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Trichological problems related to menopause

Problemy trichologiczne okresu menopauzy

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S u m m a r y

The menopause is associated with a cessation of ovarian synthesis of estrogens, what undoubtedly affects human skin functions and may cause some changes in hair distribution. An increase in androgen to estrogen ratio leads to a reduction in hair density over the crown and frontal scalp with a relative sparing of the anterior hair line, what is described as female pattern hair loss (FPHL). Some other diagnoses, including chronic telogen effluvium (CTE) should be also excluded, what may require a scalp biopsy, but the trichoscopy is essentially useful diagnostic technique. The frontal fibrosing alopecia (FFA) is a distinct condition that mainly affects postmenopausal women and typically starts 2-12 years after the beginning of menopause. An essential problem of aging is an increasing number of systemic diseases that occur soon after the menopause begins. The majority of them requires a long-term drug interventions and some agents has been reported to affect hair growth. The impact of medications on hair physiology is distinguished and some drugs can lead to increased hair loss. Changes in hair distribution in menopause may also consider an unwanted facial hair growth. Some cases of excessive hair growth should be differentiated from acquired hypetrichosis languinosa (AHL), that may coexist with internal malignancy. The pathogenesis of the most of trichological disturbances stay not clear, but some of these hair changes can comprise a significant marker of systemic disorders and the knowledge of them may have an essential, vital significance.

S t r e s z c z e n i e

Menopauza jest związana z ustaniem jajnikowej produkcji estrogenów, co niewątpliwie wpływa na funkcjonowanie skóry oraz może powodować zmiany w rozmieszczeniu owłosienia. Obserwowany relatywny wzrost stosunku androgenów do estrogenów prowadzi do redukcji gęstości włosów na szczycie głowy oraz w okolicy czołowej ze względnym zaoszczędzeniem przedniej linii włosów, co określa się jako żeński typ łysienia. Równocześnie należy wykluczyć kilka innych przyczyn takich jak telogenowe wypadanie włosów, co też może wymagać biopsji skóry, jednakże pomocna okazuje się być także trichoskopia. Kolejnym problemem, który dotyczy przede wszystkim kobiet okresu pomenopauzalnego, jest łysienie włókniejące czołowe, pojawiające się typowo w pierwszych 2-12 latach menopauzy. Istotnym problemem starzenia jest wzrastająca liczba schorzeń układowych, które pojawiają się na początku menopauzy. Większość z nich wymaga długoterminowych interwencji farmakologicznych, a część leków charakteryzuje się oddziaływaniem na wzrost włosów. Wpływ leków na fizjologię włosów jest zróżnicowany i część środków może powodować zwiększone wypadanie włosów. Zmiany rozmieszczenia owłosienia mogą również dotyczyć niepożądanego wzrostu włosów w zakresie twarzy. Niektóre przypadki nadmiernego wzrostu włosów powinny być różnicowane z nadmiernym wzrostem włosów typu meszkowego (*hypetrichosis languinosa acquista*), który może towarzyszyć procesom nowotworowym. Patogeneza większości problemów trichologicznych pozostaje niezbyt jasna, ale część z tych zaburzeń może stanowić ważny marker schorzeń układowych, a ich znajomość może mieć istotne, życiowo ważne znaczenie.

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Menopause is defined as the last menses, recognized after 12 months of amenorrhea that is not associated with a pathologic cause. On average, the age of onset of the menopause is 50 years, but it may vary among women, ranging from 45 up to 56 years of age (1, 2).

The menopause is a result of a transition from full ovarian function to a complete lack of ovarian estrogen biosynthesis. It is now apparent, that estrogens have additional, important and diverse functions (3). Undoubtedly, decrease in estrogens synthesis leads to climacteric changes, which hinder life of woman and worsen the quality of life. Typical menopausal symptoms comprise hot flushes, sweating, insomnia and vaginal dryness or urinary frequency. Up to 75% of menopausal women experience one or more of such symptoms. Postmenopausal disturbances are observed in the cardiac system (progressive coronary heart disease, increased blood pressure), in a loss of bone mineral density or as metabolic changes (worsening lipid profile, altered body fat distribution with central obesity, altered glucose and insulin balance) (4, 5).

