General information about positive NIPT results: XXY syndrome (Klinefelter syndrome)

My patient's NIPT is positive for XXY syndrome (Klinefelter syndrome). What does this mean?

Your patient's noninvasive prenatal testing (NIPT) result suggests the presence of an extra copy of the X chromosome. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have XXY syndrome depends on many factors, including the patient's clinical and family history.

Next steps to consider: You should discuss the results and the potential clinical implications with your patient. Globally, professional medical societies recommend that all women with a positive screening result should have genetic counseling and a comprehensive ultrasound evaluation with an opportunity for diagnostic testing to confirm the results.[1,2] Confirmation prior to birth can also help with pregnancy and neonatal management.

See below for more information about XXY syndrome.

What is XXY syndrome?

XXY syndrome is a condition that is caused by a male having an extra copy of the X sex chromosome (two copies of the X chromosome and one copy of the Y chromosome rather than the usual one copy of each).

What are the features of XXY syndrome?

XXY syndrome is likely to result in live birth. Males with XXY syndrome have variable phenotypes. Some of the common features of XXY syndrome include learning disabilities, delayed speech and language development, taller stature, hypogonadism, and risk of infertility. Prenatal ultrasounds are usually normal.

What is the prevalence of this condition?

Approximately 1 in 600 males are born with XXY syndrome. This condition usually happens by chance and can be associated with advanced maternal age.

What testing could be considered?

Specialized genetic tests such as karyotyping, fluorescence *in situ* hybridization (FISH), quantitative polymerase chain reaction (qPCR), and microarray are available to confirm the presence of XXY syndrome.

These confirmatory tests are generally performed on cells from chorionic villus sampling (CVS) or amniocentesis during pregnancy, on cord blood or peripheral blood sample after the baby is born, or on products of conception (POC) in the case of a miscarriage. The type of invasive procedure and diagnostic testing should take into account the underlying chromosome anomaly.[3,4]

Ultrasound evaluation is not expected to be useful in aiding with a prenatal diagnosis of XXY syndrome, as ultrasound is usually normal. Normal ultrasound cannot exclude this condition.

Resources for XXY syndrome

MedlinePlus Genetics
medlineplus.gov/genetics/condition/klinefelter-syndrome

National Organization for Rare Disorders
rarediseases.org/rare-diseases/47-xxy-klinefelter-syndrome

Support Group UK
ksa-uk.net

References

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Additional resources

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