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АЛОПЕЦИЯ В СТРУКТУРЕ КЛИНИЧЕСКИХ ПРОЯВЛЕНИЙ ЭНДОКРИНОПАТИЙ: ПАТОГЕНЕТИЧЕСКИЕ И ДИАГНОСТИЧЕСКИЕ АСПЕКТЫ

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Alopecia and Clinical Presentation of Endocrinopathies: Pathogenetic and Diagnostic Aspects

Резюме

В обзоре рассмотрены ключевые аспекты патогенеза алопеции при патологии эндокринной системы. Продемонстрирована роль целого ряда гормонов, факторов роста, цитокинов и других биологически активных веществ. Показано, что клиническое значение алопеции — весьма распространенного в популяции симптома — далеко не исчерпывается геронтологической проблематикой, и может быть проявлением эндокринопатий. Указанное обстоятельство диктует проведение в целом ряде случаев широкого дифференциально-диагностического поиска, выполнение которого наиболее перспективно при условии реализации мультидисциплинарного подхода с участием эндокринолога, гинеколога, андролога, дерматолога / трихолога и других специалистов.

Ключевые слова: *алопеция, эндокринная система, эндокринопатии, трихология, мультидисциплинарный подход*

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Abstract

The review examines the key aspects of the pathogenesis of alopecia in endocrine system pathology. The role of hormones, growth factors, cytokines and other biologically active substances has been demonstrated. Alopecia is a frequent symptom that can be the result of not only gerontological, but also endocrinological problems. Therefore, time-consuming differential diagnosis is often necessary. Diagnosis is more effective if a team of specialists is involved: endocrinologist, gynecologist, andrologist, dermatologist / trichologist, and others.

Key words: *alopecia, endocrine system, endocrinopathies, trichology, multidisciplinary approach*

Conflict of interests

The authors declare that this study, its theme, subject and content do not affect competing interests

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5-AR — 5-alpha reductase, AGA — androgenetic alopecia, HF — hair follicle, SHBG — sex hormone binding globulin, DHT — dihydrotestosterone, DHEA-S — dihydroepiandrosterone sulfate, TE — telogen effluvium, BMI — body mass index, IGF-1 — insulin-like growth factor-1, LH — luteinizing hormone, MS — metabolic syndrome, DM — diabetes mellitus, PCOS — polycystic ovary syndrome, TRH — thyrotropin-releasing hormone, TNF-alpha — tumor necrosis factor-alpha

In the clinical practice, there are quite often cases when a symptom that should serve as a key to a correct and accurate diagnosis escapes the doctor's analytical field due to its low specificity and the diagnostic procedure based on it seems unpromising. An example is alopecia, which can be the only sign and nevertheless deserves close attention and requires a comprehensive examination of the patient. Diagnostic search should include a range of diseases and conditions that can cause this symptom. The type of alopecia can also have a diagnostic value, and hair loss itself can serve as the first symptom of the disease.

Optimal treatment of the patient requires an understanding of the hair loss progression and awareness of the plurality of its possible causes. An individual treatment plan can be implemented if work with the patient is carried out sequentially: starting with the most simple and obvious tasks and gradually moving on to more complex ones. It should be borne in mind that hair loss is most often caused not by a single cause but by a whole range of factors [1].

Alopecia is a term that refers to any hair loss. The daily rate of hair loss is about 100, and hair loss can be defined as a condition in which more than 100 hairs fall per day. However, given the individual physiological processes, excessive hair loss, not typical for a particular person, can be called alopecia [2]. There are two main groups of alopecia: reversible and irreversible (scarring, in which hair cannot be restored, and the goal of therapy is to achieve remission to prevent the expansion of the lesion). Reversible forms include AGA, telogen and anagen effluvium, and alopecia areata.

The hair follicle (HF) is a highly organized structure with a high mitosis rate. It is sensitive to many factors, such as growth factors (insulin-like growth factor, endothelial vascular growth factor, fibroblast growth factor), cytokines (interleukin 1-alpha, TNF-alpha, etc.) and the state of the endocrine system, which largely regulates hair growth via androgens, prolactin, thyroid hormones, melanocyte-stimulating hormone, etc.

This article discusses the main points of hormonal regulation of HF functioning.

