Klinefelter Syndrome

Klinefelter syndrome is due to an extra copy of an X chromosome in males (47,XXY). Adult males have hypergonadotrophic hypogonadism and are invariably infertile. However, lifespan is normal and many males may never be diagnosed.

Epidemiology

- Prevalence is ~1/600–1/800 male births.
- There is a significant maternal age effect with 1/300 at maternal age 43 years.

Genetics

- Cases occur sporadically
- The extra X chromosome is of maternal origin in 56%.
- It usually arises by non-disjunction
- Mosaicism may occur, e.g. 46,XY/47,XXY, some of these males are fertile
- There is an increased incidence of chromosome abnormalities in conceptuses fathered by 47,XXY males following intracytoplasmic sperm injection (ICSI) with IVF.

Clinical presentation

- 47,XXY may present antenatally following chorionic villous sampling (CVS) or amniocentesis.
- Babies appear normal
- Increased incidence of undescended testes
- Delayed puberty
- Gynaecomastia
- Infertility

Physical signs

- Males tend to have a taller final height (186cm 47,XXY vs. 176cm 46,XY)
- Gynaecomastia
- Increased carrying angle
- Centripetal obesity
- Hypogonadism
- Normal intelligence

Diagnosis

- Routine karyotype

Complications

- IQ: usually only lower by 10-15 points compared to siblings. Overall intelligence is normal as an adult although ~60% will need some degree of additional educational help. The majority of patients tend to be passive and good natured.
- Cancer risk: there is no good evidence for a general increased risk of cancer although there is a 3% risk increase in breast cancer. There is a <1% risk of primary germ cell tumour.
- In adult life there is an increased risk of diabetes and cardiovascular disease.
- Hypogonadism: delayed puberty, gynaecomastia, infertility
- Osteoporosis

Treatment

- Hormone replacement with IM or transdermal testosterone improves libido, facial hair, self esteem and may reduce the risk of osteoporosis.
- Management of infertility, sperm donation and adoption. ICSI may be offered to the few patients that have viable sperm.
- Surgery for gynaecomastia
- Genetic counselling: prenatal diagnosis should be offered to parents with a previously affected child although recurrence risk is <1%.

Surveillance:

- From 10 years of age: FSH, LH, testosterone measurements
- Height, weight and development

Pictures
Gynaecomastia
Habitus
Karyotype