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Dermatological manifestations in obesity

Obesity is one of the most common diseases seen in medical practice. It is a growing problem worldwide, both in industrialized and developing countries. It ranges from 7% in France to 32.8% in Brazil (13). In Poland obesity ranges from 14.4% to 19.1% in women and 14.6% in men (6). Obesity is a heterogeneous disease. The favouring factors of obesity are probably related to genetic predispositions like leprin deficiency, age, sex, socio-cultural background, environmental factors related to increasing food consumption and declining physical activity. Excess of calories is stored as a fat tissue in different parts of the human body causing android (with femoral predominance), gynoid (with abdominal predominance), or mixed type of obesity. Obesity is easier to recognize than to treat. Body mass index (BMI) is commonly used to diagnose overweight and obesity. BMI is calculated as weight in kilograms divided by height squared in meters (m^2). Normal BMI is less than 25, overweight is between 25 and 30, and obesity is more than 30. When BMI is higher than 40, it is regarded as severe obesity. Excess body weight is an important risk factor of circular, hemodynamic and metabolic disorders. Overweight and obesity can lead to insulin resistance, hyperinsulinemia, diabetes mellitus type 2, hypertension, hyperurykemia, incidence of malignancy, asthma and lipid disorders: an elevated level of LDL and a decreased level of HDL. Obesity is a great cosmetic problem but also a medical one that may need a specialistic treatment.

SKIN TAGS

Skin tags, or achrochordon, are small, painless, benign lesions composed of loose fibrous tissue (7). They are more common in patients with diabetes or glucose intolerance (13). Skin tags are usually noticed as flash-coloured or more deeply pigmented lesions and may have a thin stalk connecting the skin bump to the surface of the skin (7). They can be found mostly anywhere on the body but favourite areas are the neck, armpits, trunk, face and body folds. They are usually asymptomatic, except for occasional irritation from rubbing by clothing or other friction (7, 13). Histologically skin tags are characterized by thinned epidermis, flattened basal cell layer and loosely arranged fibrous stroma with capillaries (7). They may be surgically removed by using cryotherapy, electrodesiccation or liquid nitrogen to destroy them, with or without prior local anesthesia (7, 13).

ACANTHOSIS NIGRICANS

Obesity is the most common metabolic condition associated with acanthosis nigricans. It is characterized by symmetrical, velvety, light brown to black, thickened plaque with formation of irregular

folds of the skin (2, 5). Acanthosis nigricans is observed in obese patients, with positive correlation with the obesity severity. However, black obese patients demonstrated greater propensity for this disorder than white obese individuals (2, 3, 13). Acanthosis nigricans is usually limited to a few specific areas of the body especially the armpits, the side of the neck, the nape, the groin and anogenital areas. It has also been observed on the face, the inner area of thigh, antecubital and popliteal fossae, the umbilical region, eyelids, knuckles, palms, soles, nipples and even mucosal surfaces. The back of the neck is the most commonly involved and, often, most severely affected area (2, 5). The early lesions are usually pigmented, dry and rough but the older ones turn to verrucous or papillomatous plaques (2). There are often skin tags within or just around the lesions. Having subtle or atypical appearance they may be easily overlooked or misdiagnosed. Acanthosis nigricans should be considered in obese patients with hyperkeratotic plaques. Histologically acantosis nigricans is characterized by papillomated, acanthotic epidermis with orthohyperkeratosis and increased deposition of glycosoaminoglycans, particularly hyaluronic acid, in the dermis (2, 5). It is important to recognize acanthosis nigricans because it can be a symptomatic manifestation of systemic disease, especially the polycystic ovary syndrome, diabetes mellitus or pre-diabetic condition, dyslipidemia and arterial hypertension (5). Patients with acanthosis nigricans can present various endocrine abnormalities such as: acromegaly, hyperprolactinemia, Cushing's syndrome, hirsutism, hypothyroidism and Adison's disease (2). Several reports have revealed that formation of acanthosis nigricans is due to insulin resistance and hyperinsulinemia. Biochemical mechanisms involve: binding of insulin to the insulin-like growth factor-I receptors on keratinocytes and dermal fibroblasts, binding of tumor growth factor-alpha to epidermal growth factor receptors in the epidermis with a subsequent induction of keratinocyte and dermal fibroblasts proliferation that lead to the skin hyperplasia. There is considered a possible role of testosterone as a growth factor involved in the development of acanthosis nigricans (2, 3, 5). The most effective treatment is to reduce calories in diet. The skin changes may slowly regress, with weight decrease, although the pigmentation often persists. In the literature it is reported that synthetic analog of somatostatin-octreotide, topical calcipotriol ointment, topical or systemic retinoids and keratolytics can be useful in treatment of acanthosis nigricans (2, 3, 5).

