Klinefelter Syndrome

Carla Fedor, RN

Introduction

In 1942, Dr. Harry Klinefelter and his coworkers first described the combination of features that has come to be recognized as Klinefelter Syndrome. By the late 1950's, researchers discovered that men with this group of symptoms had an extra sex chromosome, XXY instead of the usual male arrangement of XY. Although, XXY is common, the syndrome itself is uncommon. Many men live out their lives without ever even suspecting that they have an additional chromosome. For this reason, the term Klinefelter syndrome" has fallen out of favor with the medical community and many experts prefer to describe males having an extra chromosome as "XXY males."

Chromosomes are carriers of DNA, the hereditary material. Men and women usually have 2 sex chromosomes. Women inherit 2 X chromosomes, one from each parent. Men inherit an X chromosome from their mother and a Y chromosome from their father.

Causes

Klinefelter's syndrome is caused by an extra X chromosome and affects only males. No one knows what puts a couple at risk for conceiving an XXY child. A biological accident occurs during a process called meiosis causing XXY. Meiosis is experienced by all cells which will become an egg or sperm. Before meiosis is completed, chromosomes pair and exchange bits of genetic material. In women, the X chromosomes from each parent form a pair. In men, the X from the mother and the Y chromosomes from the father, form a pair. After the exchange, the chromosomes separate and meiosis continues. In some cases, the two X chromosomes or the X and Y chromosomes fail to pair and fail to exchange genetic material. When a sperm with X and Y chromosomes fertilizes an egg having a single X chromosome, or a normal sperm with a Y chromosome fertilizes an egg having two X chromosomes, an XXY male is conceived.

Frequency

Older mothers may have a slightly higher risk of having a boy with XXY. But studies have shown that about 50 % of the time, the extra chromosome comes from the father and the other 50 % comes from the mother. In the US, it occurs in about 1 in 500-1000 male births; over 3,000 males are affected yearly. It affects all races equally. Mortality rate is not significantly higher than in healthy individuals.

Diagnosis

Because XXY males often don't appear any different from anyone else, many XXY males probably never learn that they have an extra chromosome. Diagnosis, when made, usually occurs in adolescence or adulthood.

Other times that the diagnosis may occur are before or shortly after birth and early childhood. More recently, many XXY males have been diagnosed before birth, through amniocentesis. In amniocentesis, a sample of the fluid surrounding the fetus is withdrawn. The fluid is then examined for chromosomal abnormalities. This test is usually not done unless there is a family history of problems or if the pregnant woman is older than 35.

The next most likely time for diagnosis is when the child begins school. The doctor may suspect the boy is an XXY male if he is slow in learning to talk or has difficulty reading and writing.

In adolescence, diagnosis may occur as a result of excessive breast development. Like some normal males, many XXY males undergo slight breast enlargement at puberty. Only a small fraction of XXY males develop breasts large enough to embarrass them.

The most common time that an XXY male is diagnosed is as an adult. It is usually the result of testing for infertility. The examining doctor may also notice small testes which are characteristics of an XXY male.

Infertility and gynecomastia (enlarged breast tissue) are the two most common complaints leading to diagnosis. Other complaints include fatigue, weakness, erectile dysfunction, language impairment, academic problems, subnormal libido, poor self-esteem, osteoporosis and behavior problems.

Testing for Klinefelter's syndrome may include:

- Physical examination
- Karyotyping or a study of the person's chromosomes
- Semen exam showing low sperm count
- Decreased serum testosterone levels
- Increased serum luteinizing hormone
- Increased serum follicle stimulating hormone

Clinical Signs

Severity of symptoms may vary and may include:

- Small penis and testes
- Decreased facial, body and pubic hair
- Height taller than average
- Long arms and legs
- Enlarged breast tissue (gynecomastia)
- Inability to produce sperm
- Learning disabilities especially language difficulties
- Personality impairment

Treatment

There is no treatment for infertility associated with this syndrome.

The most widely used form of therapy is an intramuscular preparation of testosterone. Individuals respond to testosterone treatment in different ways and although most will benefit, a few will not. It is generally safe and well tolerated by most people. Regularly scheduled testosterone injections will improve the development of secondary sexual characteristics. The best time to begin testosterone replacement therapy is at age 11 or 12. Even if the syndrome is not diagnosed and treated early, testosterone therapy can have positive effects. It will increase facial and pubic hair, increase muscle size, increase strength and increase libido. It can help improve their mood and behavior, improve self-esteem and they tend to become more energetic and less irritable. It will not have any effect on the size of the testicles, enlarged breast tissue or sterility.

Many XXY males have a history of learning disabilities, poor body image, lack of self esteem and difficultly with relationships. For these reasons, as soon as a diagnosis is made, it is encouraged that they be referred to a qualified mental health specialist to receive psychological counseling. They can greatly benefit from the support of speech and language pathologists, teachers, special education services and support groups.

Complications

The syndrome is associated with an increased risk of osteoporosis, breast cancer, varicose veins, prostate problems, impotence and psychological problems.

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