MEDIBEATS
The Medical Bulletin

In Syndrome

Klinefelter syndrome is the most frequent chromosome disorder in males defined by 47XXY karyotype.

History : Klinefelter syndrome is named for Harry Klinefelter, an American physician who in 1942 described a set of symptoms that characterized the condition. The syndrome was first identified with a specific chromosomal abnormality in 1959 by British researcher Patricia A. Jacobs et al.,

Etiology : The most common karyotype of Klinefelter syndrome is 47, XXY (greater than 90%). Mosaic karyotypes such as 46XY / 47XXY and other aneuploidies such as 48XXXY and 49 XXXXY have been described. The acquisition of the extra X-chromosome is random and usually due to meiotic nondisjunction or post-zygotic nondisjunction. Overall severity of the phenotype appears to be correlated with the amount of additional X chromosome material present.

Epidemiology : 1:500 to 1:1000 males.

Clinical Features : Tall-stature & long limbs, reflected in a low upper/lower segment ratio. Mean height is at the 75th percentile, with weight and head circumference at the 50th percentile. In childhood - phallus and testes may be relatively small. During adolescence - discordant pubertal development with fairly normal phallus and pubic hair development, although testes rarely exceed 4 mL and are characteristically firm due to hyalinization and fibrosis. Testosterone levels - low to the low-normal range. Gynecomastia IQ is between 85 to 90. Verbal IQ is higher than performance due to problems with expressive language and auditory processing. Behavioral difficulties, including immaturity, insecurity, shyness, poor judgment, and the formation of meaningful peer relationships, may be affected. Between 20% to 50% have intention tremors.

Diagnosis : It is made by prenatal or postnatal karyotype or chromosomal microarray. Non-invasive prenatal testing for cell-free DNA can detect upto 67%. Additional prenatal testing or postnatal testing is suggested to confirm any suspected case.The initial evaluation may include a workup for hypogonadism or infertility. Gonadotropins are usually elevated when testicular hyalinization and fibrosis are present.The finding of hypergonadotropic hypogonadism indicates primary gonadal failure. FSH elevation typically predominates over LH, though both are elevated above normal. Testosterone concentrations are usually low or low-normal in both adolescents and adults. A minority of children may demonstrate low inhibin B and elevated AMH, reflecting abnormal Sertoli cell function.

Treatment : The management of patients with Klinefelter syndrome is multidisciplinary.Treatment is basically symptomatic and complete recovery is not possible. Supplemental testosterone treatment under the supervision of a pediatric endocrinologist

may prevent some of the physical manifestations of the "classic KS phenotype." Advanced reproductive technology such as testicular sperm extraction (microTESE) has been successful in allowing up to half of the men with KS deemed "infertile" to have an opportunity to have a biological child. Small pockets of gonadal tissue producing sperm may be identified, extracted, and then injected by intracytoplasmic sperm injection into an ovum for fertilization.

Prognosis : The overall prognosis is guarded.

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