Androgens

Testosterone is produced not only in the adrenal glands and gonads from its predecessors — androstenedione, dihydroepiandrosterone and dihydroepiandrosterone sulfate, but also locally by the dermal papilla. Therefore, the hair follicle is not only the target but the site of testosterone synthesis [3].

The link between androgens and alopecia was first noted by Hamilton J. B. (1960), stating that AGA did not develop in eunuchs and boys castrated before puberty [4, 5]. However, with severe testosterone deficiency, telogen effluvium (TE) may develop. Most likely, this is due to its anabolic effect on the formation of protein structures, which are also the hair shaft. The relationship between the androgen receptor gene with androgenic insensitivity and hair loss has been shown in Kennedy's disease, which is a neurodegenerative disease that triggers muscular atrophy of the spine, testicular atrophy and reduced virilization [3]. Significant improvement in hair condition was also shown in patients taking tamoxifen for breast

cancer. Therefore, in the absence of genetic sensitivity of the HF to dihydrotestosterone (DHT), hormone replacement therapy with testosterone can have a positive effect on hair growth [6, 7].

During puberty, young men and women develop terminal hair (secondary sexual characteristics) in the axillary, pubic areas, and lower extremities, and young men in the trunk and beard (the so-called androgen-dependent hair growth zones). In these areas, androgens extend the hair growth phase, change the ability of keratinocytes to divide and increase the pigmentation and size of the dermal papilla.

These processes involve 5-alpha reductase (5-AR), enzyme that converts testosterone to dihydrotestosterone. It can also convert 4-androstenedione and progesterone into their corresponding reduced forms. 5-AR is synthesized in two molecular forms, each encoded by a separate gene. The distribution of 5-AR of the first and second types, their ratio and expression intensity vary in different areas. The expression of second-type 5-AR is higher in the dermal papilla of the HF on the head, which intensifies the negative effect of androgens.

A five-fold increase in the androgenic activity of testosterone due to its conversion to DHT demonstrates the important role of 5-AR in androgen action. With a genetic predisposition under the influence of DHT, microinflammation develops in the perifollicular zone in the scalp skin. This leads to the gradual miniaturization of the follicle and a shorter hair growth phase, and the development of fibrosis, with slow replacement of the follicle with connective tissue. Therefore, with high activity of the 5-AR and HF genetic sensitivity to DHT, a type of hair loss called AGA develops. In contrast, in rare cases of 5-AR deficiency syndrome, hair loss on the head was not observed [3]. In this regard, finasteride, a second-type 5-AR inhibitor mainly used to treat benign prostatic hyperplasia, is effective in treating AGA.

The role of androgens in the development of AGA in women is contradictory. Most studies have shown no hyperandrogenism in more than 60% of women with AGA [6].

Estrogens

Estrogen (and androgen) receptors are located on epidermal keratinocytes, dermal fibroblasts, sebaceous glands and HF. On the scalp, the predominant estrogen receptors are beta-estrogen receptors [6]. Estradiol alters the metabolism of androgens in the pilosebasial structures, which itself exhibits a noticeable activity of aromatase, a key enzyme in the conversion of androgens to estradiol. In addition, estradiol can affect androgen metabolism by inhibiting aromatase activity, which determines the conversion of testosterone and androstenedione androgens to estrogens estradiol and estrone [8]. That is, the HF is simultaneously a target for estrogens and their source [9].

Estrogens are believed to have a positive effect on the prolongation of the hair growth phase by binding to locally expressed estrogen receptors, stimulating the synthesis of glycosaminoglycans, elastin, and collagen in the skin [10]. This partially explains the active postpartum hair loss due to a drop in the system level of estrogen (and progesterone). The same applies to women during menopause: with a drop in estrogen levels, changes in the skin and hair are significantly accelerated, accompanied by loss of turgor, dryness, thinning and hair loss due to depletion of the microvasculature of the dermis, trophic innsufficiency of the dermal papilla, relative increase in androgenic effect, activation of pro-inflammatory cytokines with the formation of zones of chronic inflammation in the HF [3]. Most women receiving aromatase inhibitors develop some form of alopecia (androgenetic or diffuse) [11].