A number of studies have shown that estrogens have many important, beneficial and protective roles in the skin physiology. An impact of estrogens on human skin is recognized as changes that are observed in post-menopausal women, with a number of studies documenting differences seen following the menopause. Many women report a sudden onset of skin aging several months after climacteric symptoms begin (6).

The menopause leads to skin aging, which becomes thinner with a loss of collagen content, decreased elasticity and increased wrinkling (3). The decline in estrogen, which occurs during the menopause, reduces the mitotic activity in the epidermal basal layers as well as modyfing epidermal lipid synthesis, causing xerosis (7). There are fewer blood vessels and their walls are often damaged, resulting in easier occurance of skin extravasations. Further, unpleasant symptoms, include numerous teleangiectases, roughness, sallowness, sagging and pigment alternations (8).

Aging associated with climacteric hormonal changes also affects some hair characteristics and is responsible for decreased hair coverage in middle-aged women (9). With menopause, the hair distribution of the female body starts to change, but some changes can occur both in a distribution and in a structure of hair. Age related decrease in hair copper and calcium concentration is observed in perimenopausal women (2, 10, 11). The optical fibre diameter analysis reveals that diameters of hair in the frontal and parietal scalp are lower in postmenopausal women, but there is no change in the occipital hair diameter (12).

The hair follicles are often affected in menopausal women, and indeed, hair represents a specific receptor structure expressing declines related to fluctuations in circulating levels of sex steroids (9). As it is was mentioned above, one of the major changes during menopause is the virtual cessation of ovarian estrogen production. The major source of estrogen after the menopause is from conversion of adrenal androgen to estrogen by the enzyme aromatase in the peripheral tissues (12). There is an evidence that an estrogen receptor pathway within the dermal papilla regulates the telogen-anagen transition of the hair follicle (13). In humans, estrogens reduce the rate of hair growth, but prolong the duration of growing phase of hair cycle growth and probably shorten its resting phase (14, 15). Estradiol has also been noted to induce aromatase activity in human scalp follicles and it is the possible one mechanism by which it may exert own biological activity (12). While it has been recognized, that estrogens stay important modulators of hair growth, the details of molecular regulatory pathways have not been well characterized. In contrast, the role of androgens on hair growth has dominated the field of hair biology and they are the most important among sex hormones, that regulates hair growth (16). Androgens can lead to the conversion of fine vellus hairs to terminal hairs in pubic and axillary areas, but they cause the opposite hair conversion on the scalp (17). In postmenopausal women, testosterone levels decrease compared to young women, although the residual ovarian synthesis after the menopause appears to contribute to a higher proportion of circulating testosterone, relative to estrogens. This may be due to higher LH levels and their effect on ovarian stromal steroidogenesis. As there is a free available to cells and SHBG (sex hormone binding globulin) bounded – testosterone, in the postmenopausal period, estrogens dependant SHBG levels decline and may account for higher bioavailability of testosterone (18). The increase in androgen to estrogen ratio may cause some changes in hair distribution seen during menopause. Hair loss occurs for example in axillary and pubic areas, whereas some women also start to lose hair on the scalp and androgenic alopecia or frontal fibrosing alopecia should be considered. It is observed that, the frequency of all-over thinning and frontal hair loss increases with age of women, whereas hair loss at the temples do not increase with age (19, 20). In contrast, some women may also experience an increase in facial hair (2, 7, 17).

As the role of androgens in perimenopausal alopecia has not been clearly established, the most preferred term for female androgenetic alopecia is currently female pattern hair loss (FPHL). It much better describes diffuse hair loss patterns in women with uncertain relationship between androgens and this entity (7, 21). The term FPHL distinguishes from male pattern of hair loss described by James Hamilton, which features the fronto-temporal recession and hair loss over the vertex while the occipital scalp is preserved (17, 22, 23). A studies supporting a notion of nonandrogen pathways involved in FPHL show, that sebum secretion, a marker of end-organ androgen response, is not elevated in perimenopausal women (12). It is rather suggested, that the FPHL occurs in genetically pre-

disposed women due to androgens (16, 24, 25). Summarizing, neither the androgen-dependent nature nor the genetic basis of the FPHL has been clearly established (26).

