STUDENT PROBLEM-BASED LEARNING SESSION

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

LOYOLA UNIVERSITY MEDICAL CENTER

Topic: **Prenatal Genetic Counseling and Diagnosis**

Recommended Reading:

American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics Committee on Genetics Society for Maternal-Fetal Medicine Screening for Fetal Chromosomal Abnormalities, Obstetrics & Gynecology: October 2020 - Volume 136 - Issue 4 - p e48-e69

Embryology, Anatomy and Reproductive Genetics, Chapter 3 in Obstetrics and Gynecology for Medical Students, Beckmann et al.

Case Presentation:

Jill is a 38 year old G3 P1011 Caucasian female seen for her first prenatal care visit. Her LMP was approximately 11 weeks ago. She began taking prenatal vitamins when she discovered she was pregnant at 6 weeks.

The patient's OB history includes 1 term vaginal delivery of a healthy female and 1 first trimester termination for anencephaly.

Jill's family history includes 1 brother and 1 maternal aunt's son with intellectual disabilities.

Jill's husband, Jack, is 40 years old and in good health. Jack's sister died in early childhood from cystic fibrosis. Both report Ashkenazi Jewish ancestry.

From the history

(1) List the disorders that this couple is at increased risk for.

Carrier Screening

(2) What kind of carrier screening would you offer this patient?
(3) What carrier screening would you offer a patient not of Ashkenazi Jewish ancestry?
(4) The patient and her partner elect to pursue the following tests. You receive the following results 4 weeks later:

Jill:

Fragile X CGG repeats = 36 (normal) and 62 repeats (premutation)
CBC = Hgb 10.2 MCV 69
Hb Electrophoresis (WNL): Hb A = 98%, Hb A_2 = 2%
CFTR gene sequencing = no mutations detected

Jack:

Hexosaminidase A = 62% (WNL)
DNA analysis for Tay-Sach's disease = no mutations detected
DNA analysis for Canavan disease = no mutations detected
CF carrier screening in 2010 = negative for 32 common mutations

Jill's brother:

46, XY karyotype
Fragile X CGG repeats = 300 repeats (full mutation)

(5) With these results what is the risks of the genetic disorders you were concerned about from question 1?
(6) Based on these results are there any additional genetic disorders to be concerned about and what testing would you recommend?

Prenatal Screening and Diagnostic Testing

(7) What genetic screening options do you offer Jill at this point?
(8) Would it be different if she was 23 years old?

Jill elects for NIPS (Cell free DNA) which returns low risk for common aneuploidies (Trisomy 21, 13 and 18) and XY sex chromosomes

(9) How do you counsel the patient on these results?

At 20 weeks, Jill has a detailed anatomic ultrasound. The fetal head shows ventriculomegaly with lemon shape and banana sign.

(10) What congenital anomaly are you concerned about? What is the inheritance pattern of this anomaly?
(11) Which blood test could we have offered that would have signaled an increased risk of this anomaly?
(12) What recommendations would you make for future pregnancies?

Given this diagnosis, Jill and Jack desire further genetic testing.

(13) What options does the couple have for invasive genetic testing?

The patient has an uncomplicated amniocentesis that gives 46, XY karyotype and normal microarray. The couple plans to meet with pediatric neurosurgery and neonatology during the pregnancy.

	Screening	Diagnostic
Preconception	-Carrier screening -Pre-implantation genetic testing/screening	
First Trimester	-First trimester screen (incl. NT ultrasound) -Integrated part 1 -Cell-free DNA screening	-Chorionic villus sampling (CVS)
Second Trimester	-Quad screen (blood) -Integrated part 2 -Cell-free DNA screening	-Amniocentesis -Cordocentesis/PUBS