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Anna Otlewska[1], Paweł Hackemer[2], Fryderyk Menzel[2]

Hirsutism

Hirsutyzm

[1] Chair and Department of Physiology, Wroclaw Medical University, Wrocław, Poland
[2] Department of Urology and Urologic Oncology, University Hospital in Wroclaw, University Hospital in Wroclaw, Wrocław, Poland
Correspondence: Anna Otlewska, Wiązowa 7/1, 53-127 Wrocław, Poland, tel.: +48 500 074 744, e-mail: a.otlewska@gmail.com

Abstract

Hirsutism is defined as excessive hair growth in androgen-dependent areas and it affects about 5–10% of the female population. The majority of cases are either idiopathic or due to polycystic ovary syndrome. Other causes include adrenal glands disorders, congenital adrenal hyperplasia as well as adrenal and ovarian tumours and some medications. The Ferriman–Gallwey score is used to diagnose hirsutism. However, it should be noted that the assessment of the severity of hirsutism using this score is subjective. A thoroughly collected medical history and a detailed physical examination supplemented with laboratory and imaging diagnosis plays an important role in the diagnostic process. It is important to differentiate hirsutism from hypertrichosis, which is not associated with hyperandrogenaemia. Increased androgen levels can also cause other complications in women, such as masculinisation of the external genital organs, male-pattern hair loss, deepening of voice. The treatment uses pharmacotherapy and mechanical methods for excess hair removal. It should be noted that excessive hair in women may also have psychosocial consequences.

Keywords: hirsutism, polycystic ovary syndrome, idiopathic hirsutism, congenital adrenal hyperplasia, Ferriman–Gallwey score

Streszczenie

Hirsutyzm polega na występowaniu nadmiernego owłosienia w okolicach androgenozależnych i dotyczy około 5–10% populacji kobiet. Za większość jego przypadków odpowiadają zespół policystycznych jajników oraz hirsutyzm idiopatyczny. Do pozostałych przyczyn należą: choroby nadnerczy, przede wszystkim wrodzony przerost nadnerczy, a także guzy nadnerczy i jajników oraz niektóre leki. Do rozpoznawania hirsutyzmu wykorzystuje się skalę Ferrimana–Gallweya. Trzeba jednak pamiętać, że ocena nasilenia hirsutyzmu przy wykorzystaniu tej skali ma charakter subiektywny. Istotną rolę w procesie diagnostycznym odgrywają dokładnie zebrany wywiad i dokładnie przeprowadzone badanie przedmiotowe, uzupełnione diagnostyką laboratoryjną i obrazową. Ważne jest różnicowanie hirsutyzmu z hipertrichozą, w przebiegu której nie obserwuje się hiperandrogenemii. Podwyższone stężenie androgenów może prowadzić także do innych powikłań u kobiet, takich jak: maskulinizacja zewnętrznych narządów płciowych, łysienie typu męskiego, obniżenie tembru głosu. W leczeniu wykorzystuje się farmakoterapię oraz mechaniczne metody usuwania nadmiernego owłosienia. Występowanie nadmiernego owłosienia u kobiet może mieć również konsekwencje psychospołeczne.

Słowa kluczowe: hirsutyzm, zespół policystycznych jajników, hirsutyzm idiopatyczny, wrodzony przerost nadnerczy, skala Ferrimana–Gallweya

INTRODUCTION

Hirsutism is defined as excessive terminal hair growth in areas where it is typically seen in men[1,2]. It is estimated that about 5–10% of women are affected[3,4]. Hirsutism may have a negative impact on the well-being of patients[5], reduce their quality of life[6], cause anxiety and depression[7,8], and even lead to social withdrawal[9].

In women, androgens are produced in the ovaries and the adrenal glands. These include: testosterone, androstenedione, dihydrotestosterone, dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS). DHEAS is mainly produced in the adrenal glands[10]. It has a slight androgenic activity[11]. Other hormones are produced by both mentioned endocrine glands[10]. Testosterone is produced via peripheral conversion from androstenedione (50%) and by the ovaries and adrenals (50%)[12]. About 98–99% of testosterone is bound to proteins, while the remaining 1–2% is free testosterone, which is the active form of the hormone[13]. Androstenedione is produced in the ovaries and adrenals in similar proportions. It is produced from DHEA and 17-hydroxyprogesterone. The hormone shows poor androgenic activity[11,14].

