

REI Case 2 – Mentor Answer Key

Part A. Case Questions:

1. What is this patients' differential diagnosis?

The differential diagnosis for secondary amenorrhea includes pregnancy, chronic anovulation, acquired uterine outflow abnormalities (Asherman's syndrome), hypogonadotropic hypogonadism or hypergonadotropic hypogonadism (premature ovarian failure).

2. Are you concerned about anything in particular in her medical history or physical exam?

Her history of a prior uterine instrumentation procedure is concerning for risk for Asherman's syndrome. Her vaginal atrophy suggests low serum estradiol. Her low BMI is concerning for low BMI as a cause of hypogonadotropic hypogonadism.

3. What tests will you order initially and why?

The initial evaluation should exclude pregnancy and measure thyroid stimulating hormone and prolactin. It is common to proceed with a progestin withdrawal at this time. These tests are initially ordered as pregnancy and chronic anovulation are the most common causes of secondary amenorrhea and will often lead to the diagnosis.

Part B. Case Questions:

1. What is your suspected diagnosis at this time?

Chronic anovulation

2. Do you need to do any further testing?

No further testing is indicated at this time to diagnose her secondary amenorrhea.

3. What is your next course of action?

If she does not desire pregnancy, would regulate her menses with oral contraceptives or cyclic progestin. Progestin exposure to the uterus could also be accomplished by depot medroxyprogesterone or a levonorgestrel intrauterine device.

If pregnancy is desired, would proceed with ovulation induction.

4. What would you do next if she had not bled in response to the Provera?

Confirmation of a normal uterine lining is essential. This can be accomplished by a sequential estrogen challenge followed by a progestin withdrawal. Menstrual flow is expected with a normal uterine lining. If she has a normal withdrawal, assessing the level of Follicle Stimulating Hormone (FSH) can distinguish between hypogonadotropic hypogonadism or hypergonadotropic hypogonadism (premature ovarian failure).

Part C. Case Questions:

1. What are possible causes for her sudden lack of response?

Pregnancy

Hypogonadotropic Hypogonadism

Hypergonadotropic Hypogonadism (Premature Ovarian Failure)

2. Do you need any further evaluation now?

Pregnancy Test

Serum level of FSH

3. Do you need to treat her amenorrhea? If so, how?

Her amenorrhea does need to be treated. Assuming she is not pregnant, she would need estrogen therapy as well as progestin therapy.

4. What long term issues does she face?

Osteoporosis

Infertility

Part D. Case Questions:

1. What do you anticipate when she stops the pill?

She will either have irregular menses or become amenorrheic.

2. How do you counsel women during the pre-pregnancy period?

Risk assessment for pregnancy should include evaluation of her age, medical history, reproductive history, medications, family history, environmental exposures and habits (such as smoking and alcohol use).

Laboratory screening includes rubella and varicella titers, a complete blood count, HIV and Hepatitis B antigen screening. Other evaluation, based on the individual's risk, could include screening for diabetes, genetic screening, TB or Hepatitis C antibody testing, screening for sexually transmitted diseases or obtaining toxoplasmosis or CMV titers.

Any woman of childbearing age should have an intake of folic acid at a dose of 0.4 mg/day.

3. What are her treatment options and the costs/risks of each option?

If she is anovulatory, ovulation induction with oral medications, such as clomiphene citrate, is possible. The side effects include hot flushes, moodiness and an increased risk of multiple pregnancy (6-8% twins, <1% of higher-order pregnancies). The cost is less than \$50-100/cycle.

If she has hypogonadotropic hypogonadism, her options include weight gain, gonadotropin ovulation induction and in vitro fertilization. Both gonadotropin ovulation induction and in vitro fertilization carry the risk of ovarian hyperstimulation syndrome. The risk of higher order multiple pregnancy is higher with gonadotropin ovulation induction due to the loss of control of number of embryos transferred. The recommended embryo transfer number recommended by American Society of Reproductive Medicine has dramatically decreased recently, leading to a decrease in higher-order multiple pregnancy. In 2011, the cost of gonadotropin ovulation induction combined with intrauterine insemination is about \$3-4000/cycle, and the cost of IVF is about \$20,000/cycle.

If she has premature ovarian failure, fertility therapies have not been shown to improve her limited chance for pregnancy. These women may need to consider donor oocyte IVF, adoption or remaining childless.