HYPERANDROGENISM

Hyperandrogenism observed in obesity can be a consequence of hyperinsulinemia that increases the production of ovarian androgens. Otherwise adipose tissue synthesizes testosterone. In women, abdominal obesity is associated with hyperandrogenism and low sex hormone-binding globulin levels (3, 13). Moreover, hyperandrogenism in females may manifest with acne, excess hair growth, male pattern baldness, menstrual disturbance and acanthosis nigricans (3). These symptoms can be observed in girls or women with the polycystic ovary syndrome. Obesity in these patients should be treated, because weight loss can improve hormonal abnormalities and skin symptoms (13). Initial recommendation consists in lifestyle changes including dietary modification and increased physical activity. Otherwise they can be treated with metformin, contraceptives and antiandrogenic agents, such as cyproterone acetate, flutamide and spironolactone. Keratosis pilaris is also associated with hyperandrogenism (3, 13). An increase of androgens stimulates pilosebaceus unit. Examination of skin biopsy specimens revealed hypertrophy of sebaceous glands, increased skin surface lipids, populations of *Propionibacter acnes*, cholesterol and free fatty acids. These people are more susceptible to acne, hirsutism, striae atrophicae and furunculosis (3).

XANTHOMAS

There are various clinical forms of xanthomas, such as xanthelasma and tuberous, planar, eruptive, and tendinous xanthomas. The most common are xanthelasma which are seen clinically as bilateral, symmetrical, oval or elongated yellowish plaques arranged around the eyelids. Palpation may reveal a soft, semisolid or calcified texture (11, 12). It is a common form of xanthoma, a cutaneous deposit of fatty materials. Histologically it is seen as accumulation of lipid-laden macrophages, termed histiocytes, within the dermis (12). Xanthomatosis may occur in obese patients with hyperlipidemia of triglyceridis and chylomicrons. Eruptive xanthomas are red to yellow papules on extensor surfaces and buttocks, which often appear in crops and often acutely (11). Xanthelasma are considered as cosmetically unacceptable. They can be treated by using chemocautery agents, such as trichloracetic acid, electrodesiccation, cryotherapy, CO_2 or argon laser ablation or surgical excision. In patients with elevated serum lipid levels, they can involute surprisingly quickly after the lipid levels are lowered. Antioxidants such as vitamin E may be effective in the long term (11, 12).

STRIAE DISTENSAE

Striae distensae, or stretch marks, are characterized by linear, smooth bands of atrophic-appearing skin that are initially reddish, then purple and finally white, atrophic and depressed. They are seen more often in people with obesity (3, 13). Abdominal striae are one of the signs in patients with Cushing's syndrome, as a result of exogenous glucocorticoid therapy and in pregnancy. They are related to stretching of the skin, as in rapid weight gain or mechanical stress, as in weight lifting. Pathogenesis of striae distense is unknown but may be due to changes in the fibroblast phenotype (3). They occur most commonly in areas with the most adipose tissue – on the lateral abdomen, buttocks, breasts, and thighs (3, 13). They are a type of dermal scarring. Histologically they are characterized by a densely packed area of thin, eosinophilic collagen bundles, horizontal to the surface in a parallel fashion. There is lack of rete pegs, adnexal structures and normal dermal undulations in striae distensae. Hair follicles and other appendages are absent (13). Tsuji T. et al. (14) reported that in early striae distensae there are more fine elastic fibers, while thick elastic fibers predominated in older lesions. Besides, in early lesions the periphery showed thick and tortuous elastic fibers, but in older lesions it was of normal appearance. The authors concluded that elastic fibers in striae were newly synthesized and gradually increased and thickened with age. The latest research by Viennet et al. (15) revealed that fibroblast from early striae distensae were the richest cells in alpha-smooth muscle actin filaments and generated the highest contractile forces in comparison to normal fibroblasts. There was no significant difference in force generation between old striae fibroblast and normal fibroblast with cells expressing no alpha-smooth muscle actin. Therapy for striae distensae has been unsatisfactory up till now. Effective treatment must be started during the early, active stage. It is recommended to use topical tretinoin, but it should be used for almost one year. Another possible treatment of striae involves pulsed dye laser (3, 13).

