classic form as they do in other populations.

THE PHYSIOLOGY OF OBESE SKIN

Obesity has many effects on the skin and is associated with a number of dermatoses. Normal subcutaneous fat is comprised of white adipose tissue; whereas, brown adipose is primarily only seen in newborns and is physiologically distinct. The adipocytes of white adipose tissue serve as storage units of energy and, as a whole, provide insulation and serve as a frictionless surface between body structures. Chemically, adipose tissue is involved in the production of many substances, including but not limited to: cytokines, hormones, fatty acids, and functional mast cell progenitors[3-5]. Adipokines (such as leptin and resistin) and pro-inflammatory cytokines [such as tumor necrosis factor-α and interleukin (IL)-6] are assumed to have a more complex role in cutaneous physiology and pathophysiology due to activation of modulators of insulin resistance, inflammation and wound healing.[6,7]

In obesity, there is excessive accumulation of adipose tissue and weakness of the skin. Low me-

Table 1 Obesity-related changes in skin physiology

	Physiologic changes	**Cutaneous manifestations**
Skin barrier function	Erythema Altered epidermal barrier	Impaired skin barrier repair Vulnerability to infection
	Increased transepidermal water loss	Dry skin
Sebaceous glands and sebum production	Androgens, insulin, growth hormone & IGFs frequently elevated, which activate sebaceous glands	Acne exacerbations and increased acne severity
Apocrine and eccrine sweat glands	Increased sweat gland activity due to thick layers of subcutaneous fat	Increase frictional & moisture components
Lymphatics	Interference of lymphatic flow Reduced tissue oxygenation	Lymphedema Fibrosis
Wound healing	Altered collagen structure and function	Impaired wound healing Less manifestations of facial wrinkles
Vascular	Microvascular dysfunction Increased BMI Lower peak capillary blood cell velocity Impaired capillary recruitment Acetylcholine-mediated vasodilation Altered vagosympathetic activity	Microangiopathy Hypertension Increased cutaneous blood flow Impaired skin microcirculatory responses to mental stress Reduction in cutaneous vasoconstrictive response to sympathetic activation
Subcutaneous tissue	Increased subcutaneous fat	Increased insulation
Hormonal effects	Hyperandrogenism Hyperinsulinemia	Increased adiposity results in increased production of endogenous androgens Increases production of ovarian androgens
Thermoregulation	Direct relationship between adipose thickness and required cooling time	Longer cold application after injury

chanical strength of the skin in obese mice was found to result from an insufficient quantity of collagen deposition to match the increase in skin surface area.[8] The association between obesity and changes in skin physiology may be related to an increase in sweat gland activity, dry skin, high transepidermal water loss, altered collagen structure and function, and impaired wound healing.[5, 9-11] There is also reduced microvascular reactivity in obese skin, yet the activity of sebaceous, apocrine or eccrine glands remain unchanged.[12,13]

COMMON DERMATOLOGIC CONDITIONS

Acanthosis nigricans

The most common dermatologic manifestation of obesity is unarguably, acanthosis nigricans. It is characterized by symmetric, velvety-brown, poorly - demarcated plaques accentuating the skin folds that occur almost anywhere. Lesions are commonly observed in the axilla, groin, and posterior neck but may occur in the knuckles, elbows and face, especially in individuals of darker complexion. Skin proliferation (secondary to acanthosis and papillomatosis of the epidermis) is frequently associated with a state of hyperinsulinemia with insulin resistance.[14] A proposed mechanism of how insulin-resistant states lead to epidermal changes that result in acanthosis nigricans focuses on possible interaction with excess circulating insulin with insulin-like growth factor (IGF) receptors on both keratinocytes and dermal fibroblasts.[15] Excess insulin depletes the number of functioning insulin receptors, causing a shift of increased binding to the IGF receptors, leading to growth-promotional effects.[15,16]

Obesity is a common finding in children with benign acanthosis nigricans, however it is reversible.[17,18] Acanthosis nigricans is frequently found in obese, hirsute, hyperandrogenic women, most commonly in the vulva.[19] In one particular study, Hud et al observed a positive correlation between acanthosis nigricans and the severity of obesity and found a prevalence of acanthosis nigricans in 74% of a healthy, adult obese population.[20] Acanthosis nigricans is also a feature of Alstrom's syndrome, a rare autosomal recessive disorder characterized by childhood obesity and multiorgan dysfunction.[21] Acanthosis nigricans may be managed with weight loss and a low-calorie diet improving the insulin-resistant state, thus decreasing the severity of cutaneous manifestations.[22] Other treatment options include: long-term octreotide; retinoic acid; vitamin D3 analogs; metformin; rosiglitazone; and laser therapy.[23] New methods with variable success include: photothermolysis with Q-switched lasers, long-pulsed alexandrite laser, and dermabrasion; surgical excision may be attempted if conservative therapy fails.[24-26]

