9 Polycystic Ovarian Syndrome (PCOS)

David Buckley

Key Points

- Polycystic ovarian syndrome (PCOS) occurs in women of child bearing age and causes excess androgen production.
- This can lead to skin, gynaecological, psychological and sometimes general health problems. Long term complications are type 2 diabetes and heart disease.
- It is not essential to demonstrate polycystic ovaries to make the diagnosis of PCOS.
- Treatments are targeted towards the primary gynecological cause and obesity reduction as well as to the secondary skin and metabolic problems.

What to Tell the Patient

- PCOS is a treatable condition.
- Weight loss is important if the person is overweight.
- Oral contraceptives with a relatively high oestrogen and a progesterone can help most of the skin and gynaecological problems associated with PCOS.
- Do not smoke if you are prescribed the pill.

9.1 Introduction

PCOS is a multi-system disease that occurs in women after the menarche and before the menopause which causes excess androgen secretion. Polycystic ovaries can be seen with ultrasound in up to 20% of healthy women [1]. However, the majority of women with polycystic ovaries do not have features of polycystic ovary syndrome (PCOS) and do not require intervention. Prevalence figures vary depending on diagnostic criteria used, but PCOS is thought to affect 5–15% of women of reproductive age [2, 3]. It is probably more common than realised as many cases go undiagnosed or undetected.

9.2 Clinical Features and Diagnosis

Women with PCOS may present with dermatology and gynaecology problems, weight gain, psychological symptoms [1] (mood swings, depression, anxiety, poor self-esteem) or sleep apnoea. PCOS signs and symptoms tend to be more severe in obese patients.

In dermatology, most patients with PCOS present with either acne, hirsutism or female pattern alopecia (androgenic alopecia) (Fig. 9.1a, b). Many of these women may also have weight problems, menstrual abnormalities, and fertility issues.

D. Buckley (✉)
The Ashe Street Clinic, Tralee, Co. Kerry, Ireland
e-mail: info@asctralee.com

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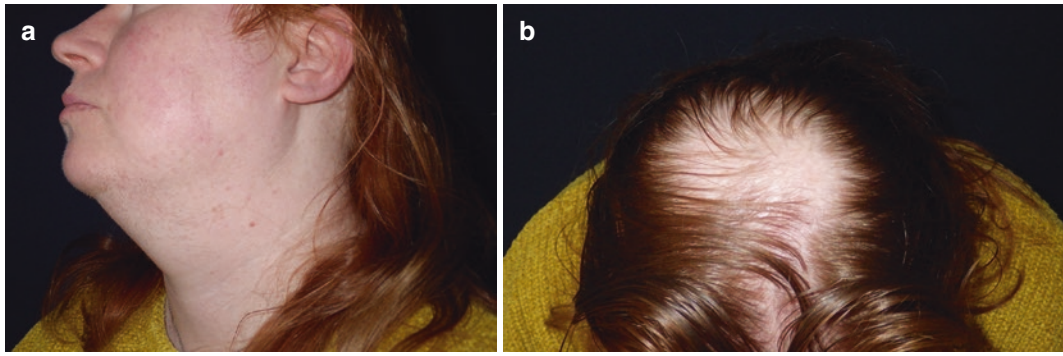

Fig. 9.1 (**a**) Hirsutism in a 33 year-old-female with PCOS who is on spironolactone 100 mg daily. (**b**) Same female with male patterened hair loss and PCOS

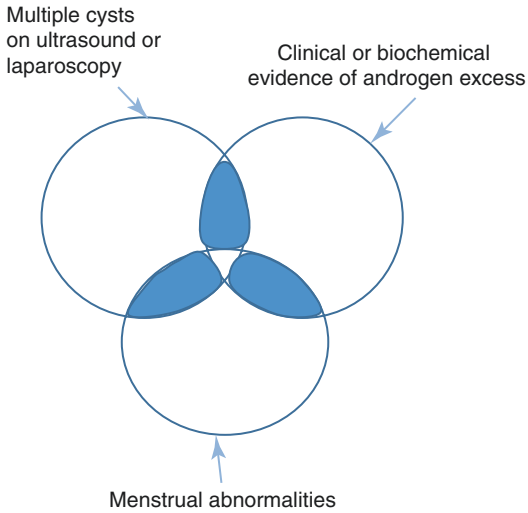

Fig. 9.2 Diagnosis of PCOC (2 out of 3)

Diagnosis of PCOS is based on the presence of any two of the following:

- Polycystic ovaries on ultrasound or laparoscopy.
- Menstrual irregularities (no periods or very occasional periods).
- Clinical and/or biochemical evidence of androgen excess.

