General information about positive NIPT results: Partial deletion (CNV ≥ 7 Mb)

My patient's NIPT is positive for a partial deletion. What does this mean?

Your patient's noninvasive prenatal testing (NIPT) detected a partial deletion of 7 Mb or larger. See the report for details regarding the size and the region of the chromosome involved. NIPT is a screening test; false positives can occur. The actual chance for the pregnancy to have a partial deletion 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 partial deletions.

What is a partial deletion?

A partial deletion is a loss of part of a chromosome. It can be either interstitial (within a chromosome) or terminal (at the end of the chromosome). It results in loss of genomic material for the region of the deleted segment of the chromosome. Deletions of 7 Mb or larger are likely to be seen on karyotype analysis.

What are the features of a partial deletion?

The clinical significance is variable and is based on the size and location of the deletion, as well as presence of additional deletions or duplications. In general, partial deletions that are 7 Mb or larger are likely to be associated with a clinical phenotype, which can include intellectual disability, structural anomalies, dysmorphic features, and possibly other medical issues. There are certain recurring deletions for which the clinical features are well described. Some examples of these include 4p- syndrome, 5p- syndrome, and 1p36 deletion. However, other deletions may not be associated with a specific syndrome. The exact phenotype will depend on the region of the chromosome involved. This will require a specific literature search to better understand the clinical significance. Confined placental mosaicism (CPM; when cells with partial deletions are present in the placenta, but not in the fetus) has been reported.

What is the prevalence of this condition?

Birth prevalence is approximately 1 to 2 per 10,000.[3] Prevalence in NIPT is reported to be 0.12% to 0.16% (includes deletions and duplications). Positive predictive value (PPV) in one study was 32%.[4]

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 a partial deletion.

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.[5,6]

Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of partial deletion, but a normal ultrasound cannot exclude these conditions.

Special considerations

The presence of a maternal copy number variation (CNV) may lead to a positive NIPT result (causing a false positive fetal result). Some of these CNV are likely to be benign.

One study has indicated that 10q25-ter deletions identified on NIPT are due to maternal low-level mosaic deletion associated with FRA10B expansions, and are likely to be benign.[7]

Presence of partial deletion may be due to a balanced parental rearrangement, and it may be appropriate to consider parental karyotyping.

Resources for partial deletion

ClinGen Clinical Genome Resource
clinicalgenome.org

Unique, The Rare Chromosome Disorder Support Group
rarechromo.org

References

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7. Huijsdens-van Amsterdam K, Straver R, van Maarle MC, et al. Mosaic maternal 10qter deletions are associated with FRA10B expansions and may cause false-positive noninvasive prenatal screening results. *Genet Med*. 2018;20(11):1472-1476.

Additional resources

Gardner RJM, Amor DJ. *Gardner and Sutherland's Chromosome Abnormalities and Genetic Counseling*. 5th ed. Oxford University Press; 2018.

Jones KL, Jones MC, del Campo M. *Smith's Recognizable Patterns of Human Malformation*. 7th ed. W.B. Saunders Company; 2013.

Snyder MW, Simmons LE, Kitzman JO, et al. Copy-number variation and false positive prenatal aneuploidy screening results. *N Engl J Med*. 2015;372(17):1639-1645.

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