INTERTRIGO

Intertrigo is a combination of skin irritation and infection. Obesity, diabetes mellitus and vascular diseases facilitate infections and effect unsatisfactory immunity. Obese persons have more numerous and deeper skin folds where heat, moisure, maceration, friction, lack of air circulation and inadequate hygiene are predisposing factors to bacteria, yeast and dermatophytes growth. The most frequent is colonization of *Candida* especially in patients with diabetes mellitus. Significantly higher skin pH was observed in these

patiens in intertriginous areas (3). Intertrigo is usually located in the axilla, underside of the breast, abdominal folds, genitocrural and gluteal areas. It manifests in scaling erythema with macules, papules or satellite pustules (3). Patients can complain of itching, oozing or burning over the affected area. The treatment of intertrigo involves keeping the affected area dry and separated with cotton or linen cloth, using antiperspirants and antibacterial soap. *Staphylococcus aureus* and *Streptoccocus apyogenes* can be healed with appropriate antibiotics. *Candida* infection is treated topically with antifungal powder, cream or oinment. Widspread or severe infections should be treated with either antifungal drugs orally. Fluconazole is effective in a wide range of fungal skin infections (3). Topical steroid cream can be used for a short period. Weight loss is helpful.

LYMPHEDEMA

Obesity is a risk factor for the development of lymphedema. It happens when lymphatic return is impaired. This results in an abnormal accumulation of protein-rich interstitial fluid principally in the subcutaneous adipose tissue (3). Fibrosis, edema and chronic inflammation is observed. Skin over the affected area can be warm, tender and erythematous. Initially lymphedema has a soft manifestation – painless pitting edema. When the process develops, swelling becomes indurated and pitting is gone. Thickened skin, papillomas and hyperkeratosis may occur. Lymphedema with severe enlargement can cause complications like fatigue, severe impairment of daily activities. Reduced tissue oxygenation and worst lymph and blood circulation determine perfect conditions for bacteria and fungi growth with recurrent infections. On the contrary, the presence of infection may enlarge the limb volume, fibrosis and even sepsis. Often happen recurrent infections which may cause the development of cellulite. It is most commonly observed over the shins (13). Finally lymphedema may manifest as elephantosis nostras verrucosa. Prevention of skin injury and inflammation is an important factor in healing lymphedema as well as leg elevation, elastic stockings, manual lymphatic drainage and external pneumatic compression. Moreover, appropriate hygiene is necessary, cleaning skin with mild soap and careful drying. Regular moisturing may improve skin condition preventing from cracks, furrowing and hyperkeratosis. In case of infection appropriate antibiotic therapy should be administered.

PERIPHERAL VASCULAR DISEASE

Obesity is a risk factor for varicose veins. Prolonged standing, female sex, sedentary lifestyle, parity, smoking and hypertension can cause varicose veins (3). Obese patients have higher intra-abdominal pressure that affects externity veins. Changes in vessel wall and valves result in extravasation of the red cells into dermis. Stasis pigmentation is the result of inflammatory reaction to the hemosiderin from degenerated red cells. Other symptoms include oedema, eczema, cellulitis, lypodermatosclerosis with extensive fibrosis causing inverted 'champagne bottle' shape and *atrophie blanche* (9). The combination of venous insufficiency, diabetes, obesity and in some cases arterial alterations may cause leg ulcers that are a therapeutic problem (13). The ulcers are characteristically situated on the medial ankle or lower calf where the pressure is the highest and veins are structurally the weakest. Prevention and treatment goal is swelling reduction. Elevating of legs and elastic stocks are recommended. Corticosteroids topically help in itching and inflammation. If cellulitis is present, antibiotics therapy is necessary.

CELLULITE

Cellulite (gynoid liphodystrophy, panniculopathy, panniculosis) is a common phenomenon, not exclusively related to the obesity. It is clinically characterised by an 'orange peel' skin surface. Genetic predispositon is necessary. Other predisposing factors are: diet abounding with fats and carbohydrates, sedentary lifestyle, tight clothes, high heeled shoes, smoking, alcohol, stress, some drugs and pregnancy, however, the cause of cellulite is still not clearly known. It is observed mainly among women because adipocytes in femoral region present slow metabolism and they are more resistant to lipolysis, additionally they are influenced by female sex hormones (10). Cellulite manifests as puckered, dimpled skin in the pelvic regions, lower limbs and abdomen. It is related to changes in skin architecture and microcirculatory alterations in the fatty layer beneath the dermis and down to the level of muscles. Diffuse pattern of extrusion of underlying fat tissue into dermis correlate with cellulite grading (8). Moreover, there are morphological, histochemical, biochemical and ultrastructural modifications (10). Pathophysiologically it is initially related to the microcirculatory alterations. Capillary insufficiency causes an oedema. A number of water-binding dermal glycosaminoglycans is increasing (3). Fluid accumulation results in hyperplasia and hypertrophy of the reticular framework. The next stage is micronodules forming with adipocytes binding by colagen fibres and finally sclerosis causes macronodules (10). Basing on clinical and histopathological changes there are 4 grades of cellulite. Grade 1 and 2 have no distinct clinical manifestations. There are circular alterations and histopathological modifications. Incipient cellulite is identified with the 'mattress phenomenon'. Orange peel becomes visible in grade 3 with micronodules and neoformation of capillaries. Grade 4 is similar to grade 3 but nodules are more visible, palpable, and painful (10). Treatment of cellulite is difficult and more effective in early grades than when a lumpy-bumpy skin is observed. The anti cellulite creams with caffeine, vitamins and green tea extract improve the skin appearance more than the influence of the adipocytes. Topical retinol and aminophyline are commonly used in the treatment because of their modulating effect on cellulite. Mesotherapy is used as well. Physical and mechanical methods include: iontophoresis, ultrasound, thermotherapy, pressotherapy, lymphatic drainage, electrolipophoresis (10). However, the most recommended is well balanced diet, increased water intake and change in a life-style resulting in weight loss.