(Rotterdam criteria): [3, 4] (see Fig. 9.2)

It is not essential to have cysts visible on ultrasound. Neither is a hormone analysis essential for diagnosis (Table 9.1). For instance, a woman with acne and/or hirsutism with oligimenorrhoea or amenorrhoea may be diagnosed as having PCOS. In this situation, neither an ultrasound nor hormonal analysis needs to be done to confirm the diagnosis.

An elevation of free testosterone in combination with a low sex hormone binding globulin (SHBG) is the most sensitive way to establish the presence of hyperandrogenism. If the total testosterone is normal (in the absence of the oral contraceptive pill), the diagnosis of PCOS is effectively ruled out. The patient needs to be off the OCP for at least 1 month before testing.

Table 9.1 Investigations for women suspected of having PCOS[a]

Full blood count, urea and electrolytes, liver function tests
FSH/LH (LH elevated >10 IU/L, LH:FSH ratio increased (>2), with FSH normal)
Oestradiol
Sex hormone binding globulin (SHBG- reduced)
Free Testosterone: (rased >2.5 nmol/l). If total testosterone is >5 nmol/L, exclude androgen-secreting tumours and congenital adrenal hyperplasia
Random Blood Sugar
HBA1C
Thyroid function tests (TFT's)
Lipid Profile
B12, folate, ferretin
Prolactin
Ultrasound of the ovaries and the adrenals (the presence of cysts does not prove PCOS and cysts do not have to be present to make the diagnosis of PCOS)
Dehydroepiandrosterone sulphate (DHEAS) (for those with severe or rapidly progressive hyperandrogenism)
17-hydroxyprogesterone

[a]Bloods best taken during the first week after menstruation when not on any hormone treatment

Table 9.2 Differential diagnosis for PCOS

Cushing's disease
Later onset congenital adrenal hyperplasia
Androgen secreting tumours (ovary or adrenal)
Ovarian hyperthecosis

Table 9.3 Clues that there may be a more serious cause of androgen excess

Abrupt onset of symptoms
More severe disease
Rapid progression
Older age of onset
Very high serum androgens (testosterone of >5 nmol/l)
Free testosterone level more than double the normal
Signs of virilisation (deep voice, cliteromegaly)

9.3 Differential Diagnosis

Most women with clinical and/or biochemical evidence of androgen excess and menstrual irregularities will have PCOS. However, other more sinister and serious factors can be responsible (Table 9.2).

Some of the signs and symptoms of PCOS can be mimicked by **androgen secreting tumours**. This should be investigated if there is rapid onset of severe acne or hirsutism especially if these problems start in women over the age of 35 (Table 9.3). Deepening of the voice, cliteromegaly, total testosterone of >5 nmol/l or free testosterone level more than double the normal might also give clues to an underlying androgen secreting tumour of the ovary or adrenal gland. Measurement of dehydroepiandrosterone sulphate (DHEAS) should be included for those with severe or rapidly progressive hyperandrogenism to screen for a primary adrenal source, as DHEAS is a marker for adrenal hyperandrogenism. Raised 17 OH progesterone suggests late onset congenital adrenal hyperplasia.

9.4 Pathophysiology

Polycystic ovaries are thought to develop when ovaries are stimulated to produce excessive amounts of male hormones, particularly testosterone. This stimulation is caused by excess LH produced by the anterior pituitary in response to increased gonadotrophin-releasing hormone (GnRH) or through high levels of insulin caused by insulin resistance. High insulin levels also suppress hepatic production of sex hormone-binding globulin (SHBG) leading to higher levels of free circulating androgens, further adding to the hyperandrogenaemia. The underlying endocrine disturbance can exist in the absence of polycystic ovaries. Androgen levels may not correlate with clinical presentation and serum androgen levels may be normal [5].

9.5 Treatment

The first line treatment for all forms of PCOS is diet and exercise to reduce weight in the overweight. Specific treatments should be tailored to the patient's major presenting complaints:

Acne can persist into the thirties or forties in women with PCOS and often responds poorly to oral antibiotic and topical therapies. Acne in PCOS may require long term treatment to prevent relapse (see Chap. 7—acne in women).

If a woman with PCOS and acne is overweight even a 5% drop in weight can help. Topical treatments such as topical retinoid, benzoyl peroxide or azelaic acid gel may help but most women with troublesome acne in PCOS will also need systemic treatment. While they may get some response from oral antibiotics, best results are obtained with hormonal treatments such as an oral contraceptive pill (OCP) with relatively high oestrogen dose and a progesterone with low androgenic action (e.g.:"Yasmin®" or "Cilest®").