With a genetic predisposition, a violation of the ratio of estrogens and androgens can be a triggering factor in hair loss in women [12]. Combined oral contraceptives or hormone replacement therapy with androgenic progestogens (norethisterone, levonorgestrel, tibolone) often cause hair loss, especially in genetically predisposed women [1, 13–15]. In the overwhelming majority of cases, severe hair loss occurs after oral contraceptives are discontinued, and AGA often occurs, which argues against prescribing these drugs to treat alopecia (not to mention other side effects — changes in blood rheology and lipid profile, increased SHBG level, gonadotropin synthesis inhibition by the hypothalamus, acne, hirsutism, decreased libido, osteoporosis, adrenal gland dysfunction, impaired venous outflow, and vaginal atrophy) [1, 16].

AGA in women, which differs externally from men, is also explained by the fact that scalp skin in women has higher aromatase activity and more estrogen receptors [17]. On the other hand, a mouse study showed that parenteral and local estrogen agonists cause deep and long-term inhibition of hair growth, while estrogen antagonists stimulate hair growth by initiating anagen, that is, an active growth phase [4]. Therefore, unlike androgens, the role of estrogens in the regulation of hair growth is debatable.

Progesterone

The effects of progesterone that have an impact on the phases of hair growth include vasodilating and anti-inflammatory effect (due to inhibition of lipid peroxidation, TNF-alpha, mast cells), suppression of the effects of excess testosterone and estrogen, as well as inhibition of

5-AP activity. It was shown that the topical application of progesterone to the scalp skin significantly reduces 5-AR activity and the level of DHT in the perifollicular zone (the synthesis of DHT is inhibited by 97% and estradiol by 41%) [18]. The effect of progesterone, which partially intensifies hair growth, is also due to its central action via inhibiting the secretion of luteinizing hormone (LH), which, in turn, causes a decrease in the stimulation of ovarian theca cells (androgen synthesis) [8].

Progesterone is considered a female steroid hormone. However, since it is also produced in the testes and adrenal glands in men (in lesser amounts than in women), it also has its biological effects (anti-inflammatory, antioxidant activity, and participation in the synthesis of neurohormones). Progesterone could be a tool in hormonal modulation and treatment of hair loss in men and treating disorders caused by high activity of 5-AR of both types and system hyperestrogenia (which leads to gynecomastia, prostate hyperplasia, and erectile dysfunction) [19]. Therefore, progesterone deficiency affects the course of AGA in women and, to a lesser extent, in men.

Among the main reasons for a decrease in progesterone are an increase in estrogen and cortisol levels, polycystic ovary syndrome, oral contraceptives and cortisone use, menopause, and vitamin D deficiency.

Prolactin

Prolactin levels also affect the pilosebial structures: on the phases of hair growth and sebaceous gland, affecting the follicle not only directly, but also indirectly, through an increase in the proandrogen content in the adrenal cortex and tissue androgen metabolism [20]. Consequently, hyperprolactinemia can be the cause of not only TE, but also AGA, as well as acne and hirsutism [21, 22]. A decrease in blood prolactin levels to physiological values usually offsets symptoms of hyperandrogenism.

Human scalp hair follicles express prolactin receptors. Exposure of the follicle to high doses of prolactin leads to significant inhibition of anagen and premature development of catagen, along with a decrease in proliferation and increased apoptosis of hair follicle keratinocytes. The significant inhibitory in vitro effect of high doses of prolactin suggested that prolactin acts as an autocrine inhibitor of hair growth [23]. This may explain hair loss in patients with high prolactin levels. Hyperprolactinemia is one of the possible causes of TE in women in the postpartum period [2].

Thyroid Hormones

The thyroid diseases accompany more than half of alopecia cases. The main functions of thyroid hormones are the maintenance of basic metabolism and the regulation of tissue respiration: they increase general metabolism, oxygen consumption and heat production in tissues. It has been shown that thyrotropin-releasing hormone (TRH) acts as an inducer of hair growth and pigmentation [24, 25]; TRH and thyroid-stimulating hormone are powerful promoters of mitochondrial activity and regulators of keratin expression [25], and triiodothyronine and tetraiodothyronine stimulate hair growth by regulating the function of stem cells of the dermal papilla and prolonging anagen [26]. Working mainly at the level of the cell nucleus, they can directly affect processes in the mitochondria and the cell membrane, stimulating RNA formation and leading to stimulation of protein synthesis, which is manifested by both growth and differentiation reactions [25]. Since thyroid hormones affect the growth and differentiation of tissues, the metabolism of many substrates, vitamins, hormones, oxygen consumption, protein synthesis, mitosis, they are of great importance for the formation and growth of hair.