Dihydrotestosterone, which is derived from conversion of testosterone by 5α–reductase, is the most active form of androgens[1].

At this point, the sex hormone binding globulin (SHBG) should be mentioned. This protein transports androgens, mainly testosterone, in the blood. Furthermore, it binds estrogens, DHEA and dihydrotestosterone. Therefore, the levels of free serum hormones depend on the level of SHBG[15]. The following factors play a crucial pathogenetic role in hirsutism: androgen levels, hair follicle sensitivity to androgens, and local activity of 5α-reductase[16].

DIAGNOSIS

Hirsutism is diagnosed based on the Ferriman–Gallwey score (FG score). The tool is used to quantify hair growth in nine androgen-dependent areas[3]. The following body areas are evaluated using the FG score: upper lip, chin, chest, upper abdomen, lower abdomen, upper back, lower back, arms and thighs[17]. A score of 0–4 is assigned to each area examined, based on the density of hair[18]. A score of 8 or higher is regarded as indicative of hirsutism[5].

HYPERANDROGENAEMIA

Increased androgen levels may also induce seborrhoea, acne, androgenetic alopecia[1], menstrual disorders[19], impaired libido and fertility as well as deepening of voice and clitoral hypertrophy[20].

CAUSES OF HIRSUTISM

The majority of cases (95%) of hirsutism are either idiopathic or due to polycystic ovary syndrome (PCOS)[5].

Literature data shows that PCOS may affect 4–12% of women of childbearing age[21]. The Rotterdam criteria are used for diagnosing PCOS. The syndrome is diagnosed if two of the following criteria are met: abnormal menstrual cycle in the form of amenorrhoea or oligomenorrhoea, clinical or laboratory indices of hyperandrogenisation and polycystic ovaries on ultrasonography[21,22]. Up to 60% of women with PCOS may develop hirsutism[23]. The syndrome may be accompanied by other disorders, such as insulin resistance, overweight, obesity[23,24], and other symptoms of hyperandrogenism: male-pattern hair loss, acne or clitoral hypertrophy[25]. PCOS can also lead to infertility[23]. Talaei et al. showed a positive correlation between hirsutism and insulin resistance[26]. PCOS is diagnosed after puberty[27].

Idiopathic hirsutism (IH) may account for 5–15% of cases[28]. IH is diagnosed in women with normal androgen levels, menstrual cycles and ovaries[29]. It may be caused by increased 5α-reductase activity, androgen receptor gene polymorphism or increased hair follicle sensitivity to androgens[26]. Onset of IH occurs after puberty, with slow progression[13].

Increased production of androgens may be caused by adrenal gland disease: congenital adrenal hyperplasia, most often caused by 21-hydroxylase deficiency[30], hormonally active adenomas and adrenal carcinomas[31] or ovarian tumors[32].

Congenital adrenal hyperplasia caused by enzymatic deficiency impairs cortisol synthesis, which consequently leads to increased levels of adrenocorticotropic hormone (ACTH), which in turn stimulates adrenal glands, inducing their hypertrophy[33]. In the most common form of congenital adrenal hyperplasia, resulting from 21-hydroxylase deficiency, increased levels of 17-hydroxyprogesterone are observed. Additionally, the ACTH test, which stimulates an increase in the elevated hormone, is used in the diagnosis[34]. It should be also noted that hirsutism may be caused by non-classical form of congenital adrenal hyperplasia, which may manifest at different ages[35].

High testosterone levels (>200 ng/dL or 2 μg/mL) may suggest the presence of a virilising tumour[36], while increased DHEAS may indicate adrenal origin of androgens. A dexamethasone suppression test is used for differential diagnosis. Reduced DHEAS levels during the test indicate adrenal hypertrophy, while the lack of suppression indicates adrenal tumour[37]. A suspicion of virilising tumour may be also raised in the case of rapidly progressing hirsutism[38] accompanied by masculinisation[37]. Ovarian cancer accounts for 1% of hirsutism cases. Androgen-secreting ovarian tumours include gonadal tumors and Leydig and Sertoli cell tumours[12].

