General information about positive NIPT results

My patient's NIPT is positive for a deletion of 15q11.2-q13. What does this mean? Your patient's screening test detected a deletion of 15q11.2-q13 which is associated with Prader-Willi and Angelman syndromes. NIPT cannot distinguish between a risk for Prader-Willi syndrome or Angelman syndrome. NIPT is a screening test; false positives can occur.

Next steps to consider: You should discuss the results and the potential clinical implications with your patient. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."[1] Confirmation prior to birth can also help with pregnancy and neonatal management.

Please see below for the general description of Prader-Willi syndrome and Angelman Syndrome and additional resources.

What is Prader-Willi syndrome? Prader-Willi syndrome (PWS) is a rare genetic condition that causes difficulty feeding and failure to thrive in infancy, with obesity, developmental delay, and other medical problems as the child gets older. NIPT is only able to detect PWS caused by a deletion, which accounts for ~70% of cases; the remaining cases are caused by different underlying molecular mechanisms.

What is Angelman syndrome? Angelman syndrome (AS) is a rare genetic syndrome that includes intellectual disability and other serious medical problems. NIPT is only able to detect AS caused be a deletion, which accounts for ~68% of cases; the remaining cases are caused by different underlying molecular mechanisms.

What are the features of PWS? People with PWS have severe hypotonia and feeding difficulties in early infancy, followed in later infancy or early childhood by excessive eating and gradual development of morbid obesity. Motor milestones and language development are delayed. All individuals have some degree of cognitive impairment, and may also have behavior problems. A normal lifespan is expected.

What are the features of AS? Common features in individuals with AS include: intellectual disability, severe developmental delay, speech impairment, ataxia, seizures and dysmorphic features. A normal lifespan is expected.

What is the prevalence of these conditions? 1 in 10,000 to 1 in 25,000 newborns have PWS. 1 in 12,000 to 1 in 20,000 newborns have AS.

What testing could be considered?

- NIPT cannot distinguish between a risk for PWS or AS.
- NIPT can only screen for cases of PWS or AS caused by a deletion.
- Specialized genetic tests such as fluorescence in situ hybridization (FISH) and microarray are available to confirm the presence of Prader-Willi or Angelman 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 products of conception (POC) in case of a miscarriage.
- Ultrasound evaluation may be useful in aiding with a prenatal diagnosis of these conditions, but a normal ultrasound cannot exclude this condition. Usually, ultrasound is normal.

Resources for PWS:

Prader-Willi Syndrome Association http://www.pwsausa.org/

Prader-Willi syndrome-Genetics Home Reference
http://ghr.nlm.nih.gov/condition/prader-willi-syndrome

Resources for AS:

Angelman Syndrome Foundation, Inc. http://www.angelman.org/

Angelman syndrome-Genetics Home Reference
http://ghr.nlm.nih.gov/condition/angelman-syndrome

Angelman syndrome- National Organization for Rare Disorders
https://rarediseases.org/rare-diseases/angelman-syndrome/

The information provided in this sheet is based on literature search performed on 11/28/16. This Information Sheet is intended to provide some general overview of the key issues relating to its subject matter. This sheet is not intended to be an exhaustive discussion of the subject covered by the sheet nor should it be used to substitute for the exercise of a Clinical Laboratory or a Healthcare Provider's legal or professional duties relative to interpreting the test results to which this Information Sheet relates. This sheet is also not intended to serve as a recommendation of management. This sheet is not intended to be a substitute for genetic counseling.

Reference:

1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. *Obstet Gynecol.* 2016;127:e123-137.

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