Hypothyroidism occurs ten times more often in women than men. With hypothyroidism, hair is dry, dull, coarse, brittle, and TE, growth retardation, loss of lateral areas of the eyebrows (madarosis) develop. With a genetic predisposition, AGA may occur, and the probable development mechanism involves a decrease in SHBG and an increase of free androgens in plasma [27, 28].

The most common symptoms of hyperthyroidism are systemic, not cutaneous, and are caused by the state of hypermetabolism. TE is observed in 20–40% of cases, and axillary hair loss in 60%. The severity of hair loss does not correlate with the severity of thyrotoxicosis. The hair itself is thin, soft, straight, and not amenable to permanent waving. It should be borne in mind that hair loss can result from side effects of drugs used for treatment (carbimazole, methyluracil, levothyroxine, lithium, amiodarone, etc.) [1, 29].

D-Hormone

The outlook on vitamin D has expanded significantly in recent decades. In terms of its chemical structure, metabolic characteristics and interaction with nuclear receptors, vitamin D has more similarities with steroid hormones than with vitamins, which is why it is called D-hormone in many publications [30, 31]. The hormone-active form of vitamin D reportedly acts as a regulator of a number of enzymes involved in the metabolism of steroid hormones: both adrenal and sex hormones [32, 33].

In experiments on animals, on cell cultures and in vivo, it was shown that the vitamin D receptor gene is expressed in ovarian tissues, modulating the steroidogenesis pathway in granulosa cells, which can lead to improved follicular development and maturation [31,

34]. The expression of these genes in keratinocytes is necessary for the regulation of the hair follicle cycle, and vitamin D deficiency leads to impaired epidermal differentiation and regulation of hair growth [35, 36]. It was shown that alopecia develops in mice and humans due to the inactivation of vitamin D receptors [2, 37].

It was found that the biologically active form of vitamin D — 1,25(OH)2D — stimulates the production of progesterone, estrone and, in synergy with insulin, increases the production of estradiol by 60% [38]. In autoimmune diseases, vitamin D stimulates apoptosis of immune cells, inhibits NO production, reduces T-helper tissue infiltration and T-cell activation, and inhibits the maturation of antigen-presenting cells, thus possessing a powerful immunomodulatory effect [39]. Therefore, vitamin D may be a defense factor in some autoimmune diseases, including alimentary and fibrotic alopecia [40]. In particular, in patients with alopecia areata, the vast majority of cases involve a critically low level of 25(OH)D (6 to 15 ng/l using liquid chromatography and tandem mass spectrometry). In patients with fibrotic forms, the correlation is not so obvious. The study conducted by Aksu Ceman, et al. (2014) showed that vitamin D deficiency is detected in 91% of patients with alopecia areata and correlates with the severity of the disease [41].

A meta-analysis of recent studies showed that vitamin D deficiency plays an important role in the pathogenesis of irreversible alopecia — TE, AGA, alopecia areata: most studies showed a decrease in serum vitamin D concentration in patients with various forms of alopecia compared with control groups [42].

Growth Hormone

Growth hormone affects the growth and differentiation of cells, playing a role in the development of hair follicles and hair growth. It was found that insulin-like growth factor 1 (IGF-1) is produced in the dermal papillae, and the presence of matrix RNA of the IGF-1 receptor in keratinocytes has been proven. IGF-1 in the presence of insulin is believed to induce hair growth by stimulating the proliferation of hair follicles and inhibiting apoptosis [43]. For example, hypertrichosis is observed in acromegaly [44].

In Laron's syndrome (mutation in the IGF-1 encoding gene), the hair is thin, with a significantly shorter growth phase [45]. Growth hormone enhances the effect of androgens on hair growth in areas of secondary sexual characteristics. Therefore, boys with growth hormone deficiency require five times more testosterone to induce axillary hair than hypogonadal boys with a sufficient amount of it. The effects of growth hormone are probably mediated by insulin, similar to growth factor 1 [43, 46].

Insulin

The anabolic effects of insulin have a positive effect on prolonging the hair growth phase (similar to growth hormone). In particular, its dose-dependent stimulating effect was shown in the in vitro study [43], but its ability to initiate type-2 5-AR activity aggravates the course of AGA in the presence of genetic predispositions.