Typically, hair in FPHL is fine textured and the pull test is negative, but some visibility occurs on the scalp and increases spacing between hair on the vertex compared with the occiput (12, 27). There is a diffuse reduction in hair density over the crown and frontal scalp with relative sparing of the anterior hair line, leaving there 2-3 cm of frontal hair zone (7, 17, 21, 24, 28). Women who present with a reduction in hair density, frequently exhibit thinning and widening of the area of hair loss on the central part of the scalp, which when it includes a breach of the frontal hairline is described as Christmas tree pattern, the one observed in the majority of women with FPHL (17, 29).

The clinical evaluation and definition of the FPHL has traditionally relied on the Ludwig scale, which divides the severity of hair density reduction over the crown into three grades. Further estimation of hair loss, was developed as Savin density scale, which classifies FPHL into 8 stages of increasing crown balding, in addition to a special subcategory to detect frontal anterior recession. The simplification of Savin's scale, which assesses the degree of hair loss using the midline part, was created by Sinclair as five-point visual analogue scale (21, 23, 29, 30).

A scalp biopsy in woman with FPHL, shows a normal follicular count, preserved sebaceous glands, but there are observed a progressive follicular miniaturization and the accompanying conversion of terminal follicles into vellus-like follicles. The anagen phase of these vellus hair follicles is briefer and leads to production of shorter and finer hairs (12, 25, 27, 29). Clinical and histopathological observations are consent to trichoscopy which indicates lower average hair thickness in the frontal area in comparison to the occiput, more than 10% of thin hair (below 0.03 mm) in the frontal area and the ratio of vellus hair number (frontal area to occiput) above 1.5:1 (20, 31). The presence of more than 6 vellus hairs in the frontal scalp at 20-fold magnification can be used as an additional criterion of FPHL, especially in the initial phases of the disease (32). Another important trichoscopy finding is perifollicular discoloration of the skin in FPHL. A ratio of such hair follicles with perifollicular discoloration in frontal to occiput higher than 3:1 (calculated at 20-fold magnification) is highly indicative of FPHL. Data shows that a number of single-hair pilosebaceous units is significantly increased in the frontal area in patients with FPHL compared to the occiput (a ratio above 2:1). Essentially, trichogram in FPHL reveals an increased percentage of hair in telogen in affected area, what in early disease the diagnosis may demand to exclude chronic telogen effluvium (CTE) (25, 31).

Increased hair shedding is common in the early stages of FPHL, but when little or no reduction in hair volume over the mid-frontal scalp is seen, the other differential diagnoses, including acute and chronic telogen effluvium should be considered. While acute telogen effluvium is a self-limiting event, the CTE typically presents an abrupt hair shedding that can have fluctuating course lasting at least 6 months and may continue for 6-7 years, but ultimately not leading to balding. Following the FPHL without treatment, it invariably leads to a progressive reduction in hair volume over the frontal scalp (21, 33). Indeed, it has been proposed, but not confirmed, that decreasing estrogen levels may also contribute to CTE (16). As the CTE is a diagnosis of exclusion, a scalp biopsy is required to differentiate CTE from the early FPHL. It is considered to use the ratio of terminal to vellus-like hair assessed at $\leq$ 4:1 as diagnostic for the FPHL, while ratio $\geq$ 8:1 is considered as diagnostic for CTE. Ratios 5:1, 6:1, 7:1 persist indeterminate (16, 21, 26). Another research reveals that, FPHL may be differentiated from CTE basing solely on trichoscopy criteria. A major trichoscopy criterion of FPHL is the presence of yellow dots, which reflect hair follicle ostia lacking any hair (empty hair follicles) and it is one of the most important trichoscopy features distinguishing FPHL from CTE. Intrinsically, CTE has no specific trichoscopy features apart from an increased proportion of short, sharp-ended hair (31).