Acrochordons

Acrochordons, or skin tags, are flesh-colored or light-brown pedunculated papules with smooth or irregular surfaces. Like acanthosis nigricans, skin tags are often seen in obesity in similar locations, such as the neck, axillae, groin, and eyelids. Skin tags are unsightly in appearance and may become symptomatic if twisting of the pedicle compromises the blood supply, resulting in infarction. In a study done by Garcia-Hidalgo et al. on 156 patients, the percentage of individuals with acrochordons had a positive correlation with the degree of obesity.[27] Acrochordons are frequently observed concurrently with acanthosis nigricans; however, they are more strongly associated with diabetes than with obesity. Kahana et al's study of skin tags found no association with increased incidence of obesity compared to the general population, however there was an association with impaired carbohydrate metabolism, suggesting a means for identifying patients at risk of diabetes mellitus (DM).[28] More research is needed to establish the incidence of obesity and acrochordons as well as its relationship to insulin resistance. Several effective options for removal include: excision with curved scissors, cryotherapy, and electrodessication.

Adiposis dolorosa

Adiposis dolorosa, also known as Dercum’s disease, is a rare progressive disorder featuring numerous, tender, subcutaneous lipomas more commonly noted inmarkedly obese, middle-aged women.[29] These painful lipomas are symmetric and may either be local or diffuse, usually occurring in the chest, back, and lower extremities, especially the knees. They may occur anywhere, but typically do not affect the head/neck area. A common characteristic is a chronic, disabling pain out of proportion to physical findings often resistant to analgesics.[30,31] Most patients are above 50% of ideal weight for their age and notably, the intensity of pain increases with BMI.[13] Other characteristic features include: hyperalgesia of the subcutis, swelling, purpura, and telangiectasias. fatigability, weakness, confusion, dementia, and depression.[32] Although many different mechanisms have been proposed, the exact etiology has not been confirmed.[29] The diagnosis is primarily clinical, after excluding other possibilities. Unfortunately, imaging tools such as ultrasound and more importantly, MRI may be helpful at identifying the lipomas.[33] Management options include analgesics, immunomodulatory medications, corticosteroids, calcium channel modulators, hypobaric pressure, liposuction, surgery and psychotherapy, however treatment is usually ineffective for pain control. Medications target the symptoms yet do not alter how this disease unfolds. An interdisciplinary team may help patients reach goals for therapy, such as pain relief.[29]

Cellulite

Cellulite represents a modification of skin topography characterized by skin dimpling, herniation of subcutaneous fat within fibrous tissue, and dermal edema that contributes to the pad or “orange peel” appearance.[34] It often occurs in postpubertal women in the abdomen, pelvic region, buttocks, and thighs. In cellulite, there are changes in lipid metabolism and structural alterations in the dermis, the microcirculation, and within adipocytes.[34] Although it is not exclusively associated with obesity, its presence may be accentuated by it. Additionally, fatty tissue distribution is an important hereditary predisposing factor. A non-balanced diet with excess fat intake, leading to an increase in lipogenesis, may also play a role.[34] Cellulite is difficult to treat and there is no single treatment that is completely effective.[35] There are treatments ranging from topical creams to invasive therapies, such as weight loss, endermologie, liposuction, subcision, mesotherapy, topical phosphotidylcholine and lED, radiofrequency devices, ultrasonography, lasers, pharmacologic agents, cryolipolysis, topical retinoids, physical massage, topical aminophylline, and other commercial products; however, there is no substantial evidence for efficacy.[35] According to Smalls et al. weight loss may improve the severity of cellulite, however the resulting loose skin may adversely affect skin dimpling.[36]

Hidradenitis Suppurativa

Hidradenitis suppurativa (HS) is a chronic, recurrent suppurative disease of apocrine gland-bearing skin characterized by abscesses, fistulas, and scarring tracts. It is a common disorder affecting up to 4% of individuals and usually involves the axillae, anogenital region, inframammary regions, and rarely the scalp.[37] The etiopathogenesis was long thought to be of apocrine origin, however now it is thought to be caused by follicular occlusion.[38] Although not a primary cause, obesity has a strong relationship with HS. Several ways it may aggravate disease include: sweat retention and maceration, shearing of follicular or ductal outlets, and abnormal hormonal metabolism.[38] Additionally, obesity propagates retention of sweat, further aggravating the role of perspiration as an irritant. Furthermore, changes in production, metabolism, and biologic activity of sex hormone binding globulin, androgens, and estrogens are associated with obesity, leading to a state of androgen excess; this may result in coarsening of hair shafts and subsequent follicular occlusion.[39]