PLANTAR HYPERKERATOSIS

Excess body weight influences infavourably normal foot anatomy (3). Obese persons comparing to non-obese have an icreased forefoot width and higher plantar pressures during standing and walking. Hills et al. found that the highest pressure is observed under the longitudinal arch of the foot and the metatarsal heads. Moreover, obese women as compared to the obese men have higher pressure under the mid-foot and the middle of the forefoot during standing (4). All these changes in pressure distribution appear to favour acquired flat foot, sacrodynia, podalgias and reduce ligaments strength, which can cause pain and discomfort in the lower extremity. Foot deformity and exerting abnormal pressure increase keratinocyte activity and result in accumulation of several layers of epithelium histologically and clinicaly characterised as hyperkeratosis (1). Using insoles and appropriate footwear may help to alleviate the symptoms.

CONCLUSIONS

A number of complications affecting skin is observed in people with obesity. Dermatologists might play an important role in diagnosing and treating the dermatoses of obesity. Dermatological examination may have significant importance in recognizing some systemic disorders, for example hyperlipidemia, the polycystic ovary syndrome, insulin resistance or other hormonal abnormalities or even cardiovascular disease where skin defects are present. There is a higher incidence of skin infection found in obese patients than in general population, which must be diagnosed and treated. Apart from pharmacological treating the most important task is to encourage patients to the healthy lifestyle and to lose weight, which may result in subsequent regress of the skin symptoms.

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SUMMARY

Obesity is associated with various skin diseases. Acanthosis nigricans and skin tags develop commonly in obese individuals with insulin resistance and hyperinsulinemia. Hyperandrogenism, due to increased volumes of adipose tissue and hyperinsulinemia, may also be present. The excess of fat tissue forms fat folds that favour humidity and warmth easily leading to maceration and intertrigo. These are main factors that increase the incidence of cutaneous infection including bacterial, fungal or yeast grow. Peripheral vascular disease is related to stasis pigmentation. Leg ulcerations, a frequent consequence of the venous insufficiency may be often observed. Excess weight changes foot architecture, which results in plantar hyperkeratosis. Disturbed blood and lymph flow in the fat tissue is related to lymphedema and additional inflammation factors can cause cellulitis. Some skin lesions such as striae distense due to over extension and cellulite are regarded as mostly cosmetic defects. Effective control of obesity contributes greatly to regress of the skin manifestations.

Skórne objawy otyłości

Z otyłością wiąże się występowanie różnych zmian dotyczących skóry. Niektóre z nich obserwuje się głównie u osób ze stwierdzoną opornością tkanek na insulinę oraz hyperinsulinemią. Ponadto nadmiar tkanki tłuszczowej i hyperinsulinemia mogą prowadzić do wystąpienia skórnych objawów hyperandrogenizmu. Nagromadzona tkanka tłuszczowa tworzy fałdy skórne, przyczyniając się do maceracji skóry i powstawania wyprzeń. Dodatkowo zwiększona wilgoć i ocieplenie sprzyjają zakażeniom bakteryjnym, grzybiczym i drożdżakowym. Przewlekła niewydolność naczyniowa prowadzi do wystąpienia brunatnych przebarwień skóry goleni, a w skrajnych przypadkach owrzodzeń podudzi. Zwiększona masa ciała powoduje deformację struktur kostnych stopy oraz może prowadzić do nadmiernego rogowacenia podeszew. Obrzęk limfatyczny oraz zapalenie tkanki podskórnej są związane z zaburzeniami przepływu krwi i chłonki w naczyniach tkanki tłuszczowej. Niektóre z obserwowanych zmian skórnych, tj. rozstępy, celulit, są postrzegane głównie jako defekt kosmetyczny. Jednakże zmniejszenie masy ciała może przyczynić się do ustąpienia lub ograniczenia większości zmian skórnych wynikających z otyłości.