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Fifteen-minute consultation: Approach to the adolescent presenting with hirsutism

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Abstract

Hirsutism, unwanted terminal hair growth in androgen dependent areas, is a common presentation to general paediatricians, dermatologists and endocrinologists. Polycystic ovarian syndrome is the commonest cause but can be challenging to diagnose in young people due to the significant overlap of features with the healthy adolescent population. There are other rare, but important, causes to consider such as nonclassic congenital adrenal hyperplasia and androgen secreting tumours. Hirsutism carries a significant psychological burden for those living with it. This fifteen-minute consultation piece describes the causes of hirsutism, introduces a novel assessment tool, and suggests an approach to investigations and management, including signposting to psychological support.

Competing interests:

None declared

INTRODUCTION

Hirsutism is the growth of excessive terminal hair in females in an adult male distribution.[1] Terminal hair is thicker and darker than small, fair vellus hair. Growth of terminal hair, from vellus hair, is androgen dependent and influenced by plasma androgen levels and hair follicle androgen sensitivity.[1] Hirsutism should be differentiated from hypertrichosis, generalised excess hair growth in non-androgen dependent areas e.g., forearms.[2] Hirsutism is a common condition, estimated to affect 3-20% of adolescent girls[3] with high associated psychosocial morbidity.[1]

WHAT CAUSES HIRSUTISM?

Idiopathic hirsutism, with or without hyperandrogenism, is common, but the commonest cause in adolescents is polycystic ovarian syndrome (PCOS).[3,4] The diagnosis of PCOS is challenging in adolescents due to a considerable overlap with the healthy population as features like acne and irregular menstrual cycles are commonplace. Modified diagnostic criteria should be used.[5] Rarer conditions, including nonclassic congenital adrenal hyperplasia (NCCAH), androgen secreting tumours and other endocrinopathies may present with hirsutism and are important to consider (table 1).[3]

Table 1. Causes of hirsutism in adolescents with the key diagnostic features and supportive investigations.

Aetiology	Relative prevalence in patients with hirsutism	Diagnostic features	Supportive investigations
Polycystic Ovary Syndrome	20-40% in adolescent girls[3]	• Clinical (hirsutism, severe cystic acne) and/or biochemical evidence of hyperandrogenism[4] AND irregular menses*. • Associated but non-diagnostic features include: obesity, insulin resistance (acanthosis nigricans)[4] • Ovarian USS should not be routinely performed until eight years post menarche as the PCO morphology of large multi-follicular ovaries are common in adolescents.[6,7]	• ↑ testosterone (although may be normal) or ↑ FAI (FAI calculation= (total testosterone/ SHBG) x 100) • Diagnosis of exclusion. • Patients with amenorrhoea/ oligomenorrhoea for less than 3 years,[6] who have evidence of hyperandrogenism are "at risk" of PCOS and should be followed up.[4]
Idiopathic hyperandrogenism	10-15% [8]	• No other identifiable cause of elevated androgen levels • Normal menses	• ↑ testosterone or ↑ FAI. • Diagnosis of exclusion.
Idiopathic hirsutism	6-10% [8,9] (half of mild hirsutism)[10]	• Normal androgen levels and menses. • No features of other endocrine disorder. • Often familial or related to ethnicity.[11]	• Normal testosterone. • Diagnosis of exclusion.
Nonclassic CAH	4-14% [3,9]	• Family history of CAH, ↑ risk ethnicity (Ashkenazi Jew, Hispanic, Slav) • Premature pubarche (before age of eight years), • Accelerated growth,	• Indicative USP • ↑ 17OHP, early morning in follicular phase • 17OHP level >30 nmol/L basal or after Synacthen stimulation diagnostic.[12]

