49,XXXXY Syndrome

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49,XXXXY syndrome is a chromosomal condition in boys and men that causes intellectual disability, developmental delays, physical differences, and an inability to father biological children (infertility). Its signs and symptoms vary among affected individuals.

Keywords: genetic conditions

1. Introduction

Boys and men with 49,XXXXY syndrome have mild or moderate intellectual disability with learning difficulties. Speech and language development is particularly affected. Most affected boys and men can understand what other people say more easily than they themselves can speak. People with 49,XXXXY syndrome tend to be shy and friendly, but problems with speech and communication can contribute to behavioral issues, including irritability, difficulty tolerating frustration, defiant behavior, and outbursts or temper tantrums.

49,XXXXY syndrome is also associated with weak muscle tone (hypotonia) and problems with coordination that delay the development of motor skills, such as sitting, standing, and walking. Affected infants and young boys are often shorter than their peers, but some catch up in height later in childhood or adolescence.

Other physical differences associated with 49,XXXXY syndrome include abnormal fusion of certain bones in the forearm (radioulnar synostosis), an unusually large range of joint movement (hyperextensibility), elbow abnormalities, curved pinky fingers (fifth finger clinodactyly), and flat feet (pes planus). Affected individuals have distinctive facial features that can include widely spaced eyes (ocular hypertelorism), outside corners of the eyes that point upward (upslanting palpebral fissures), skin folds covering the inner corner of the eyes (epicanthal folds), and a flat bridge of the nose. Dental abnormalities are also common in this disorder.

49,XXXXY syndrome disrupts male sexual development. The penis is often short and underdeveloped, and the testes may be undescended, which means they are abnormally located inside the pelvis or abdomen. The testes are small and do not produce enough testosterone, which is the hormone that directs male sexual development. The shortage of testosterone often leads to incomplete puberty. Starting in adolescence, affected boys and men may have sparse body hair, and some experience breast enlargement (gynecomastia). Their testes do not produce sperm, so all men with 49,XXXXY syndrome are infertile.

2. Frequency

49,XXXXY syndrome affects an estimated 1 in 85,000 to 100,000 newborn boys. It is among the rarest of the sex chromosome disorders, which are conditions caused by changes in the number of sex chromosomes (the X chromosome and the Y chromosome).

3. Causes

49,XXXXY syndrome is a sex chromosome disorder in boys and men that results from having three extra X chromosomes in each cell. People typically have 46 chromosomes in each cell, two of which are the sex chromosomes. Females have two X chromosomes (46,XX), and males have one X chromosome and one Y chromosome (46,XY). Boys and men with 49,XXXXY syndrome have the usual single Y chromosome, but they have four copies of the X chromosome, for a total of 49 chromosomes in each cell.

Boys and men with 49,XXXXY syndrome have extra copies of multiple genes on the X chromosome. The activity of these extra genes affects many aspects of development, including sexual development before birth and at puberty. Researchers are working to determine which genes contribute to the specific developmental and physical differences that occur with

49,XXXXY syndrome.

49,XXXXY syndrome is sometimes described as a variant of another sex chromosome disorder called Klinefelter syndrome. Boys and men with Klinefelter syndrome have one extra copy of the X chromosome, for a total of 47 chromosomes in each cell (47,XXY). Like 49,XXXXY syndrome, Klinefelter syndrome affects male sexual development and can be associated with learning disabilities and problems with speech and language development. However, the features of 49,XXXXY syndrome tend to be more severe than those of Klinefelter syndrome and affect more parts of the body. As doctors and researchers have learned more about the differences between these sex chromosome disorders, they have started to consider them as separate conditions.

3.1. The chromosome associated with 49,XXXXY syndrome

- x chromosome

4. Inheritance

This condition is not inherited; it occurs as a random event during the formation of reproductive cells (eggs) in an affected person's mother. During cell division, an error called nondisjunction prevents X chromosomes from being distributed among egg cells as they form. Typically, as cells divide, each egg cell gets a single X chromosome. However, because of nondisjunction, a single egg cell can end up with four X chromosomes that would usually have been distributed among four separate egg cells. If a sperm cell containing a single Y chromosome fertilizes this egg cell, the resulting child will have four X chromosomes and one Y chromosome (49,XXXXY) in each of the body's cells.

5. Other Names for This Condition

- 49,XXXXY chromosomal anomaly
- chromosome XXXXY syndrome
- XXXXY aneuploidy
- XXXXY syndrome

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