The frontal fibrosing alopecia (FFA) is a distinct condition, firstly described by Kossard in 1994, that mainly affects postmenopausal women (34-39). The mean age of onset of FFA ranges 56-60 years and typically it starts 2-12 years after the beginning of menopause (34, 36, 37, 40). It is characterized clinically by a slowly progressive symmetrical band of frontotemporal or frontoparietal hairline recession (37). The alopecic skin appears pale, smooth and devoid of sun-damage signs in contrast with the adjacent skin of the forehead (38). The condition develops slowly with spontaneous stabilization over several years, but it is impossible to predict the degree of expression prior to stabilization (35). The disease is widely recognized as a clinical variant of lichen planopilaris (LPP), as it shares aspects with LPP both clinically and histopathologically (37, 41, 42). The histologic features of FFA and LPP are similar: both demonstrate inflamed follicles containing keratinous plugging, apoptotic keratinocytes in the external root sheath, perifollicular fibrosis, and marked follicular dropout with fibrotic traxcts at the sites of previously existing hair follicles. Scattered melanophages can be seen among the inflammation (36, 41). A striking feature of FFA is a loss of both terminal and vellus hair (36). The pathogenesis of FFA has remained still unknown. Although an autoimmune reaction and hormonal factors seem to play a role, the exact mechanism of development of scarring alopecia in the typical pattern of FFA is unknown. Laboratory abnormalities typically include positive anithyroid antibodies or positive antinuclear antibodies (34). Several autoimmune diseases such as thyroid dysfunction (a significant prevalence of hypothyroidism) or vitiligo seem to be associated with FFA, supporting an autoimmune mechanism in

the pathogenesis of FFA (34, 39). Interestingly, FFA has been reported to occur also in such pathologies as sarcoidosis, lymhoidal disorders, skin cancers or metastatic tumors to the scalp – especially a cancer of breast, stomach, colon, parotid salivary glands, kidney or melanoma (24, 42). Some observations indicate a high incidence in a rate of early menopause is found among female patients with FFA, what indicates a possible hormonal role in its etiology (34, 37, 39). The decrease of estrogens associated with menopause may alter the control of the hair cycle and in some matter predispose to the development of FFA (34). Some response to treatment with finasteride (an inhibitor of α5-reductase), also suggests that androgens may be partially responsible in the pathogenesis of the disease (38). A considerable coexistence of FPHL is found in patients with FFA. (34, 40) Other findings in patients with FFA, encompass a loss of eyebrow that is reported in more than 70% of cases and may be the initial sign of presentation of FFA (34, 36). Alopecia of eyelashes and body hair (axillary, pubic and limb) can also be observed, although less frequently (34-37). Histological findings reveal, some fibrotic changes in the accompanying loss of eyebrow, while concomitant alopecia of other sites seems to be non-inflammatory and non-scarring (37).

An essential problem of aging is an increasing number of systemic diseases that occur soon after the menopause begins. The majority of them requires a long-term drug interventions and some agents has been reported to affect hair growth. The impact of medications on hair physiology is distinguished and some drugs can lead to increased hair loss while others, can stimulate hair growth or even change their shape or color. The drug-induced alopecia affects predominantly a scalp and has typically a diffuse pattern with non-scarring and transient course. The hair loss usually results from toxic influence of the drug on the hair follicle, which depends on the dosage, type of drug and patient susceptibility. As a consequence, medications can lead to telogen effluvium, anagen effluvium or both. Therapeutic options are mostly lacking, however an elimination of drug is often sufficient and some dietary supplement with vitamins or biotin can facilitate hair regrowth (43, 44). Cardiology patients may report hair loss due to: lipid lowering agents, angiotensin converting enzyme inhibitors, β-blockers and calcium channel blockers (45). Toxic effects of drugs used in a therapy of hypertension, coronary heart disease and cardiovascular insufficiency vary, however they are usually transient. This is apparent with regard to alopecia induced by angiontensin converting enzyme inhibitors, which occurs in up to 5% of the treated patients, and depends on the type of drug. Such hair loss affects usually the scalp, is reversible after discontinuation of the treatment (46, 47). Lipid lowering agents such as statins and fibrates are responsible for alopecia in 1-5% of the patients admitted to the therapeutic regimen. The hair loss is usually transient, and affects not only the scalp but also other body regions (28, 47-49). Anticoagulants cause balding in 50% of the patients, which occurs 1-12 weeks after the last dose is administered. Originally unfractioned heparin was mainly blamed for this condition, however it has recently been demonstrated that low molecular weight heparins and warfarin have the same side effect. Anticoagulants belonging to the vitamin K antagonist group involve hair thinning usually between 3 and 20 weeks after the onset of the therapy. Most cases of hair loss are of benign nature and only 20% of patients display pronounced clinical symptoms, initially present on the scalp and later occurring in the eyebrow, armpit and pubic areas (50, 51). Drugs used in psychiatry and neurology are also responsible for drug induced alopecia. Carbamazepine induces hair loss in up to 10.0% of individuals, Valproic acid in 2.6-12%, lithium salts in 12-17% and dopaminergic drugs in up to 30% of patients submitted to the therapeutic regimen (52, 53). The group of drugs that induce changes in hair growth related to hormonal changes is very wide. Drugs used in thyroid gland diseases, such as propylotiouracyl or metizole, may be responsible for iatrogenic hypothyroidism and therefore lead to alopecia (44).

