20.29 Anti-androgen therapy

Mechanism of action	Drug	Dose	Hazards
Androgen receptor antagonism	Cyproterone acetate	2, 50 or 100 mg on days 1–11 of 28-day cycle with ethinylestradiol 30 µg on days 1–21	Hepatic dysfunction Feminisation of male fetus Progesterone receptor agonist Dysfunctional uterine bleeding
	Spironolactone	100–200 mg daily	Electrolyte disturbance
	Flutamide	Not recommended	Hepatic dysfunction
5α-reductase inhibition (prevent conversion of testosterone to active dihydrotestosterone)	Finasteride	5 mg daily	Limited clinical experience; possibly less efficacious than other treatments
Suppression of ovarian steroid production and elevation of sex hormone-binding globulin	Oestrogen	See combination with cyproterone acetate above *or* Conventional oestrogen-containing contraceptive	Venous thromboembolism Hypertension Weight gain Dyslipidaemia Increased breast and endometrial carcinoma

Fig. 20.16 Polycystic ovary. A transvaginal ultrasound scan showing multiple cysts (some indicated by black arrows) in the ovary (highlighted by white arrows) of a woman with polycystic ovary syndrome.

chest hair but are expensive. Eflornithine cream inhibits ornithine decarboxylase in hair follicles and may reduce hair growth when applied daily to affected areas of the face.

If conservative measures are unsuccessful, anti-androgen therapy is given (Box 20.29). The life cycle of a hair follicle is at least 3 months and no improvement is likely before this time, when follicles have shed their hair and replacement hair growth has been suppressed. Metformin and thiazolidinediones are less effective at treating hirsutism than at restoring menstrual regularity. Unless weight is lost, hirsutism will return if therapy is discontinued. The patient should know that prolonged exposure to some agents may not be desirable and they should be stopped before pregnancy.

Turner syndrome

Turner syndrome affects around 1 in 2500 females. It is classically associated with a 45,X karyotype but other cytogenetic abnormalities may be responsible, including mosaic forms (e.g. 45,X/46,XX or 45,X/46,XY) and partial deletions of an X chromosome.

Clinical features

These are shown in Figure 20.17.

Individuals with Turner syndrome invariably have short stature from an early age and this is often the initial presenting symptom. It is probably due to haploinsufficiency of the *SHOX* gene, one copy of which is found on both the X and Y chromosomes, which encodes a protein that is predominantly found in bone fibroblasts.

The genital tract and external genitalia in Turner syndrome are female in character, since this is the default developmental outcome in the absence of testes. Ovarian tissue develops normally until the third month of gestation, but thereafter there is gonadal dysgenesis with accelerated degeneration of oöcytes and increased ovarian stromal fibrosis, resulting in 'streak ovaries'. The inability of ovarian tissue to produce oestrogen results in loss of negative feedback and elevation of FSH and LH concentrations.

There is a wide variation in the spectrum of associated somatic abnormalities. The severity of the phenotype is, in part, related to the underlying cytogenetic abnormality. Mosaic individuals may have only mild short stature and may enter puberty spontaneously before developing gonadal failure.

Diagnosis and management

The diagnosis of Turner syndrome can be confirmed by karyotype analysis. Short stature, although not directly due to growth hormone deficiency, responds to high doses of growth hormone. Prophylactic gonadectomy is recommended for individuals with 45,X/46,XY mosaicism because there is an increased risk of gonadoblastoma. Pubertal development can be induced with oestrogen therapy but causes fusion of the epiphyses and cessation of growth. The timing of pubertal induction therefore needs to be carefully planned. Adults with Turner syndrome require long-term oestrogen replacement therapy and should be monitored periodically for the development of aortic root dilatation, hearing loss and other somatic complications.

Klinefelter syndrome

Klinefelter syndrome affects approximately 1 in 1000 males and is usually associated with a 47,XXY karyotype. However, other cytogenetic variants may be responsible, especially 46,XY/47,XXY mosaicism. The principal pathological abnormality is dysgenesis of the seminiferous tubules. This is evident from infancy (and possibly even in utero) and progresses with age. By adolescence, hyalinisation and fibrosis are present within the seminiferous tubules and Leydig cell function is impaired, resulting in hypogonadism.

Clinical features

The diagnosis is typically made in adolescents who have presented with gynaecomastia and failure to progress normally through puberty. Affected individuals usually have small, firm testes. Tall stature is apparent from early childhood, reflecting characteristically long leg length associated with 47,XXY, and may be exacerbated by androgen deficiency with