		• Signs of virilisation (clitoromegaly, increased muscle mass, voice change).	• 17OHP levels >6 nmol/L in prepuberty.[12]
Androgen secreting tumours	0.2% (half of which are malignant)[3]	• Evidence of virilisation • Rapid onset. • Abdominal/pelvic mass. • Progressive hair growth despite treatment.[3]	• Raised testosterone (>5 nmol/L or >2-3x ULNR). • Indicative USP.[3] • ↑ DHEAS (>19 mmol/L) (adrenal source). • ↑ androstenedione (ovarian source). • Adrenal or ovarian mass on USS or MRI.[3]
Other		• Other symptoms likely to predominate: • Cushing syndrome: Lack of height gain despite ↑ weight, central obesity, plethoric facies, proximal muscle weakness. • Pregnancy: Amenorrhoea, nausea, fatigue. • Hyperprolactinaemia: galactorrhoea, amenorrhoea, features of space occupying lesion e.g., bitemporal hemianopia	• Urinary cortisol, late night salivary cortisol, dexamethasone suppression test.[13] • ↑ urine or plasma beta HCG. • ↑ prolactin (exclude macroprolactin).[14]
Drugs		Access to drugs including: • Anabolic steroids, testosterone, valproate.[10]	• USP

* Irregular menses are normal in the first years after menarche although cycles <19 days or >90 days are considered abnormal.[2]

Abbreviations: 17OHP, 17-hydroxyprogesterone; CAH, congenital adrenal hyperplasia; DHEAS, dehydroepiandrosterone sulphate; FAI, free androgen index; HCG, human chorionic gonadotropin; MRI, magnetic resonance imaging; NCCAH, nonclassic congenital adrenal hyperplasia; SHBG, sex hormone binding globulin; ULNR, upper limit normal range; USP, urinary steroid profile; USS, ultrasound scan.

ASSESSMENT

Adolescents presenting with excess hair growth require a thorough evaluation. We have developed a clinical assessment proforma for this purpose (figure 1).

History

"Patient important hirsutism" is any excessive terminal hair growth causing the patient sufficient distress to seek treatment. Consultations should be conducted sensitively, with the clinician proactively assessing the psychosocial impact of the unwanted hair, including the patient's perception of their hair growth and effects on their confidence, self-esteem, relationships, school and activities. It is important to explore the patient (and parent/carer)'s expectations to aid empathic discussion of realistic and achievable treatment outcomes. Detailed history should be sought about the age/stage of puberty at onset and speed of hair growth (prepubertal onset and rapid progression are concerning for androgen secreting tumours).[3] Often patients have removed the hair, so a description of the hair and its distribution will help assess severity and differentiate from hypertrichosis. The efficacy and side effects of hair removal techniques should be noted. Ask appropriate questions to identify features of the differential diagnoses in table 1.

Examination

Hirsutism is typically assessed using the modified Ferriman-Gallwey (mFG) score, with hair growth recorded in nine androgen sensitive areas: upper lip, chin, chest, upper arms, upper back, lower back, upper abdomen, lower abdomen, and thighs. Each area is scored from zero to four: zero denoting absence of terminal hair, one representing minimal hirsutism and four signifying frank virilisation, equivalent to a "hairy" man. A total score of eight is suggested as the threshold for mild hirsutism, 16-24 for moderate and >24 for severe hirsutism.[15] The mFG score has not been validated in adolescents, who may have lower scores due to reduced exposure time to androgens.[6] No standardised cut-offs for different ethnicities have been agreed. It is suggested higher thresholds are used in patients of Mediterranean or South Asian origin and lower scores in those of East Asian heritage (figure 1),[1,10,15] however specific cut-offs have not been validated in adolescents from different ethnicities.[3] The mFG does not account for patients with extensive but localised hair growth. Each body area is equally represented, meaning patients affected by only facial hair growth may not score highly but are likely to experience distress and would benefit from treatment.[1]

Investigations

Investigation of patients presenting with hirsutism should be guided by the clinician's assessment, mFG score, and presence of red flag features of hyperandrogenism or an

endocrinopathy (figure 3). In patients with isolated hair growth or low mFG scores biochemical investigation is usually not required. Most patients will have mild hirsutism and, in the absence of red flag features, require only testosterone and sex hormone binding globulin (SHBG) enabling calculation of the free androgen index (FAI), a surrogate marker of free and therefore active testosterone. There is no universally agreed normal range for FAI so local laboratory cuts off need to be employed. 17-hydroxyprogesterone (17OHP) should be measured in patients with raised testosterone levels or features of NCCAH (table 1).[12] Patients with a moderate-severe mFG score or features of a hyperandrogenic endocrine disorder need a more detailed work-up (figure 3).