The development of hyperinsulinemia (insulin resistance) intensifies glycation mechanisms (oxidation of substrates by glucose acting as a free radical), which leads to an increase in oxidative stress at the cellular level, while maintaining inflammation in the perifollicular zone and contributing to diffuse hair loss. The course of AGA worsens as the blood insulin level increases since insulin has a stimulating effect on 5-AR, and, therefore, the level of DHT increases [47]. Therefore, through the stimulation of 5-AR, hyperinsulinemia promotes the development of AGA in genetically sensitive individuals with DHT, and through the development of inflammation and oxidative stress in combination with comorbidity, it can trigger diffuse hair loss.

There are numerous studies showing the relationship between metabolic syndrome (MS) and AGA in both men and women [62]. The early onset of AGA in young men indicates, among other things, excessive activity of 5-AR and the development of related conditions in the future (erectile dysfunction, prostate hyperplasia); a significant relationship between AGA and coronary disease was also found. In young men with MS and AGA, total cholesterol, blood pressure, and insulin resistance index are significantly higher than in men without AGA [48]. It is well known that insulin resistance and MS in women have a clear association with polycystic ovary syndrome, which is the most common cause of hyperandrogenism, accompanied by anovulation. Starka L., et al. (2005) suggested that the combination of early AGA and insulin resistance can be a male analogue of polycystic ovary syndrome [49].

In addition, according to Cannarella R., et al. (2020), a hormonal profile similar to that of polycystic ovary syndrome (PCOS) and characterized by a decreased level of follicle-stimulating hormone (FSH) and sex hormone binding globulin (SHBG), increased levels of LH, androstenedione and 17α-hydroxyprogesterone (17α OHP), as well as hypertension, insulin resistance, and weight gain, is also characteristic of men with early onset of AGA [50]. It is noteworthy that all patients with early AGA had a significantly higher body mass index (BMI) and seru, 17 α-hydroxyprogesterone level compared with the control group ($p < 0.05$). The authors report a tendency to an increase in dehydroepiandrosterone sulfate (DHEA-S), a decrease in the level of total testosterone, as well as a higher percentage of sperm apoptosis compared with the control group ($p < 0.05$) [50]

Androgenetic Alopecia (AGA)

AGA is usually divided into male type and female type hair loss. Androgen-dependent zones (forehead, crown, and, in some cases, temporal zones) are identified on the scalp skin, where the amount of 5-AR and DHT is significantly higher. Despite the similarity of mechanisms in the development of AGA in both sexes, hair loss in women is characterized by less pronounced zonality, which is associated with greater aromatase activity in the scalp skin and a large number of estrogen beta-receptors [51, 52].

It is already established that 287 genes are responsible for the development of AGA, i.e., polygenic multifactorial inheritance takes place. However, the main gene is located on the X chromosome [17]. Polymorphism of one of the two main hair loss susceptibility genes in men — the androgen receptor gene EBA2R on the X chromosome — is associated with the early onset of AGA [11]. The role of aromatic compounds CYP19A1 genes has been suggested but not confirmed [6].

AGA in both men and women should raise concern over the development of metabolic syndrome, and coronary disease. Possible mechanisms explaining the relationship between these conditions are the presence of 5-AR and receptors for DHT in blood vessels [6, 53]. Studies have confirmed a significant relationship between body mass index, systolic and diastolic blood pressure, levels of aldosterone, cholesterol, triglycerides, glucose, fasting insulin and AGA. MS was observed significantly more often in patients with AGA — in 60% of men and 48.6% of women (12.5% and 8.1% without AGA, respectively, $p < 0.0001$) Patients with AGA also have more significant atheromatous plaques [54, 55].

A 2020 case-control cross-sectional study by Jingwen Ma et al. showed the following results: men with AGA (n = 1,312) had a higher mean uric acid level (6.25 mg/dl versus 5.97 mg/dl; $p < 0.001$) and a higher prevalence of hyperuricemia (25.0% versus 15.6%; $p < 0.001$) than men without AGA (n = 2,624). A significant relationship between the severity of AHA and hyperuricemia was not demonstrated ($p = 0.295$) [56]

Figure 1. *Androgenetic alopecia (female-type hair loss)*

In a population-based prospective cohort study, the relationship between the mortality rate from diabetes mellitus (DM) and cardiovascular diseases and the severity of AGA was evaluated in 7,252 participants After about five years of follow-up, there was a significantly higher risk of mortality from diabetes and cardiovascular diseases with moderate and severe AGA compared with normal or moderate AGA in men and women after adjusting for age, a family history of diabetes mellitus or cardiovascular disease and MS (adjusted risk ratio: 2.97 and 2.28, respectively). Therefore, despite the different mechanisms of alopecia in men and women, the occurrence of cardiovascular diseases and mortality from them increases in both gender groups [55].