HS is a debilitating disease with much morbidity, such as pain, scarring, and pus-like discharge.[41] There is no uniformly effective therapy and physicians will likely have to try various treatment modalities depending on the case at hand. Several treatment options of varying efficacy include: antibiotics, retinoids, antiandrogens, immunosuppressive and anti-inflammatory agents, botulinum toxin, radiotherapy, light, radiofrequency, and other procedures.[38] Because obesity may play an important role in the pathogenesis, weight loss is highly encouraged.Surgical resection of aprocrine gland-bearing tissue can significantly improve quality of life and alter the natural course of disease for patients with extensive HS.[40-42]

Hirsutism

Hirsutism is excessive, unwanted hair growth in women in androgen-dependent hair patterns secondary to increased androgenic activity. Androgens convert vellus to terminal hairs in androgen-sensitive hair follicles in areas such as the beard, face, chest, breasts, lower back, buttocks, external genitalia, thighs, and linea alba of the abdomen. According to Ruutiainen at al, women with severe facial hirsutism had more teenage obesity and a higher maximum weight than other hirsute patients.[43] Results also indicated that facial hirsutism was significantly associated with BMI independently of age and testosterone levels.[43] In a systematic review to evaluate the efficacy of various drug treatments, a significant reduction in hirsutism was found for flutamide, spironolactone, cyproterone acetate combined with an oral contraceptive, thiazolidinediones, oral contraceptive pills, finasteride, and metformin.[44] Additionally, the response to treatment was inversely associated with BMI.[44] Obesity has a negative impact on outcome regardless of which treatment option is chosen, thus weight loss and appropriate lifestyle advice is necessary.[44]

Hyperandrogenism

Other manifestations of androgen excess in obesity may result from increased synthesis of endogenous androgens due to the production of testosterone from adipose tissue, as well as increased production of ovarian androgens due to hyperinsulinemia.According to Barth et al., cutaneous virilism includes a combination of dermatoses related to hyperandrogenism, such as: hirsutism, acne vulgaris, HS, androgenic alopecia, and keratosis pilaris.[46] Compared to normal controls, these patients demonstrated a significant relationship with insulin resistance, elevated fasting plasma insulin. In addition, the total serum testosterone correlated with insulin resistance.[46] Skin biopsies from individuals administered high doses of testosterone in hyperandrogenic patients and anabolic androgenic steroids show sebaceous gland hypertrophy, greater lipids in the skin’s surface, cholesterol, free fatty acids, and increased colonies of *Propionobacterium acnes.*[45] Goals for management should focus on ruling out a more serious problem such as a virilizing tumor or endocrinologic disorder, and secondly, to determine if there is a state of insulin resistance, glucose intolerance, or dyslipidemia. Weight loss may also improve the local skin environment that predisposes to disease onset and progression.

INFECTIONS

Obesity and a high-fat diet play important roles for pathogens and immunity. Estimates indicate that approximately half of obese individuals have skin infections.[46] The associated malnutrition in nutritionally compromised obese patients alters the incidence and severity of fungal, bacterial, viral, and parasitic infectious diseases.[47] The setting of infections in both the hospital and community encourages awareness of these conditions among dermatologists and other healthcare providers. Early diagnosis and management of these conditions in at-risk populations, such as the obese, may prevent further complications.

Bacterial

Obesity is related to bacterial complications ranging in complexity from folliculitis, furunculosis, and erythrasma, which occur in the skin folds, to more complicated infections such as gas gangrene, erysipelas, and necrotizing fasciitis that require hospital level of care.[21, 48-53] Erysipelas is an acute, spreading infection of the dermis and subcutaneous tissue usually caused by streptococcal species. It is characterized by a red, warm, tender area of skin often originating at a site of bacterial entry. Erysipelas is a frequent complication of lymphedema; the most important risk factor for this infection is lymphedema since protein-rich edema contributes to infection.[54] Obesity is also an independent risk factor for development and recurrence of erysipelas.[48,49,55] Of several comorbidities, obesity was the only predisposing factor for local complications of erysipelas, such as hemorrhagic, bullous, necrotic lesions, and abscesses.[56] Hence, obese patients should be evaluated carefully due to the potential severity of disease and increased risk of failure of empirical antibiotics.