Changes in hair distribution in climacteric women may also consider some kind of unwanted hair growth. Body hair in women usually tends to rise until menopause, however facial hair tends to increase even in the elderly (9). The frequency of facial hair gain varies with site, with the prevalence on the chin over the upper lip (19). The prevalence of hirsutism in postmenopausal women has not been fully documented, but it is supposed that about 50-70% of women report excessive facial hair growth after menopause, even though there is no hormonal replacement therapy (9, 54). Although the occurrence of hirsutism in the elderly women is often, the causes and its intensity should be differentiated. In more than 95% of cases in women, hirsutism is due to benign condition, but some pathological issues should be also considered (7). Potential etiologies encompass both tumors or non-neoplastic such as PCOS, obesity-induced hyperandrogenic anovulation, Cushing's syndrome, persistent congenital adrenal hyperplasia, iatrogenic hyperandrogenism and ovarian stromal hyperplasia or ovarian hyperthecosis (54-56). According to the classical or modified Ferriman-Gallway scale, a score of $\geq$ 8 is considered to represent hirsutism, however this scale may be not suitable for menopausal women. It results from changes which encompass both the hair distribution as well as the character of hair, what differs them from such observed in women at reproductive age (7).

Some cases of excessive hair growth should be differentiated from increased lanugo hair growth. Essentially, the report of lanugo-like hair growth in areas that were previously hair free should be considered as an important indicator, known as acquired hypetrichosis languinosa (AHL), that may coexist with internal malignancy (57, 58). It is a rare paraneoplastic dermatosis

that was first described by Turner in 1865 in a female patient with breast cancer (58). The term hyperthisosis languinosa refers to increased growth of thin and soft hair, typically with the sudden onset (58, 59). These lanugo hair, which are fine and nonpigmented, can reach unusual length (57). The syndrome is more often observed in women than in men (70 vs. 30%) with an average age of onset 40-70 years (58, 60). In women, AHL should be differentiated from hirsutism, which is distributed in an adult male pattern (60). AHL is preferentially located on the face, but it may also involve the thorax and extremities, spreading in a craniocaudal manner (58, 60). This cutaneous syndrome is most commonly associated with adenocarcinoma of the lung and colon, but occurance of AHL in other malignancies have been reported, such as breast cancer, gastric adenocarcinoma, Ewing's sarcoma or myeloid leukemia (59 63). There is observed a strictly parallel development of AHL and the tumor, with complete disappearance of hypertrichosis in the weeks following surgical removal of the tumor, but the most characteristic is that it usually occurs when the tumor is disseminated (60, 61). The syndrome may represent the inappropriate and perhaps ectopic production of a hormone normally produced during fetal development (59). This factor leads to a prolongation of the anagen phase of vellus hair follicles, resulting in hypertichosis (60). The AHL often precedes tumor diagnosis in about two and half to three years, with mean survival of less than three years after diagnosis (58, 60). Sometimes, AHL occurs concurrent with acanthosis nigricans, papillary hypertrophy of tongue and glossitis, taste or smell disturbances, angular cheilitis (57, 58, 60). The occurrence of AHL has been also reported in metabolic and endocrine disorders, such as hyperthyroidism, anorexia nervosa, porphyria or as pharmacologically induced (Cyclosporine, Minoxidil, Diazoxide, Interfeon, Corticosteroids or Phenytoin). In contrast, hypertichosis in such cases, is rather characterized by terminal-type hair, which is mostly coarse and dark (57, 60).