In the event of AGA, men should be wary of the development of metabolic, coronary syndromes, prostate diseases, which underlines the importance of preventive measures, especially in young men and adolescents with AGA.

In the case of AGA in women and adolescent girls, the following should be excluded: polycystic ovary syndrome (the most common endocrine disease in women with AGA [6]), congenital adrenal cortical dysfunction, hyperprolactinemia and other causes of systemic hyperandrogenism (often also accompanied by acne and/or hirsutism, galactorrhea, anovulation), insulin resistance and type 2 DM. As in the case of male hair loss, in women, more than half of the cases do not show any concomitant disease; only a genetic predisposition is detected. In this case, a family history is important.

In the presence of a genetic predisposition, the androgen-estrogen ratio can play a decisive role. However, in clinical practice, among patients diagnosed with AGA, the majority have a reduced/normal level of testosterone in the blood and a normal/undetectable level of DHT. This is because 5-AR is a tissue enzyme, and the conversion of testosterone to DHT occurs directly in the skin (this phenomenon is called "cutaneous hyperandrogenism"). Therefore the measurement of DHT in the blood is of no diagnostic value in the absence of systemic disorder [57].

Sugar-lowering drugs have a positive effect on the course of AGA [24], again proving the relationship between this condition and hyperinsulinemia. Among these drugs, one of the most effective is metformin, since besides regulating carbohydrate metabolism, it has a positive effect on the microvasculature.

In 2017, a hypothesis was published. It summarized a large number of studies and suggested that the thinning

and hair loss characteristic of AGA is a consequence of fibrosis, which develops due to calcification of the microvasculature due to systemic vascular disorders in patients with heart diseases accompanied by hypercholesterolemia and deposition calcium in the walls of the arteries. Fibrosis is usually believed to be a consequence of perifollicular microinflammation as a result of the damaging effect of DHT [58]. However, regardless of the sequence of processes, it was found that metabolic disorders and AGA are associated, and AGA may be one of the markers of MS and cardiovascular risks [59.60].

AGA usually does not reverse itself, and patients need lifelong therapy with topical and systemic drugs after all possible comorbid conditions are excluded, or during treatment.

Telogen Effluvium (TE)

It is a common condition that is not associated with increased sensitivity to DHT, in which there is no progressive thinning of the hair shaft. Alopecia does not have a clear zonality; hair loss occurs evenly throughout the scalp. TE has various causes, mostly endocrine: thyroid diseases (hypo- and hyperthyroidism), Addison's disease and hypopituitarism. The severity of hair loss usually does not correlate with the severity of endocrine disease, and for a long time, may be the only symptom of the disease [6].

In TE management, treatment of the underlying disease is crucial. When the triggering factor is eliminated, complete hair restoration occurs.

Alopecia Areata

Alopecia areata is an immune-mediated disease characterized by sudden onset of hair loss from any area without scarring. This is a fairly common condition without hazard to life.

It has long been known that focal alopecia occurs in various autoimmune diseases, such as rheumatoid arthritis, type 1 diabetes mellitus, vitiligo, systemic lupus erythematosus, thyroiditis, pemphigus vulgaris, pernicious anemia and celiac disease. There is evidence of impaired thyroid function or the presence of autoantibodies to thyroid tissue in 24% of examined children with focal alopecia. In adult patients with focal alopecia, antibodies to thyroid peroxidase were detected in 17.7% of cases.

The meta-analysis of 2019 studied the relationship between alopecia areata and thyroid disease. It was shown that the prevalence of thyroid diseases in patients with alopecia areata is significantly higher than in the control group (odds ratio 3.66; 95% confidence interval 2.90–4.61; p 0.001 [61].