Necrotizing fasciitis is a rare, rapidly progressing bacterial infection characterized by extensive necrosis of subcutaneous tissue and fascia, and occasionally of the overlying skin.[57] Risk factors associated with necrotizing fasciitis include obesity/malnutrition, DM, intravenous drug abuse, age > 50, and hypertension. The presence of more than three of these risk factors was predictive of a mortality rate of 50%.[53] In a retrospective analysis of gynecologic and obstetric patients with necrotizing fasciitis, approximately 87% of women had obesity as a predisposing factor.[51] Authors have also cited obesity as a major therapeutic challenge for necrotizing fasciitis; therefore, adequate therapy using antibiotics, hyperbaric oxygen, and surgical exploration must be adapted to the patient’s obesity.[58]

Fungal

Obesity may also be associated with certain fungal infections including: candida folliculitis, candidiasis, and tinea cruris, commonly observed in the skin folds.[21, 59-61] A survey of 18,102 overweight or obese patients showed skin fold mycosis was more frequent in women and present in 22.8% of the patients.[62] In one epidemiologic study, vascular disease, DM, and obesity were the three most prevalent predisposing factors in foot disease, fungal disease, and fungal nail disease.[63] In a prospective survey, obesity appears to be the most frequently occurring factor coexisting with fungal foot disease in adults; whereas, obesity and atopy were coexistent in children with toenail onychomycosis.[64] Thus, obesity is a main factor coexisting with foot diseases, such as fungal foot infection, tinea pedis and toenail onychomycosis.

Intertrigo

The term "intertrigo" originates from the Latin derivatives, inter (between) and trigo (rubbing). It is a non-specific inflammation of opposed skin characterized by macerated, erythematous plaques commonly observed in the inframammary regions, axillae, groins, abdominal pannus, gluteal folds, genitocrural area, and other areas with redundant skin folds in obese individuals. Though not primarily of infectious etiology, it is commonly exacerbated by colonization with bacteria, yeast, and dermatophytes, among which candida is most common. In a cross-sectional study on 156 obese patients, intertrigo was a cutaneous finding with statistical significance for a positive linear trend[27]. Excess skin folds in obese patients causes profuse sweating due to increased subcutaneous tissue, thus leading to friction between skin surfaces and maceration from accumulated moisture.[45] A study by Yosipovitch et al indicated that skin surface pH of the inguinal folds of diabetic patients with a BMI > 25 is significantly higher than in subjects with BMI < 25.[65] Since Candida hyphae grow best in an alkaline medium, this finding implies a possible role of skin pH in host susceptibility of skin candida infection.[65, 66]

The primary approach to intertrigo is to minimize moisture and friction. Obese patients should loss weight if possible. Physical exercise is encouraged, but patients should cleanse and dry intertriginous areas thoroughly.[67] In regards to excess skin folds, a systematic review clearly found that the percentage of women with inframammary intertrigo decreased substantially after reduction mammaplasty from 80-100%, so there is uniform evidence that surgery helps.[68] A panniculectomy or surgical excision with reconstruction may be necessary for patients with excess skin folds, especially after massive weight loss.

Insulin resistance, diabetes and obesity

The strong association between obesity, insulin resistance, and type 2 DM is widely recognized. Thus, dermatoses associated with diabetes may alsobe secondarily associated with obesity (see Table 2). Compensatory hyperinsulinemia resulting from peripheral insulin resistance is the root cause of the maladies of metabolic syndrome, such as obesity and type 2 diabetes.[69] Insulin is a growth-promoting hormone, and evidence indicates that hyperinsulinemia shifts various endocrine pathways, such as androgens, favoring unregulated growth in a variety of tissues including the skin.[69] The course of disease may promote acne, epithelial cell carcinomas, acrochordons, acanthosis nigricans, polycystic ovarian syndrome, and androgenic alopecia.[69] Diets with high-glycemic-load carbohydrates (in the context of individual susceptibility genes and hormonal effects) may enhance growth in many tissues, es-