A progressive ageing of society leads to increase in a number of women in menopause. Indeed, an increase in prevalence of reported climacteric symptoms will be observed in following years, including these associated with hair changes. A significant number of menopausal women can experience a detrimental in quality of life, caused by trichological disturbances. The pathogenesis of the most of them stay not clear, but some of these hair changes can comprise a significant marker of systemic disorders and the knowledge of them may have an essential, vital significance.

BIBLIOGRAPHY

1. Słopień R, Warenik-Szymankiewicz A: Przekwitanie. [W:] Bręborowicz GH (red.): Położnictwo i ginekologia. Wyd. I, Wydawnictwo Lekarskie PZWL, Warszawa 2010: 716-725.
2. Calleja-Agius J, Brincat M, Borg M: Skin connective tissue and ageing. Best Pract. Res Clin Obstet Gynaecol 2013; 27: 727-740.
3. Thornton MJ: Estrogens and aging skin. Dermatoendocrinol 2013; 5: 264-270.
4. Genazzani AR, Gambacciani M, Simoncini T: Menopause and aging, quality of life and Sexuality. Climacteric 2007; 10: 88-96.
5. Birkhaeuser MH, Panay N, Archer DF et al.: Updated practical recommendations for hormone replacement therapy in the peri- and postmenopause. Climacteric 2008; 11: 108-123.
6. Stevenson S, Thornton J: Effect of estrogens on skin aging and the potential role of SERMs. Clin Interv Aging 2007; 2: 283-297.
7. Blume-Peytavi U, Atkin S, Gieler U, Grimalt R: Skin academy: hair, skin, hormones and menopause - current status/knowledge on the management of hair disorders in menopausal women. Eur J Dermatol 2012; 22: 310-318.
8. Broniarczyk-Dyla G, Joss-Wichman E: Ageing of the skin during menopause. J Eur Acad Dermatol Venereol 2001; 15: 494-495.
9. Piérard-Franchimont C, Piérard GE: Alterations in Hair Follicle Dynamics in Women. BioMed Research International, vol. 2013, Article ID 957432, 5 pages, 2013. doi:10.1155/2013/957432.
10. Wlaźlak E, Dunicz-Sokolowska A, Radomska K et al.: Analysis of hair copper concentration in perimenopausal women. Prz Menopauz 2007; 6: 303-305.
11. Wlaźlak E, Surkont G, Dunicz-Sokołowska A et al.: Analysis of calcium concentration in perimenopausal women hair. Prz Menopauz 2007; 6: 51-54.
12. Mirmirani P: Hormonal changes in menopause: do they contribute to a 'midlife hair crisis' in women? Br J Dermatol 2011; 165 (suppl. 3): 7-11.
13. Oh HS, Smart RC: An estrogen receptor pathway regulates the telogen-anagen hair follicle transition and influences epidermal cell proliferation. Proc Natl Acad Sci USA 1996; 93: 12525-12530.