MANAGEMENT

If an underlying cause for the hirsutism has been identified this should be treated in the first instance. Thereafter hirsutism management falls into three categories: lifestyle, cosmetic and pharmacological. Exploring patients' expectations is important, discussing with them that no treatment will 'cure' the hirsutism and that pharmacological management can take 6 to 12 months to demonstrate an effect, due to the length of hair growth cycle.[10]

Lifestyle

Lifestyle interventions are particularly useful in patients with PCOS but should be discussed with all patients. If patients are overweight or obese, weight loss strategies should be discussed with signposting to appropriate support e.g. a local community weight management programme.[10] Weight loss of 5-7% body weight can improve testosterone levels, menstrual irregularity, reduce the risk of metabolic sequelae and result in small improvements in hirsutism severity.[4,10] Lifestyle changes are not as effective as pharmacological interventions and should not be used alone.[10]

Providing emotional support by psychological welfare discussions and connecting patients to peers is important. Increased social support has been correlated with higher levels of health related quality of life in patients living with hirsutism.[16] Patients can be signposted to resources such as Changing Faces (https://www.changingfaces.org.uk), a charity supporting people with visible differences, which offers counselling, or Verity (http://www.verity-pcos.org.uk), a charity run by people living with PCOS.

Cosmetic

Cosmetic measures include methods that remove hair shafts from the skin surface, depilation (e.g., shaving or chemical depilation); or methods that remove hairs from above the bulb, epilation (plucking, waxing or threading). A commonly cited myth is that hair regrowth is thicker

or darker after shaving. Hair may appear thicker as a blunt tip is formed rather than the tapered end of uncut hair, but patients can be reassured that no hair removal method causes increased hair shaft diameter or darkening.[10] Cosmetic hair removal is readily available but is temporary and can be painful, cause skin irritation, scarring, folliculitis, or hyperpigmentation, particularly in people of colour.[10] Bleaching is a non-removal alternative generally used on facial hair.

Topical

Eflornithine cream inhibits hair growth in the anagen phase (growing stage) of the hair cycle and is licensed for facial use.[11] Noticeable effects take 6-8 weeks but hair growth returns to pre-treatment levels when stopped and it can cause itching and dry skin.[10]

Longer-lasting hair reduction

Photoepilation and electrolysis are methods of permanently reducing hair counts. Photoepilation, or "laser" treatment, uses light pulses to thermolyse pigmented terminal hair follicles and can reduce hair by 80% after 6 months of treatment.[17] It should be avoided in patients from Mediterranean or Middle Eastern heritage because of potential paradoxical hypertrichosis.[10] Photoepilation is up to 60 times faster than electrolysis, as electrolysis uses a fine electrode to thermolyse each individual hair. It is more painful, limited to smaller areas and not available on the NHS.[17] Funding approval for NHS "laser" therapy is very limited. Private clinics may offer photoepilation but, in our experience, won't accept patients <18 years. Less powerful photoepilation devices are available to purchase for home use but are expensive and not as effective as medical photoepilation devices.[10] Eflornithine cream can be an effective adjunct, facilitating a more rapid response.[10]

Pharmacological

Combined oral contraceptive pills (COCP)

COCPs are first-line treatment for hirsutism, although they are prescribed off-label. They slow hair growth but do not remove existing hair.[10] The oestrogen decreases free androgens by increasing SHBG production, and suppresses luteinising hormone, reducing adrenal and ovarian androgen production. The progestins block androgen receptors and conversion of testosterone to the more potent dihydrotestosterone by inhibition of 5α-reductase.[4] There is no clear evidence for choosing any particular COCP, however third generation progestins e.g., desogestrel, gestodene and norgestimate are "androgen neutral" and are preferred to second generation progestins like levonorgestrel. Antiandrogenic containing COCPs, including cyproterone acetate or drospirenone, improve hirsutism more than other COCPs.[8,10]