Table 2 Classification of dermatologic conditions in obesity

Physical factors		Pressure sores (decubitus ulcers) Adiposis dolorosa Plantar hyperkeratosis Lymphedema Striae distensae Cellulite
Xerosis		Pruritus
Infectious		
	Bacterial	Necrotizing cellulitis/ fasciitis Gas gangrene Erythrasma Furunculosis Erysipelas Cellulitis
	Fungal	Candida Intertrigo Dermatophytes Candida folliculitis Tinea cruris
Infestations		Scabies Pediculosis
Inflammatory		Psoriasis Hidradenitis suppurativa
Insulin resistance		Metabolic syndrome Acanthosis nigricans Keratosis pilaris Hyperandrogenism Hirsutism Cutaneous virilism
Metabolic		
	Gout	Tophaceous gout
	Hypothyroidism	Dry skin, swollen lips, brittle nails, myxedema
Eczematous reactions		Seborrheic dermatitis Atopic dermatitis
Neoplastic		
	Benign	Acrochordons
	Malignant	Non-melanoma skin cancers (BCC, SCC) Malignant melanoma Angiosarcoma
Vascular		Chronic venous insufficiency (stasis dermatitis)
Genetic		
	Prader-Willi Syndrome	Skin picking Lymphedema Cellulitis
	Alstrom’s syndrome	Acanthosis nigricans

pecially in epithelial cells, which have rapid turnover.[59] Thus, dietary interventions may be useful in treating the cutaneous maladies that stem from insulin resistance.

Keratosis pilaris

Keratosis pilaris is characterized by small, perifollicular papules on the extensor aspects of the extremities. This benign dermatosis is significantly associated with multiple factors including a BMI> 25; dry, scaly skin; and atopy.[70, 71] In a study on young insulin-dependent diabetes mellitus (IDDM) patients, keratosis pilaris was present in 21% of patients versus 9% of control subjects and was found to be exclusively associated with a high BMI.[72] IDDM and insulin resistance may play a role in the development of this condition.[70,73] Treatment is difficult for obese and normal-weight patients alike. Some patients respond to topical retinoids, keratolytics, 12% ammonium lactate, topical calcipotriene, or mild topical steroids.

Lymphedema

In patients with obesity, lymphedema develops due to abnormal accumulation of protein-rich lymphatic fluid resulting from impaired lymphatic return. In obese patients, lymphedema most commonly occurs on the lower extremities initially presenting as swelling and pitting edema. It then spreads proximally and slowly evolves into nonpitting woody induration. Secondary soft tissue infections are common and often recurrent, leading to worsening of the condition. Prolonged lymphedema may lead to grotesque enlargement of the extremity characterized by epidermal hyperplasia with verrucosis. Elephantiasis nostras verrucosa is a result of chronic lymphedema characterized by permanent hypertrophic fibrosis that may occur in any location. Dermatologic findings consistent with this entity have been reported in the abdominal pannus of patients with morbid obesity.[74] A panniculectomy may be useful for management of these patients. Angiosarcomas are highly malignant proliferations of endothelial cells that may occur as a complication of chronic lymphedema. According to a review on cutaneous angiosarcoma arising in massive localized lymphedema of the morbidly obese, the clinical and pathological features of angiosarcoma arising in this setting were identical to those of other lymphedema-associated angiosarcomas.[75] Thus, lymphedema secondary to obesity should be recognized as a significant risk factor and it is critical that these patients be carefully examined for evidence of early angiosarcoma.

A cornerstone of treatment is prevention of acute inflammatory episodes by reducing limb girth and weight through weight reduction amongst other measures. Complete decongestive physiotherapy is comprised of manual lymphatic massages, compression bandaging, exercises, meticulous skin care, and self-care through compression or wrapping in different phases. This method is highly effective for lymphedema and maintained volume reductions in the majority of treated patients. Patients reported significant recovery and maintenance of the initial volume reductions after treatment with this method.[76]

Plantar hyperkeratosis

Plantar hyperkeratosis is described as well-demarcated, thickened, dry skin on the soles of the feet. It was first reported by Garcia-Hidalgo et al. as the most common cutaneous finding in obese patients with excess weight of greater than 76%.[27] In this study of 156 patients, the authors found significant differences in the horseshoe-shaped hyperkeratosis of the soles according to the degree of obesity.[27] The mechanism is a physiologic response to mechanical trauma because during normal gait, the metatarsal head areas are subject to more stress than any other area of the plantar aspects of the feet.[77, 78] Obese subjects show increased forefoot width and higher plantar pressures during standing and walking, especially under the longitudinal arch and under the metatarsal heads[79]. In obese patients, carrying an excessload of weight disrupts the normal foot anatomy.[45] In addition, abnormal transference of weight during ambulation alters foot alignment and likely contributes to development of plantar hyperkeratosis.[45, 78] For short-term management, patients may use protective insoles or cushions to alleviate symptoms. Weight loss to eliminate the increased pressure is the primary long-term recommendation.