14. Sinclair RD: Hair structure and function. [In:] Sinclair RD, Banfield CC, Dawber RPR (eds.): Handbook of diseases of the hair and scalp. 1st ed., Wiley-Blackwell, Oxford 1999: 3-26.
15. Conrad F, Ohnemus U, Bodo E et al.: Estrogens and Human Scalp Hair Growth – Still More Questions than Answers. J Invest Dermatol 2004; 122: 840-842.
16. Mirmirani P, Luo F, Youngquist SR et al.: Hair Growth Parameters in Pre- and Postmenopausal Women. [In:] Trüeb RM, Tobin DJ (eds.): Aging hair. Springer-Verlag, Berlin Heidelberg 2010: 49-60.
17. Imko-Walczuk B, Cegielska A, Głombiowska M: Zmiany w rozmieszczeniu włosów u kobiet w okresie pomenopauzalnym. Przegl Dermatol 2012; 99: 62-67.
18. Al-Azzawia F, Palacios S: Hormonal changes during menopause. Maturitas 2009; 63: 135-137.
19. Ali I, Wojnarowska F: Physiological changes in scalp, facial and body hair after the menopause: a cross-sectional population-based study of subjective changes. Br J Dermatol 2011; 164: 508-513.
20. Brzezińska-Wcisło L, Lis A, Kamińska G, Wcisło-Dziadecka D: Physiology and pathology of growth and loss of human scalp hair. Post Derm Alergol 2003; 20: 260-266.
21. Dinh QQ, Sinclair R: Female pattern hair loss: Current treatment concepts. Clin Interv Aging 2007; 2: 189-199.
22. Hamilton JB: Patterned loss of hair in man: types and incidence. Ann N Y Acad Sci 1951; 53: 708-728.
23. Wcisło-Dziadecka D, Brzezińska-Wcisło L, Lis-Święty A, Stankiewicz-Habrat P: Co nowego w etiopatogenezie i leczeniu łysienia androgenowego? Lekarz 2005; 11: 17-24.
24. Brzezińska-Wcisło L, Wcisło-Dziadecka D, Meszyńska E et al.: New perspectives on the pathogenesis and treatment of hair disorders. Post N Med 2012; 10: 800-805.
25. Brzezińska-Wcisło L, Lis A, Szeremeta-Bazylewicz G: Etiopatogeneza łysienia androgenowego i metody jego leczenia. Świat Med Farm 2001; 10: 24-27.
26. Sinclair R, Wewerinke M, Jolley D: Treatment of female pattern hair loss with oral antiandrogens. Br J Dermatol 2005; 152: 466-473.
27. Brzezińska-Wcisło L: Łysienie rozlane kobiet – etiopatogeneza, klinika i leczenie. Świat Med Farm 2000; 1: 23-26.
28. Brzezińska-Wcisło L, Szeremeta-Bazylewicz G: Femine diffuse alopecia, classification and views of etiopathogenesis. Wiad Lek 1999; 52: 386-392.
29. Van Zuuren EJ, Fedorowicz Z, Carter B: Evidence-based treatments for female pattern hair loss: a summary of a Cochrane systematic review. Br J Dermatol 2012; 167: 995-1010.
30. Brzezińska-Wcisło L: Assessment of minoxidil effect on hair growth in androgenetic alopecia in women. Pol Merk Lek 2002; 13: 208-211.
31. Rakowska A, Slowinska M, Kowalska-Oledzka E et al.: Dermoscopy in female androgenic alopecia: Method standardization and diagnostic criteria. Int J Trichology 2009; 1: 123-130.

