

REI Case 1 – Mentor Answer Key

A. Case Questions:

1. What is your differential diagnosis and why? What is concerning to you on physical exam?

Differential diagnoses include hyperprolactinemia (less common to have hyperandrogenism), late onset congenital adrenal hyperplasia, androgen-secreting tumors from the ovary or adrenal (not likely given mild manifestations and long duration of symptoms). Certainly, pregnancy needs to be excluded even though she states she is virginal.

2. Is it necessary to order any tests to make a diagnosis? If so, which tests will you order?

Certainly, pregnancy should be excluded. It is standard to check prolactin and thyroid stimulating hormone in a nonpregnant woman without menstruation. By the Rotterdam criteria, she has already met the requirement for Polycystic Ovarian Syndrome with her irregular menses and clinical hyperandrogenism. Further testing to make the diagnosis is not necessary. Women with PCOS should be screened for diabetes mellitus and hyperlipidemia. Excluding late-onset congenital adrenal hyperplasia can be accomplished by a morning 17-OH-progesterone level, but testing can be limited to high-risk groups.

B. Case Questions:

1. Were all of these studies necessary?

As noted above, it is not necessary to check androgen levels in this patient as her hyperandrogenism is mild and chronic. Current evaluation does not require LH or FSH testing, although it is common to have an increased LH/FSH ratio. Screening for diabetes and hyperlipidemia is appropriate. It is not necessary to do a pelvic ultrasound.

2. What is your interpretation of these results? What is her diagnosis?

Based on her clinical scenario and laboratory profile, she would be diagnosed with Polycystic Ovarian Syndrome. These results showed do not show hyperandrogenism, but she displays clinical hyperandrogenism (hirsutism). She displays increased androgen action at the level of the skin. Her pelvic ultrasound shows a thickened endometrium, which may be due to unopposed estrogen.

3. What is your basis for the diagnosis you have made?

Her clinical symptoms meet the Rotterdam criteria for Polycystic Ovarian Syndrome and her laboratory evaluation meets the recommended exclusions.

4. How will you address the issue of her infrequent periods?

Women with PCOS are often put on birth control pills. Not only will this regulate their menses, but will also lead to an increase in Sex Hormone Binding Globulin (SHBG; due to estrogen) and a decrease in free androgen levels. Alternatively, she could pursue cyclic

Provera treatment or ovulation induction with clomiphene citrate (only recommended if she desires pregnancy).

5. Will you consider an endometrial biopsy? Why or why not? Is there data to support your opinion?

Her ultrasound shows markedly thickened endometrium. It is highly probable that this results from unopposed estrogen due to her PCOS. Women with PCOS are predisposed to endometrial cancer. While endometrial biopsy is reasonable after pregnancy has been excluded, it is not likely necessary in a 20 year old. One strategy may be to withdraw her via progestin stimulation and repeat the ultrasound. There is no consensus on monitoring of the endometrium in women with PCOS, but many PCOS providers would consider endometrial biopsy earlier than the ACOG general recommendation of age 35 for abnormal uterine bleeding if they have not had intermittent progestin exposure.

6. How will you help her with hirsutism?

As noted above, combined oral contraceptives can increase SHBG and decrease free androgen levels. It is also quite common to treat PCOS women with spironolactone, a potassium-sparing diuretic with anti-androgen properties. The use of other anti-androgen compounds is investigational. Local hair therapy may also be necessary: shaving, plucking, electrolysis, laser hair therapy, etc.

C. Case Questions:

1. How will you help this patient become pregnant? Which medications and doses, if any, would you chose and why? Would you change any of her current medications and why? Does she require any testing before ovulation induction?

It is important to discuss weight loss with patients having PCOS as this may result in ovulatory status. Pharmacologically, ovulation can be induced with clomiphene citrate. The addition of metformin to clomiphene citrate has been recently investigated. Its use does not appear to improve pregnancy rates. Surgery to the ovaries, via ovarian drilling, has suggested a possible role in treating ovulatory dysfunction.

Her current medications pose a problem for pregnancy. Of course, oral contraceptives will need to be discontinued. Spironolactone is contraindicated in pregnancy, due to its diuretic and antiandrogen effects. Lisinopril is a category C medication in the first trimester and category D in the second and third trimester, and thus, should be substituted. A Beta-blocker would be an appropriate substitute.

It is appropriate to screen for pregestational diabetes before the initiation of ovulation. Routine preconceptional testing also applies in this population.

2. What counseling needs to be done regarding her long term health? What screening tests should you order?

PCOS poses several long term health risks. Obesity often complicates PCOS and weight loss counseling is a main stay of care of the PCOS patient. Women with untreated PCOS are at risk for endometrial hyperplasia and/or cancer due to unopposed estrogen stimulation to the endometrial lining. Oral contraceptives allow for cyclic progestin exposure and have other benefits for the PCOS patient. If PCOS patients are unable or unwilling to take OCPs, cyclic or continuous progestin therapy is warranted. Care of the PCOS patient often involves intermittent screening for diabetes mellitus and hyperlipidemia.

Women with PCOS are also at risk for diabetes mellitus, hypertension, and heart disease. Regular screening for these processes is recommended.

3. How would you counsel this patient on the expected course of her pregnancy? Is she at risk for complications?

Women who conceive with clomiphene citrate are at risk (6-8%) of twin pregnancy. Higher-order multiples are not common (<1%). Twin pregnancies carry a higher risk of antepartum complications, such as preterm labor and birth, pre-eclampsia and gestational diabetes. PCOS women with singleton pregnancies are at increased risk of gestational diabetes and pre-eclampsia. Obesity often complicates pregnancy in PCOS patients.

D. Case Questions

1. Does this patient need additional workup for infertility? If so, what will you order?

Many practitioners would perform a standard infertility work-up after 3-6 ovulatory cycles with timed intercourse. A standard infertility evaluation would include a hysterosalpingogram to evaluate tubal status, a semen analysis and a confirmation of ovulation. If the patient is over 30, tests of ovarian reserve may also be considered.

2. How will you optimize the Clomid regimen?

This patient appears to be ovulatory with her menstrual regularity. Strategies such as timed intercourse and sperm-friendly lubricants could be recommended. Combining Clomid use and ultrasound monitoring and/or intrauterine insemination have also been recommended.

4. How would your approach change if she had never had menses after the first cycle of Clomid?

If she had never had menses after 50 mg of Clomid, one would need to exclude pregnancy. If non-pregnant, she did not ovulate in response to the initial dose of clomiphene citrate. Increased dosing with clomiphene citrate – 100 mg initially to increase to 150 mg if she remains anovulatory. Weight loss (5-10%) has been shown

to lead to less insulin resistance and improve Clomid responsiveness in PCOS women. Supplemental medications, such as metformin or dexamethasone, have been used but it is recommended by the American Society of Reproductive Medicine that consideration for gonadotropin therapy or laparoscopic ovarian surgery be given to those unresponsive to clomiphene citrate ovulation induction.