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 white 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 white, 39 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's pregnancy is at increased risk for.

Parental Carrier Screening

(2) What carrier screening options would you offer this patient?
(3) What carrier screening would you offer a patient not of Ashkenazi Jewish ancestry?
(4) Jill elects to pursue the following tests. You receive her results 4 weeks later, along with new test results from Jill's brother.

Jill:
CFTR gene sequencing + del/dup analysis = no mutations detected
SMA = 2 copies of *SMN1* gene detected
CBC = Hgb 10.2 MCV 69 MCH 26
Hb Electrophoresis (WNL): Hb A = 98%, Hb A_2 = 2%
DNA analysis for Tay-Sachs disease = no mutations detected

DNA analysis for Canavan disease = no mutations detected
DNA analysis for Familial Dysautonomia = no mutations detected
Fragile X CGG repeats = 36 (normal) and 62 repeats (premutation)

Jill's brother:
46, XY karyotype
Fragile X CGG repeats = 300 repeats (full mutation)

(5) Given these results, what are the risks for the heritable genetic disorders you were concerned about from question 1?
(6) Based on her Fragile X test result, what counseling do you offer Jill about her own health risks?

Prenatal Screening and Diagnostic Testing

(7) Jill is at 15wks GA. What fetal aneuploidy genetic screening/testing options do you offer her at this time?
(8) Would your screening recommendation differ if she were 23 years old?

Jill elects for NIPT (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 the accuracy of 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 Jill for future pregnancies?

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

(13) What options does the couple have for invasive genetic testing at 20 wks? What genetic testing do you order with this procedure?

The patient has an uncomplicated amniocentesis that gives a normal microarray with XY chromosomes, and 36 Fragile X CGG repeats. The couple plans to meet with pediatric neurosurgery and neonatology during the pregnancy.