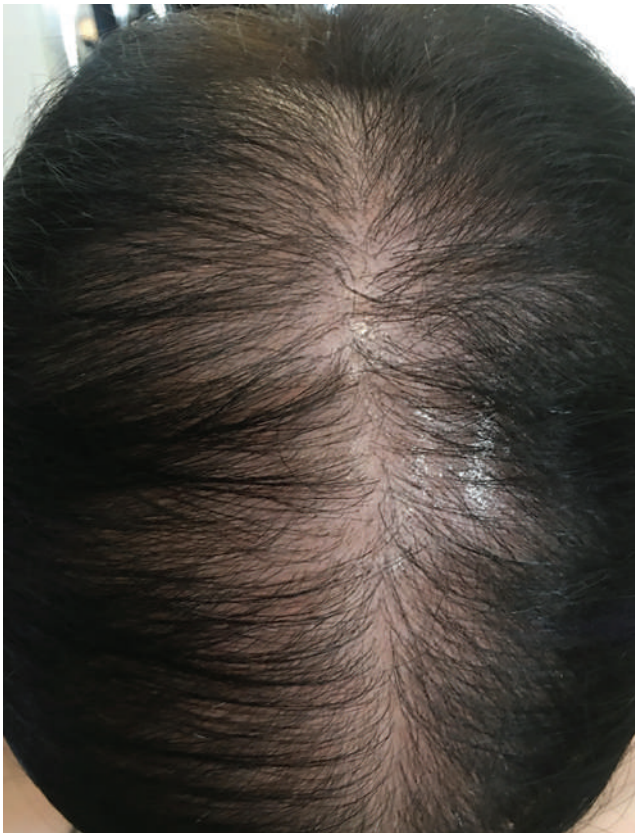

Figure 2. *Androgenetic alopecia in a patient with polycystic ovary syndrome*

Figure 3. *Diffuse telogen hair loss in hypothyroidism*

The overwhelming majority of patients with alopecia areata also have a critically low level of 25 (OH) D [59].

Treatment of alopecia areata is associated with the treatment of the underlying disease (if detected). However, in most cases, it is impossible to detect any causes of alopecia areata, while at the same time. The doctor is required to conduct a screening examination to exclude health-threatening conditions during the initial examination of such a patient.

Conclusion

Alopecia is a very common symptom in the population, and in a number of cases, it is a sign of endocrine diseases. The causes of alopecia and the clinical context of this symptom may be ambiguous in different cases. At the same time, there is no doubt that alopecia as a symptom should be subjected to clinical and diagnostic evaluation and not be ignored in the process of diagnostic search as a "purely age-related" phenomenon.

According to the information presented in the review, the problem under consideration does not always have an exclusively gerontological basis. Therefore, in most cases, the diagnostic search and the choice of therapeutic approach should be multidisciplinary with the participation of an endocrinologist, gynecologist, andrologist, dermatologist/trichologist and other medical specialists.

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Figure 4. *Alopecia Areata, multifocal form*

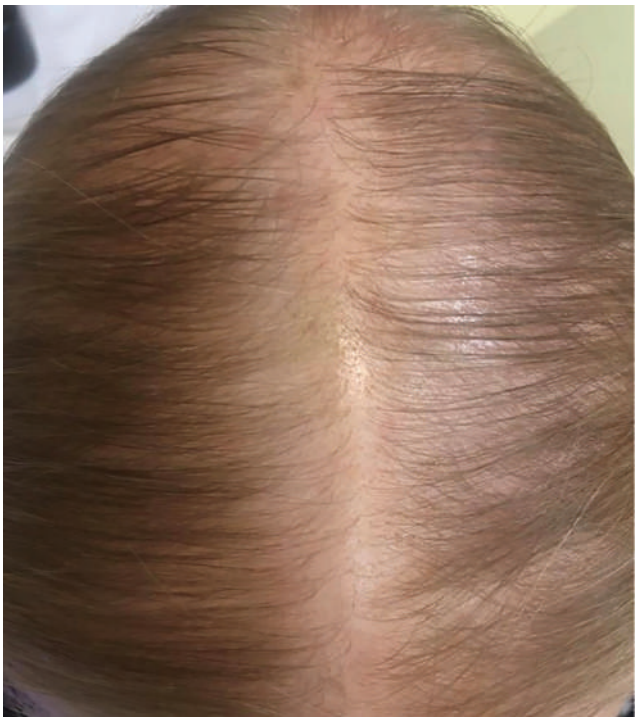

Figure 5. *Alopecia Areata, diffuseform*

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