Ethinylestradiol containing COCPs are preferred to 17-β-estradiol or estradiol valerate, which are less likely to suppress ovarian androgens due to their lower oestrogen dose.[10] Patients should be made aware of the increased risk of thromboembolism with COCPs and the related symptoms, but reassured that the absolute risk is very small.[8]

Antiandrogens

Antiandrogens are second-line treatments if COCPs are contraindicated, not tolerated or ineffective i.e. six months without improvement.[4,10] They may be used in conjunction with COCPs as part of first-line therapy in moderate to severe hirsutism.[10] Spironolactone and finasteride are the recommended anti-androgens in adolescents, but should be initiated under specialist guidance.[3,10] Spironolactone inhibits the androgen receptor and 5α-reductase.[10] Its antiandrogenic effects are dose dependent and the recommended starting dose is 25mgl.[10] Electrolytes should be monitored due to risk of hyperkalaemia. It should not be used with drospirenone containing COCPs due to the cumulative antimineralocorticoid effect.[10] Finasteride is a partial 5α-reductase inhibitor. Antiandrogens can cause feminisation of a male foetus, and should be prescribed with effective contraception and appropriate counselling.[7] Flutamide is an effective antiandrogen but can be hepatotoxic and not recommended.[10]

Metformin is an insulin sensitiser used in PCOS for its metabolic effects and improvement in menstrual regularity but has negligible effect on hirsutism.[10]

CONCLUSION

Hirsutism commonly affects adolescent girls and necessitates careful assessment and tailored investigation. Management varies depending on the severity, aetiology and individual patient factors. The psychological and social impact of hirsutism should be sought in all and appropriate support offered. Working with patients to understand the chronic nature of hirsutism and likely outcome of the available therapies may improve patient satisfaction.

5 EMQs

1. Which of the following are features of nonclassic congenital adrenal hyperplasia? You may choose more than one answer.
   A. Increased muscle mass
   B. Advanced bone age
   C. Hyponatraemia
   D. Raised 21-hydroxylase
   E. Raised 17-hydroxyprogesterone

2. A 15-year-old patient attends with concerns about dark hairs on her chin and abdomen. You find mild hirsutism on examination. She attained menarche at 11 years old and thinks she has only had two periods in the last year. You suspect she has polycystic ovary syndrome. Which of the following is the most appropriate approach to investigation?
   A. Pelvic ultrasound
   B. No investigations needed, PCOS is a clinical diagnosis.
   C. Testosterone and sex hormone binding globulin
   D. Androgen panel (17OHP, androstenedione, DHEAS and testosterone)
   E. No investigations needed, unable to diagnose PCOS at this age

3. Regarding pharmacological treatment of hirsutism, which statement is the most correct?
   A. Flutamide is a second-line treatment
   B. Oral contraceptive use alone will get decrease existing terminal hair
   C. Metformin is a useful adjunct for the treatment of hirsutism in PCOS
   D. The antiandrogenic effect of spironolactone is dose dependent
   E. The progesterone only contraceptive pill can be used if the combined pill is contraindicated or not tolerated

4. Which of following statements about cosmetic treatments of hirsutism is correct?
   A. Eflornithine cream works by disrupting the telogen, or resting, phase of hair growth
   B. Photoepilation is much faster than electrolysis
   C. Shaving causes hair to grow back thicker
   D. Photoepilation is effective on pale coloured hairs

E. COCPs should be used for at least nine months before another treatment is considered

5. Which of the following may be features of an androgen secreting tumour? You may choose more than one answer.

A. Insidious onset of symptoms

B. Voice change

C. Suppressed DHEAS

D. Raised androstenedione

E. Progression of hirsutism despite treatment

Answers

1. A, B, E
2. C
3. D
4. B
5. B, D, E

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