Psoriasis

Psoriasis is a chronic, polygenic disorder with several clinical expressions that vary among individuals from local to diffuse involvement. The lesions typically appear as chronic, recurring, scaly papules and plaques. Various studies demonstrate that patients with psoriasis have higher prevalence and rates of obesity compared to control subjects.[80-82] Inverse psoriasis, which can be indistinguishable from intertrigo, is more common in the obese population; the milieu of intertriginous skin may favor development of psoriasis.[80] Obesity affects the course of psoriasis and may have deleterious effects on the increased morbidity.[83, 84] An analysis by Sakai et al indicated that a BMI > 25 is a significant prognostic factor for long-term prognosis in patients with plaque psoriasis.[85] According to an Italian case control study, there was a significantly greater odds ratio for the frequency of psoriasis in relation to a BMI of overweight and obese, respectively.[86] However, recent evidence from a case series suggests that obesity may be a consequence, not a cause, of psoriasis.[80] Regarding dietary behavior, psoriasis patients show higher scores for consumption of alcohol, high fat foods, and saturated fats, which could explain the higher prevalence of metabolic abnormalities in these patients.[87]

Psoriasis patients are known to try alternative therapies, such as dietary manipulation with variable effects. One study showed worsening of disease severity, while another study using a low-energy diet demonstrated significant clinical improvement of moderate non-psoriasis pustular psoriasis vulgaris.[88, 89] Though some suggest particular dietary changes for prevention and treatment, much research is needed in the area of lifestyle changes for the management of psoriasis. Several studies have shown that patients with plaque psoriasis respond to certain thiazolidinediones, which contain agents that effectively inhibit rapidly proliferating epidermal keratinocytes and may be useful for the treatment of psoriasis and other hyperplastic skin diseases.[90] In one study, patients with psoriasis substantially improved with troglitazone therapy. This medication has ligands for peroxisome proliferator-activated receptor-gamma expressed in keratinocytes and also inhibits proliferation of these cells in culture.[91] In a prospective review of psoriatic patients who underwent bariatric surgery, 70% stayed in remission 6 months after surgery and 75% of patients who were previously medicated with systemic drugs discontinued their medication in relation to psoriasis.[92] Quality of life also improved significantly for these patients after the procedure, suggesting that bariatric surgery should be considered as an adjuvant treatment for obese patients with psoriasis.[92]

Striae distensae

Striae distensae, or "stretch marks," are linear dermal plaques accompanied by epidermal atrophy that appear along lines perpendicular to the direction of greatest tension and are directly related to stretching of the skin. Common distributions cover areas with the most adipose tissue, such as the breasts, lateral abdomen, buttocks, and thighs. Striae progress through several phases and colors, initially erythematous (striae rubra), then violaceous, and finally white, atrophic, and depressed plaques (striae alba). Though its pathogenesisis-controversial, striae distensae are closely related to obesity.[27] Hsu et al identified striae in approximately 40% of 89 obese children and adolescents. The incidence of striae was higher in those with a longer duration of obesity.[93] In a study of urinary steroid excretion in obese patients, urinary adrenocorticosteroids were significantly greater in obese patients, particularly in those with red abdominal striae, when compared to a normal-weight control group.[94] In another study, Angeli et al found the clinical appearance of striae in obese individuals as lighter, narrower, and less atrophic than the Cushingoid appearance.[95] Regardless of the type of regimen, weight loss does not change the degree of striae distensae.[96] Numerous therapeutic strategies ranging from topical applications to lasers are available, yet no single modality has been more consistent than the rest. Further development of effective treatment options for these patients is a much-needed area of research.

Chronic venous insufficiency (CVI)

CVI results from failure of return of venous blood and increased capillary hydrostatic pressure. Resultant changes include stasis dermatitis, edema, hyperpigmentation, ulceration, and fibrosis of the skin and subcutaneous tissue (lipodermatosclerosis). Obesity is an established risk factor for chronic venous disease.[97,98] Excess pressure in the obese abdomen opposes venous return from the lower extremities, leading to weakening of the valve commissures and subsequent dilatation.[13,45] Padberg et al found that patients with class III obesity had severe limb symptoms typical of CVI, however, approximately two thirds had no anatomic evidence of venous valvular disease; the association of increasing limb symptoms with increasing obesity suggests that obesity alone may contribute to the morbidity of CVI.[90]

