Hirsutism

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Abstract

Hirsutism is a common endocrine disorder affecting 5–10% of women of reproductive age and is commonly associated with acne and oily skin. It may be a source of social embarrassment and can negatively affect quality of life. A thorough history, physical examination and selected laboratory evaluations will confirm the diagnosis. This article reviews various causes and management of hirsutism. The most common cause of hirsutism is polycystic ovary syndrome, accounting for three out of every four cases. Pharmacologic interventions can suppress ovarian or adrenal androgen production and block androgen receptors in the hair follicle. Hair removal methods and lifestyle modifications may improve the therapeutic response. Considering the long life cycle of a hair follicle, prolonged treatment with pharmaceutical agents is required to produce improvement in hirsutism.

Keywords hirsutism; hyperandrogenism; PCOS

Introduction

Hirsutism is excess terminal hair that commonly appears in a male pattern in women. Although hirsutism is generally associated with hyperandrogenemia, one-half of women with mild symptoms have normal androgen levels. The most common cause of hirsutism is polycystic ovary syndrome (PCOS), accounting for three out of every four cases. In patients whose hirsutism is not related to medication use, evaluation is focused on testing for endocrinopathies and neoplasms, such as PCOS, adrenal hyperplasia, thyroid dysfunction, Cushing syndrome, and androgen-secreting tumours. Further workup is guided by history, physical examination, and may include thyroid function tests, prolactin level, 17-hydroxyprogesterone level, and corticotropin stimulation test. Treatment includes mechanical hair removal and pharmacologic measures. Shaving is effective but needs to be repeated often. Evidence for the effectiveness of electrolysis and laser therapy is limited. In patients who are not planning a pregnancy, first-line pharmacologic treatment should include oral contraceptives. Topical agents, such as eflornithine, may also be used. Treatment response should be monitored for at least six months before making adjustments.

Pathophysiology

Androgens, including testosterone, dihydrotestosterone and their prohormones dehydroepiandrosterone sulphate (DHEA-S) and androstenedione, are the key factors in the growth and development of terminal hair, also known as sexual hair. Hair in different areas of the body demonstrates varying levels of androgen sensitivity, depending mostly on local sensitivity of androgen receptors and 5-α-reductase activity levels. Androgens act on sex-specific areas of the body, converting small, straight, fair vellus hairs to larger, curlier, and darker terminal hairs. Hirsutism develops in women when there is excessive growth of terminal hair in sex specific areas, typically due to androgen excess. Around 70%–80% of women with androgen excess manifest hirsutism. Excessive sexual hair may be accompanied by signs of *virilisation*; male-pattern alopecia, deepening of the voice, clitoromegaly and increased muscle bulk. When present, virilisation indicates an underlying condition associated with moderately to severely elevated androgen levels.

Epidemiology

Hirsutism occurs in approximately 7% of women of reproductive age. The extent of terminal hair varies by ethnic background and the method used to evaluate it. Women of Asian background have less body hair, as compared with southern European women. Among American women (white and black), the prevalence of hirsutism, as assessed by a standard score, is 20%.

Aetiology

Based on the aetiology (Table 1), hirsutism can be divided into the following two broad categories, with approximately 50% of cases falling under each:

1. Increased local sensitivity to androgens or increased local conversion to dihydrotestosterone
2. Increased androgen levels

Diagnostic approach

Hirsutism is usually first noted in late teenage years and tends to gradually get more severe as the woman gets older. Hirsutism can involve a single site or multiple sites. A comprehensive history and physical examination can narrow the diagnosis of the underlying condition. Hormonal studies and imaging are typically used for patients with moderate to severe hirsutism.

History

The following features should be elicited from the history as they may indicate the possible causes of hirsutism.

1. Onset: rapid progression of hair growth may be due to androgen-secreting neoplasia, particularly when associated with virilisation (e.g., male-pattern alopecia, deepening voice, clitoromegaly, increased muscle bulk).
2. Age: development of excessive coarse hair after the fourth decade of life suggests ovarian hyperthecosis and malignancies.
3. Presence of virilisation: indicates high levels of androgens and raises suspicion of androgen-secreting neoplasia.
4. Family history: presence of hirsutism in other family members suggests a genetic component as well as idiopathic hirsutism.
5. Use of medications: use of androgenic medications (anabolic steroids, danazol, oral contraceptives with androgenic progestins) may be associated with excessive hair growth.
6. Menstrual cycles: irregularity (particularly oligomenorrhoea) may be due to anovulatory cycles in PCOS, non-classic congenital adrenal hyperplasia (CAH), or hyperprolactinaemia.