It is worth noting that decreased serum SHBG levels increase free serum testosterone levels. Reduced serum SHBG levels may be due to insulin resistance, obesity, acromegaly, hypercortisolism, hypothyroidism and the use of anabolic steroids[15].

Excessive hair growth may be also caused by pharmacotherapy, e.g. oral contraceptives, danazol, diazoxide, L-thyroxine[39]. Hirsutism may also develop in the course

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of steroid therapy, which is used to treat various diseases[40,41]. A small proportion of hirsutism cases may be caused by acanthosis nigricans[28], i.e. hyperpigmentation of the skin combined with insulin resistance, obesity and diabetes mellitus[16]. Furthermore, hirsutism may be due to hyperprolactinaemia[39].

Excessive hair growth in the perimenopausal period is a result of decreased estrogens, leading to altered androgen/oestrogen ratio[10,42].

DIAGNOSIS

A thorough medical history, including patient's age at which excess hair growth occurred, whether it had a sudden or gradual onset[13] as well as pharmacotherapy used and menstrual cycles, is of great importance for the diagnosis. Also, obstetric history as well as data on the presence of acne, hair loss or any additional, coexisting symptoms should be verified[28]. In addition to a thoroughly collected medical history, a full physical examination is also important[13]. Unfortunately, the assessment of hair growth severity is subjective, with differences between the grading performed by the patient and the one performed by the doctor[9].

The diagnosis of the causes of hirsutism is based on hormonal tests: testosterone, prolactin and 17-hydroxyprogesterone levels, thyroid function[43], adrenocorticotropic axis, the luteinizing hormone/follicle-stimulating hormone (LH/FSH) ratio, and the levels of other androgens: DHEAS and androstenedione. The diagnostic process may be supplemented with diagnostic imaging: abdominal and pelvic ultrasonography, computed tomography or magnetic resonance imaging[13].

HYPERTRICHOSIS

Hirsutism should be differentiated from hypertrichosis, which is a condition that causes excessive, androgen-independent hair growth. Therefore the disease is not associated with excess androgens. It may be caused by genetic factors, certain diseases, such as porphyria, anorexia, malnutrition and hypothyroidism[36]. Hypertrichosis may be also induced by drugs, such as L-thyroxine, phenytoin, penicillamine[39], inhibitors of epidermal growth factor receptor (EGFR)[44].

TREATMENT

The treatment of hirsutism is limited to pharmacotherapy and mechanical methods. Oral contraceptives are the primary treatment strategy used in the disease. They increase SHBG levels and inhibit androgen synthesis[43]. Metformin, which increases sensitivity to insulin and may reduce serum androgen levels, is an important agent used in the management of hirsutism[25]. Other drugs include antiandrogens and androgen inhibitors[45]. Flutamide, spironolactone, and finasteride are examples of antiandrogens[46]. However, due to their teratogenic effects, it is necessary to use contraception while taking these medications[43,47]. Eflornithine may be also used in the local treatment of hirsutism, in the case of excess facial hair growth[48]. Mechanical techniques for excess hair removal include electrolysis, laser hair removal and photoepilation[43]. It is believed that weight loss in obese women with PCOS may reduce the severity of hirsutism[49]. The treatment of congenital adrenal hyperplasia involves the use of glucocorticoids[50].

CONCLUSIONS

As described in the paper, hirsutism may develop in the course of various diseases. Therefore, a thorough evaluation of its causes, based on detailed medical history, physical examination and additional tests, is crucial. Hyperandrogenaemia leading to hirsutism may additionally contribute to other disorders, often having serious consequences. Infertility is one of the most serious consequences of PCOS, which is the most common cause of hirsutism. Therefore, the problem of excess hair growth in female patients should not be underestimated as it is not just a cosmetic defect, but a sign of a more serious condition.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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