Complications of CVI include lipodermatosclerosis and venous ulcerations. Lipodermatosclerosis presents as inflammation, induration, and brawny pigmentation with edema above and below the sclerotic region, resembling a "champagne bottle" or "piano leg." Although commonly seen in the legs, the abdomen is also a site of disease, particularly in individuals with large, pendulous abdominal folds.[99] Venous ulcers are the most common type of chronic wounds, accounting for approximately 70% of chronic ulcers in the lower limbs.[100] In an investigation of the impact of overweight on chronic venous disease, there was significant correlation of BMI with clinical severity including skin changes and ulceration, independent of reflux measurements.[101] This suggests an alternate mechanism besides local effects on venous flow. An overweight state appears to be a separate risk factor for increased severity of skin changes.[101] The main treatment objectives are elevation and compression. Compression dressings or stockings are prerequisites for management. Patients may benefit from preventive measures to target obesity.[98]

Tophaceous gout

Tophi are monosodium urate crystals within connective tissues as a consequence of longstanding high levels of serum uric acid. These solid deposits are usually painless, visible, palpable, and occasionally calcified. Tophi are usually seen in areas with soft tissues, cartilage, and tendons, such as the ears, forearms, elbows, knees, hands, and feet. Obesity and excessive weight gain are known risk factors for gout and several prospective studies have demonstrated this strong relationship.[102,103] In accordance with the obesity epidemic, the prevalence of gout in the United States has also risen steadily.[104] Weight reduction is protective for primary and secondary prevention of gout, and reduced protein intake may lower serum urate.[103,105] Achieving serum urate levels below 6 mg/dL ensures appropriate dosing of urate-lowering medications, which are associated with a reduction in gout flares and tophi.[106] Through continuous monitoring of serum urate, the size of tophi may be reduced and recurrences can be prevented.[107-109] Still, surgical intervention may be necessary for patients suffering from complications due to tophaceous disease.

Pressure ulcers

Pressure sores develop at body-support interfaces over bony prominences resulting from external compression of the skin, shear forces, and friction, which produce ischemic tissue necrosis. Skin/wound problems are common, particularly in those who are chronically bedridden; yet, they are more difficult to manage. In an analysis of the 2006-2007 International Pressure Ulcer Prevalence Surveys, 1 in 10 patients were extremely obese.[110] Additionally, the obese patient may experience tissue necrosis in soft-tissue areas other than those over bony prominences. For instance, ulceration and tissue destruction may be created by the pressure associated with capillary closure within folds of fat.[45] Pressure ulcers of the hip are also more common due to prolonged, unrelieved pressure from wheelchairs, bed pans, and side rails, especially in patients with large hips and those who weigh more than 350 lb (159 kg), since these devices are not designed to accommodate such weight.[111] Pressure ulcer prevention is a critical aspect in the care of morbidly obese patients. Although many studies have tested interventions to prevent or treat pressure ulcers, they have not been studied in the obese. Further research is needed to determine optimal interventions, such as turning or repositioning schedules, specialized surfaces, and other adjunctive therapies for this population.[112]

Atopic dermatitis

Many authors have found an association between obesity and atopic dermatitis (AD).[113-115] Furthermore, Silverberg and colleagues (2012) found that the association between obesity and AD in adults remained significant even when controlling for history of asthma, rhinoconjunctivitis, and food allergies.[116] Several reasons for such findings have been explored. For instance, those who are overweight were found to have higher total WBC counts and eosinophil counts.[117] Adipose tissue is also involved in the production of mast cell progenitors.[3] Radon et al. found leptin levels to be positively correlated with allergic sensitization.[118] Lastly, increased consumption of polyunsaturated fatty acids, which are found in vegetable fats and oils, has been implicated in the development of AD.[119,120]

Skin cancer

There is strong evidence that obesity increases the risk of many types of cancers, yet the strength of association varies with organ and histologic type; still, the relationship between obesity and skin cancer is poorly understood.[121] Regarding the pathophysiology between obesity and skin cancer, there is evidence that obesity-induced inflammation interactions with UV-induced inflammation to promote a favorable state for carcinogenesis.[122,123] Pro-inflammatory cytokines may contribute to development of inflammation-associated cutaneous diseases and have been implicated in cancer risk.[124] Yet, in a study on 1621 participants in Australia, BMI, waist circumference, and waist/hip ratio was not significantly associated with risk of basal cell carcinoma (BCC) independent of sun exposure.[125] In a prospective study, obesity appears to be inversely associated with development of non-melanoma skin cancers.[123] One Canadian study found a significant association between obesity and non-melanoma skin cancer and it also noted that skin cancer survivors were more active.[126] Obese individuals may be less physically active, thus decreasing the risk of developing primary skin cancer due to less cumulative sun exposure from fewer outdoor activities. As a result, behavioral influences resulting from obesity may decrease this major risk factor.

