Is my baby healthy?
Advances and New Technology in Prenatal Genetic Testing

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Disclosures

- I have no relevant financial or nonfinancial relationships to disclose.

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Learning Objectives

• Obj: 1 Review updates in non-invasive prenatal testing through clinical case presentation

• Obj: 2 Compare use of snp microarray versus standard karyotype in products of conception
Case of Mary

• 37 year old G3P2002 patient
• referred to genetic counseling for age-related risk assessment for chromosome abnormalities
• 10 weeks and 3 days by LMP and dating scan
• Desires to know the baby’s gender
• Mary is considering NIPT- are there other important pieces of information she should know?
Non-Invasive Prenatal Testing (NIPT)

• Blood draw > 10 weeks gestation
• Currently offered for patients
  - >=35 years of age at EDD
  - Abnormal screening result
  - Abnormal ultrasound
  - Family history
• Turn around time 7-10 days
• Cost
  – List price $795-$2700
  – Patient out of pocket cost dependent on insurance
NIPT may also detect a sex chromosome abnormality....

- Sex chromosome abnormalities (SCAs):
  - Turner syndrome (45,X),
  - Klinefelter syndrome (47,XXY),
  - 47, XYY and
  - 47, XXX
Screening for SCAs with NIPT

• Not all labs are reporting every sex chromosome abnormality

• Some labs will report SCAs only if gender is also elected
Case of Leslie

• 34 year old G1P0 with a twin pregnancy detected on ultrasound

• 11 weeks gestation

• Meets AMA cut-off for twin pregnancies
What are Leslie’s screening options?

• Traditional maternal serum screening?
  - First trimester
  - Second trimester
  - Sequential screening

• NIPT?
NIPT in Twin Pregnancies

• Not currently offered by all labs

• Studies performed to date demonstrate comparable detection rates to singleton pregnancies
NIPT Available to More Populations

• Egg donor
• IVF

• Average Risk populations?
  - Not currently recommended by ACOG, ISPD, NSGC
  - Limited studies with small sample size
  - Accuracy in average population is largely affected by rate of incidence
Case of Amy

- Amy is a G1P0 patient who had an IUFD at 25 weeks complicated by a large encephalocele

- The patient and her husband declined amniocentesis during pregnancy but elected genetic studies at delivery
How do you help this patient?

Post-natal studies:

• Autopsy?

• Chromosome karyotype?

• Chromosome microarray?
Chromosome Karyotype
Patient (Fetal) and Control DNAs are labeled with different fluorescent molecules, then hybridized in equal amounts to the array of DNA probes.
Microarray Analysis

- **YELLOW** signal = NORMAL equal hybridization of green fetal DNA and red control
- **RED** = DELETION more control DNA hybridized
- **GREEN** = DUPLICATION more fetal DNA hybridized

![Microarray Diagram](image)
Microarray Analysis

Ratio profile

excess of test DNA

Deficiency of test DNA

Duplication

Deletion
Karyotype vs. Microarray

Karyotype versus Microarray Testing for Genetic Abnormalities after Stillbirth

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Informatics Enhanced SNP Microarray Analysis of 30 Miscarriage Samples Compared to Routine Cytogenetics

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Abstract

Purpose: The metaphase karyotype is often used as a diagnostic tool in the setting of early miscarriage; however this technique has several limitations. We evaluate a new technique for karyotyping that uses single nucleotide polymorphism microarrays (SNP). This technique was compared in a blinded, prospective fashion, to the traditional metaphase karyotype.

Methods: Patients undergoing dilation and curettage for first trimester miscarriage between February and August 2010 were enrolled. Samples of chorionic villi were equally divided and sent for microarray testing in parallel with routine cytogenetic testing.

Results: Thirty samples were analyzed, with only four discordant results. Discordant results occurred when the entire genome was duplicated or when a balanced rearrangement was present. Cytogenetic karyotyping took an average of 29 days while microarray-based karyotyping took an average of 12 days.

Conclusions: Molecular karyotyping of POC after missed abortion using SNP microarray analysis allows for the ability to detect maternal cell contamination and provides rapid results with good concordance to standard cytogenetic analysis.
Snp Microarray for POC

• Provider more genetic information

• Can be performed using a lower quantity or quality sample

• Has simple collection and shipping logistics

• Relatively affordable for patients
Resources

• National Society of Genetic Counselors nsgc.org
• National coalition for Health Professional Education in Genetics nchpeg.org
• Society of Maternal Fetal Medicine smfm.org
• American College of Medical Genetics acmg.net
• Genetics Home Reference ghr.nlm.nih.gov
Genetic Counselors

• All of our genetic counselors are board certified and licensed
  – Beth Jiorle
  – Martha Dudek
  – Jill Nichols

• We have clinics at One Hundred Oaks, Clarksville, Columbia, and Franklin

• Appointments: 615-343-5700
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