"Dianette®" is a popular choice in women with PCOS, as it has a strong anti-androgen (cyproterone acetate) and 35 mcg of oestrogen (0.035 mg ethinylestradiol and 2.0 mg cyproterone acetate) which can be very effective. Results can be slow and can it can take 6 or 12 months before improvements are seen. Relapse is common when the treatment is stopped. "Dianette®" can only be used in women of reproductive age and should be avoided in smokers and those with hypertension, hypercholesteraemia, obesity or a history of

venous thromboembolism (VTE) (see Chap. 7, Table 7.6). All patients on Dianette® need to be warned about the possibility of VTE and be given the warning signs to look out for.

For women who cannot go on an OCP, non hormonal anti-androgens such as spironolactone combined with topical anti-acne treatments may help. Spironolactone acts as an anti-androgen and can help acne, androgenic alopecia and hirsutism. It is teratogenic so effective contraception should be used in women of child bearing age on this drug. It is usually started at a small dose (25 mg/day) and gradually increased to a maximum of 200 mg/day if required and tolerated. It can cause hyperkalemia and the Summary of Product Characteristics recommends that electrolytes should be monitored regularly. Recent research in JAMA suggests that monitoring electrolytes in healthy, young females is not necessary [6].

Some women with more resistant or severe acne may require oral isotretinoin but the relapse rate is higher in women with PCOS (see Chap. 8).

Hirsutism is defined as excessive terminal hair (long, coarse and pigmented) that grows in a male pattern (beard area, lower abdomen and chest) and is more common in women with PCOS (Fig. 9.1a). While traditional methods such as bleaching, plucking, shaving or waxing may help and are safe, many women request a more specific treatment such as the oral contraceptive pill. "Yasmen®" (ethinyl oestradiol 30 + drospirenone) and "Yasminelle®" (ethinyl oestradiol 20 + drospirenone) arrest progression but do not reverse hirsutism. "Dianette®" (ethinyl oestradiol 35 + cyproterone 2 mg) on the other hand gives substantial reduction of hirsutism.

Relapse is almost invariable when stopped, therefore these treatments may need to be taken over a prolonged period. Eflornithine 11.5% cream twice a day ("Vaniqa®") can slow down hair growth but can be slow to work. If there is no improvement after 2 or 3 months the treatment should be stopped. Laser or IPL hair removal can be helpful in women with dark hair and light skin but the success rate is limited in women with PCOS. Laser hair removal should be done after hormonal treatment, on the residual hair and not in patients that have not controlled their excess androgen levels (see Chap. 40).

Female pattern alopecia (diffuse, non-scarring hair loss that presents with prominent thinning of frontal, central, parietal scalp hair) or sometimes **male pattern (androgenic) alopecia** can occur in approximately 22% of women with PCOS [7] (Fig. 9.1b). "Dianette®" or an OCP with low androgenicity are less effective against alopecia than against acne and hirsutism, but will give some improvement of alopecia in 30% of patients. Topical minoxidil ("Regaine®") gives medium regrowth in 15% of patients. Spironolactone or hair transplant may also have to be considered (see Chap. 40).

PCOS is linked with the **metabolic syndrome and hyperinsulemia**. 10% will go on to develop diabetes at some stage, particularly if they are overweight or if there is a positive family history of diabetes. There is also an increased incidence of abnormal lipid profile in women with PCOS. Annual fasting blood sugar and lipids should tested, especially in the overweight or those with a family history suggesting increased risk of cardiovascular disease.

If there is **ologomenorrhoea or amenorrhoea**, women should consider the oral contraceptive pill or the "Mirena®" IUD to give endometrial protection and reduce the risk of endometrial cancer in later life.

Fertility issues, if they arise, are best dealt with by a gynaecologist. Clomiphene can induce ovulation in 75–80% of women but there is a risk of multiple pregnancies. Weight loss and metformin may also improve the chances of conceiving [8].

9.6 Conclusion

PCOS is a common and debilitating condition which mainly affects young women. Early diagnosis and correction of any weight problems are key to successful management. Specific treatments can be targeted towards the primary presenting features such as, dermatology (acne, hirsutism, and alopecia), gynaecology (menstrual irregularities or fertility issues) or metabolic dysfunction.

Patient information resource: "Verity" is a self-help group for women with polycystic ovary syndrome (PCOS). See their website at: www.verity-pcos.org.uk.

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