The increasing worldwide incidence of melanoma has focused more attention on the potential role of lifestyle factors, especially obesity. A prospective cohort in the Agricultural Health Study found that obesity was associated with an increased risk of melanoma.[127] An experimental study by Brandon et al determined that obesity causes rapid growth of melanoma in mice through expression of angiogenic factors such as leptin.[128] Therefore, obesity markedly increases melanoma tumor growth rate by upregulating VEGF pathways. One recent case-control study found a correlation between high levels of leptin in obesity and melanoma in these cases compared to controls; however, the hyperleptinemia normally found in obesity may serve as a confounding variable.[129,130] Results from a retrospective study provided evidence that higher 25-hydroxyvitamin D (3) levels are associated with thinner tumors and better survival from melanoma; interestingly, BMI is inversely associated with vitamin D3 levels.[131] If obesity proves to be a modifiable risk factor, more interventional research on prevention and treatment of obesity may be essential for prevention of melanoma and its diagnosis and prognosis.

Nutritional disorders with cutaneous manifestations

What if malnourishment and its cutaneous effects present in the form of obesity? Chronic malnutrition due to excess intake of some nutrients while lacking others is commonly observed in obese populations. The low cost and ready availability of foods that have low nutritional value such as refined sugars, fatty foods, and additive preservatives predispose to nutritional cutaneous disorders. Also, obesity is a growing health problem and bariatric surgery is increasingly used to treat obesity; however, nutrient deficiencies are common after surgical treatment, which indicates a progressive increase in incidence and severity of deficiency of certain vitamins and related dermatologic conditions.

The most commonly deficient vitamins and minerals following weight loss surgery include: protein, iron, vitamin B12, folate, calcium, fat-soluble vitamins, zinc, magnesium, selenium, and other micronutrients.[132] Kwashiorkor resulting from protein deficiency commonly manifests as a cutaneous eruption with dry, wrinkled skin and edema that may be accompanied by thin, brittle, fragile, slow-growing hair leading to alopecia. Vitamin B12 and/or folate deficiencies present similarly with glossitis, angular cheilitis, and a brown reticular hyperpigmentation.[133] Iron deficiency may present as pallor, pruritus, glossitis, angular cheilitis, koilonychias, and dry, brittle, dull hair. Vitamin K deficiency may lead to a variety of coagulation factor deficiencies from purpura to hemorrhage, while a lack of vitamin A may cause phrynoderma – a dry and scaly eruption.[133] Although vitamin E deficiency rarely presents with definitive physical findings, results from a study on rats suggest that deficiency promotes peroxidation of lipids and accelerates cross-linking of collagen in the skin[134]. Vitamin D deficiency is related to a number of dermatologic disorders including skin cancers, autoimmune skin disorders, photodermatoses, atopic dermatitis, and psoriasis.[135] In a systematic review by Renzaho et al, there was evidence supporting links between vitamin D deficiency and obesity-related chronic diseases including obesity, type 2 diabetes, cardiovascular disease, and metabolic syndrome, however further research in this area is needed.[136]

Zinc deficiency may lead to acrodermatitis enteropathica which is characterized by red, inflamed patches of dry and scaly skin particularly around the orifices, erosions, nail ridging, glossitis with oral ulcers, diffuse hair loss, and impaired wound healing. Selenium deficiency may also manifest in the skin as irregularly-shaped erythematous eruptions, erosions, and sparse, short, thin, and light-colored hair.[137] In rat models, subjects fed a mildly hypomagnesemic diet were prone to dermatitis.[138] As obesity continues to grow in our society, so does our need to address optimal nutrition in obese patients to prevent the consequences of improper nutrition. Dietary advice on a balanced diet with fortified foods or supplements should be evaluated in these patients.

CONCLUSION

In summary, dermatologic problems in obese individuals are extremely common. They are visible and may even add to the psychological distress in this population. As the largest organ in the body, the skin has several important roles including immune and defense functions that protect us from the external environment. In obesity, this function is impaired. The skin bears the consequences of both the internal and external environments, culminating in pathology, which can ultimately impact the health and quality of life of obese patients. Since the obesity epidemic is on the rise in the U.S. and elsewhere, a comprehensive understanding of the obesomatoses is essential for the practicing dermatologist.

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