32. Herskovitz I, de Sousa IC, Tosti A: Vellus hairs in the frontal scalp in early female pattern hair loss. Int J Trichology 2013; 5: 118-120.
33. Brzezińska-Wcisło L, Wcisło-Dziadecka D, Bergler-Czop B, Zbiciak M: Most frequent trichological problems in women. Dermatol Klin 2014; 1: 19-24.
34. Vañó-Galván S, Molina-Ruiz AM, Serrano-Falcón C et al.: Frontal fibrosing alopecia: a multicenter review of 355 patients. J Am Acad Dermatol 2014; 70: 670-678.
35. Jouanique C, Reygagne P: Frontal fibrosing alopecia. Ann Dermatol Venereol 2014; 141: 272-278.
36. MacDonald A, Clark C, Holmes S: Frontal fibrosing alopecia: a review of 60 cases. J Am Acad Dermatol 2012; 67: 955-961.
37. Chew AL, Bashir SJ, Wain EM et al.: Expanding the spectrum of frontal fibrosing alopecia: a unifying concept. J Am Acad Dermatol 2010; 63: 653-660.
38. Tosti A, Piraccini BM, Iorizzo M, Misciali C: Frontal fibrosing alopecia in postmenopausal women. J Am Acad Dermatol 2005; 52: 55-60.
39. Tan KT, Messenger AG: Frontal fibrosing alopecia: clinical presentations and prognosis. Br J Dermatol 2009; 160: 75-79.
40. Olsen EA: Female pattern hair loss and its relationship to permanent/cicatricial alopecia: a new perspective. J Investig Dermatol Symp Proc 2005; 10: 217-221.
41. Armenores P, Shirato K, Reid C, Sidhu S: Frontal fibrosing alopecia associated with generalized hair loss. Australas J Dermatol 2010; 51: 183-185.
42. Brzezińska-Wcisło L, Szeremeta-Bayzlewicz G, Talik V: Pathlogical processes of a scalp inducing cicatrical alopecia. Wiad Lek 2000; 53: 522-529.
43. Brzezińska-Wcisło L: Badania wpływu wybranych leków na dynamikę włosów przeprowadzone na podstawie wariantu doświadczalnego na modelu szczurów rasy Wistar oraz ocena skuteczności tych leków w aspekcie klinicznym i trichologicznym w łysieniu rozlanym kobiet. Rozprawa habilitacyjna, Śląska Akademia Medyczna w Katowicach, Katowice 1996.
44. Brzezińska-Wcisło L: Najczęstsze problemy trichologiczne oraz ich profilaktyka. Wiad Dermatol 2013; 2: 1-11.
45. Llau ME, Viraben R, Montastruc JL: Drug-induced alopecia: review of the literature. Therapie 1995; 2: 145-150.
46. Keplar KE: Alopecia, Hirsutism and Hypertrichosis. [In:] Tisdale JE, Miller DA (eds.): Drug-Induced Diseases. Prevention, detection and management. 2nd ed., American Society of Health-System Pharmacists, Bethesda 2010: 135-179.
47. Latusek M, Brzezińska-Wcisło L: Impact of atrovastatin and perindopril on the hair cycle in rodent model – risk of drug induced alopecia in patients with heart disease. Post N Med 2012; 10: 794-799.
48. Trüeb RM: Diffuse Hair Loss. [In:] Blume-Peytavi U, Tosti A, Whiting DA, Trüeb R (eds.): Hair growth and disorders. Springer-Verlag, Berlin Heidelberg 2008: 259-270.
49. Shapiro J: Hair loss in women. N Eng J Med 2007; 357: 1620-1630.
50. Aspner R, Horl WH, Sunder-Plassmann G: Dalteparin induced alopecia in hemodialysis patients: reversal by regional citrate anticoagulation. Blood 2001; 97: 2914-2915.
51. Wang YY, Po HL: Enoxaparin-induced alopecia in patients with cerebral venous thrombosis. J Clin Pharm Ther 2006; 31: 513-517.
52. Burrows NP, Grant JW, Crisp AJ, Roberts SO: Scarring alopecia following gold therapy. Acta Derm Venereol 1994; 74: 486.
53. Piraccini BM, Iorizzo M, Rech G, Tosti A: Drug-induced hair disorders. Curr Drug Saf 2006; 3: 301-305.
54. Wojnowska D, Juszkiewicz-Borowiec M, Chodorowska G: Menopause and skin aging. Post Dermatol Alergol 2006; 23: 149-156.
55. Somani N, Harrison S, Bergeld WF: The clinical evaluation of hirsutism. Dermatol Ther 2008; 21: 376-391.
56. Rothman MS, Wierman ME: How should postmenopausal androgen excess be evaluated. Clin Endocrinol (Oxf) 2011; 75: 160-164.
57. Slee PH, Verzijlbergen FJ, van Leeuwen JH, van der Waal RI: CASE 2. Acquired hypertrichosis: a rare paraneoplastic syndrome in various cancers. J Clin Oncol 2006; 24: 523-534.
58. Silva JA, Mesquita Kde C, Igreja AC et al.: Paraneoplastic cutaneous manifestations: concepts and updates. An Bras Dermatol 2013; 88: 9-22.
59. Davies RA, Newman DM, Phillips MJ et al.: Acquired hypertrichosis languinosa as a sign of internal malignant disease. Can Med Assoc J 1978; 118: 1090, 1095-1096.
60. Vulink AJ, ten Bokkel Huinink D: Acquired hypertrichosis lanuginosa: a rare cutaneous paraneoplastic syndrome. J Clin Oncol 2007; 25: 1625-1626.
61. Saad N, Hot A, Ninet J et al.: Acquired hypertrichosis languinosa and gastric adenocarcinoma. Ann Dermatol Venereol 2007; 134: 55-58.
62. Pérez-Losada E, Pujol RM, Domingo P et al.: Hypertrichosis lanuginosa acquisita preceding extraskeletal Ewing's sarcoma. Clin Exp Dermatol 2001; 26: 182-183.
63. Bauer HI, Kaatz M, Elsner P: Circumscribed hypertrichosis lanuginosa in acute myeloid leukemia. Dtsch Med Wochenschr 2001; 126: 845-846.

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