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Causes of hirsutism and their diagnostic clues

Cause of hirsutism	% of cases	Diagnostic clues
PCOS	72–82	Irregular periods Normal to elevated androgens Polycystic ovaries on scan Increased waist: hip ratio Sub-fertility Insulin resistance Acanthosis nigricans
Idiopathic hyperandrogenemia	6–15	Normal periods Elevated androgens Normal ovaries on scan No other identifiable cause
Idiopathic hirsutism	4–7	Normal periods Normal androgens Normal ovaries on scan No other identifiable cause
Adrenal hyperplasia	2–4	Family history of CAH High risk Ethnic group: Ashkenazi Jews (3.7%), Hispanics (1.9%), and Yugoslavians (1.6%) Classic form: ambiguous genitalia Nonclassic, late-onset form: menstrual dysfunction, oligoanovulation, infertility Elevated 17-hydroxyprogesterone
Androgen-secreting tumours	0.2	Rapid onset and progression of hair growth, Virilisation (e.g. male-pattern alopecia, deepening voice, clitoromegaly, increased muscle bulk). Early morning total testosterone level >6.94 nmol/L (>200 ng/dL) Palpable abdominal or pelvic mass
Cushing syndrome	Rare	Central obesity, facial plethora, purple skin striae, proximal muscle weakness, acne, Hypertension Impaired glucose tolerance Elevated 24-hour urine free or salivary cortisol
Hyperprolactinemia	Rare	Galactorrhoea, amenorrhoea, infertility, elevated prolactin level
Thyroid dysfunction	Rare	Abnormal thyroid Function Test (TFT)
Iatrogenic hirsutism	Uncommon	Medication such as anabolic steroids, testosterone, danazol, cyclosporine, sodium valproate and phenytoin

Table 1

7. Reproductive history: infertility may be associated with PCOS, non-classic CAH, or hyperprolactinaemia.

It is important to differentiate true hirsutism from hypertrichosis, a condition of excessive hair growth in non-male pattern distribution, which is of hereditary origin or occurs following use of certain medications (glucocorticoids, phenytoin, minoxidil, cyclosporine).

Physical examination

A modified version of the Ferriman-Gallwey visual scale is the most commonly used grading system for diagnosis and follow-up of hirsutism. The scale assesses nine areas of the body and assigns a score from 0 (absence of hair) to 4 (extensive hair growth). In non-affected women, the score is typically under 8.

Acanthosis nigricans or PCOS, particularly when associated with a family history of type 2 diabetes mellitus, suggests insulin resistance.

The presence of galactorrhoea may be associated with hyperprolactinaemia, particularly in nulliparous women.

Signs of virilisation indicate moderately to severely increased androgen levels.

Obesity is associated with increased androgen production and clearance rates. A pattern of fat distribution of truncal obesity associated with a dorsocervical fat pad and other cushingoid features (purple striae, thin skin, bruising, facial plethora) indicates that Cushing's syndrome should be considered.

Palpation of an abdominal or pelvic mass in a hirsute woman is suggestive of androgen-secreting neoplasia.

The most common cause of hirsutism is PCOS, accounting for three out of every four cases. Table 1 outlines the various causes of hirsutism and their diagnostic clues.

Investigation

Some authors recommend no investigation for patients with mild hirsutism (Ferriman-Gallwey score 8–15) and regular menses because these patients usually have idiopathic hirsutism.

Figure 1 outlines an approach to evaluation of hirsutism.

For patients with moderate to severe hirsutism (score >15), careful investigation is recommended, as there is a high likelihood of an identifiable cause. In these patients, hormonal evaluation is recommended, as follows.

Testosterone is the most important androgen to be measured. Measurement of total testosterone, using immunoassays, has a low sensitivity for diagnosing PCOS. High (e.g., with the use of oral contraceptive pills) or low (e.g., in insulin resistance or obesity) concentrations of *sex hormone binding globulin* (SHBG) may affect total testosterone values. Measurement of SHBG enables calculation of the *free androgen index* (*FAI*), which will be elevated in hyperandrogenaemia caused by PCOS. To calculate the FAI, the total testosterone concentration is divided by the SHBG concentration and multiplied by 100. Total testosterone measured by tandem mass spectrometry is being increasingly used. This has higher specificity and less interference with other androgens, such as androstenedione and DHEAS.

Elevated testosterone concentrations are seen in 60%–80% of women with PCOS. Very high levels of total testosterone concentration may be caused by an ovarian or adrenal tumour. Elevated total testosterone concentrations >2 times the upper limit of normal or a history of rapid virilisation are likely to be associated with tumour-associated hyperandrogenism. In such cases, *DHEAS* (secreted mainly by adrenals) and

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