

## > THE PATIENT

25-year-old woman

## > SIGNS & SYMPTOMS

- Hot flashes and night sweats
- Amenorrhea
- Positive home pregnancy test

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## > THE CASE

A 25-year-old G2P2 woman came to our family practice clinic because she had multiple positive home pregnancy test results despite having undergone a sterilization procedure 4 years earlier. She said that 9 months ago, she had begun to experience hot flashes and night sweats that were getting progressively worse. Her menstrual cycles had been regular until 6 months earlier, when her bleeding became very light and irregular (2- to 6-week cycles with only one day of menstruation). Then 3 months ago, she stopped menstruating.

She'd had 2 uncomplicated pregnancies with normal vaginal deliveries 3 and 4 years ago, and had undergone a transcervical sterilization procedure after delivering her second child. Her medical history included hypothyroidism diagnosed at age 15, moderate persistent asthma, and seasonal allergies. She was taking levothyroxine 250 mcg/d, inhaled fluticasone/salmeterol, albuterol, and intranasal mometasone.

Transvaginal ultrasound failed to identify an intrauterine or ectopic pregnancy, and the patient's ovaries were not visualized (uterine anatomy was normal with an endometrial stripe of 5.7 mm). The result of a serum human chorionic gonadotropin (hCG) test was 6.73 mIU/mL. (In a nonpregnant, premenopausal woman, hCG is typically undetectable.) Subsequent serial hCG measurements remained low (6.72-7.09 mIU/mL), but persistent. Given these low hCG levels, it was imperative to rule out an intrauterine or ectopic pregnancy. A urine hCG was negative.

## THE DIAGNOSIS

Because of our patient's vasomotor symptoms, we ordered additional laboratory studies, which revealed an elevated follicle-stimulating hormone (FSH) level (66.08 mIU/mL and 42.2 mIU/mL taken one year apart; normal, 1.98-9.58 mIU/mL in a premenopausal female), an elevated luteinizing hormone (LH) level (46.1 mIU/mL; normal, 2.58-15.5 mIU/mL in a premenopausal female), a low thyroid-stimulating hormone (TSH) level (0.445 mIU/mL; normal, 0.465-4.65 mIU/mL), and a normal prolactin level (12.5 mIU/mL). Based on these results, we diagnosed primary ovarian insufficiency (POI).

## DISCUSSION

POI, formerly known as premature ovarian failure, is defined as 4 to 6 months of amenorrhea or oligomenorrhea in a woman younger than 40 with an elevated FSH on 2 occasions, at least 4 weeks apart.<sup>1-3</sup>

■ **The etiology of POI** is broad. It can be caused by a failure of the pituitary gland or hypothalamus to secrete regulating hormones to stimulate the ovaries. Possible genetic causes include Turner's syndrome, fragile X permutation, and other autosomal disorders that cause follicle dysfunction or destruction.<sup>1</sup> Infections such as mumps, varicella, and tuberculosis are known to affect ovary function, as well.<sup>1,4</sup> In addition, women who are exposed to che-

motherapy or radiation are at higher risk for developing POI.<sup>1</sup>

Because POI and autoimmune disorders tend to occur together, consider screening any patient with POI for disorders such as hypothyroidism and Addison's disease. A serum analysis to evaluate for autoantibodies against steroid-producing cells may be a potential marker for POI in patients with an autoimmune disease that affects the adrenal glands or thyroid. However, patients with isolated Addison's disease, autoimmune hypothyroidism, or diabetes mellitus in the absence of POI do not appear to have steroid-specific antibodies.<sup>2</sup> In our patient's case, her hypothyroidism may have placed her at higher risk of having a second organ system adversely affected by her immune system.

**What causes a false-positive pregnancy test?** This case is unique because our patient reported multiple positive home pregnancy test results and had persistently low serum hCG levels. While she had symptoms that suggested menopause (hot flashes, oligomenorrhea that progressed to amenorrhea), she believed these symptoms were related to pregnancy. In addition to pregnancy, an elevated serum hCG measurement can be due to various malignancies, molar pregnancy, pituitary production of hCG, elevated LH, cross-reactivity with multiple animal exposures (due to the production of human anti-animal antibodies that react with testing), and recent mononucleosis infection.<sup>5</sup>

Other potential causes for false-positive urine pregnancy test results include tubo-ovarian abscess,<sup>6</sup> adenomyosis,<sup>7</sup> and cancers that produce hCG, such as colon, pancreatic, lung, liver, and urothelial bladder carcinoma.<sup>8,9</sup> Urine with significant proteinuria can also cause a positive pregnancy test result.<sup>10</sup>

Our patient likely had a false-positive hCG due to elevated LH, secondary to POI, that demonstrated cross-reactivity on the

hCG assay. The similarity in the chemical structure of the beta subunits of hCG and LH have been reported as false-positive tests in the absence of pregnancy.<sup>5</sup>

Because home pregnancy tests are designed to detect pregnancy as early as possible, they typically feature a high sensitivity by detecting very low levels of hCG, which leads to more frequent false-positive results. It is possible that different assay methods could account for the discrepancy between our patient's positive home pregnancy tests and our negative laboratory urine pregnancy test.

**Our patient** and her husband were both counseled regarding her POI diagnosis. We conducted further studies to establish a possible etiology. She was found to have a normal karyotype of 46, XX, which ruled out Turner's syndrome. Testing for permutations of the FMR1 gene was negative for fragile X syndrome, and antibody testing for thyroid and adrenal glands was negative for autoimmune disease.

Hormone therapy and supplemental calcium and vitamin D are recommended for women with POI to help prevent bone loss and other negative effects of low estrogen.<sup>11</sup> We did not take this tack with our patient, however, because she decided she wanted to pursue a tubal ligation reversal in order to get pregnant. So instead, we decreased her dose of levothyroxine to 150 mcg (since her TSH was low) and we referred her to the Reproductive Endocrinology Department.

## THE TAKEAWAY

Although many cases of POI have no discernible etiology, it is important to rule out malignancies, failure of pituitary production, genetic causes, infections, and other possible causes. Hormone therapy and prophylactic doses of calcium and vitamin D are recommended for patients diagnosed with POI. **JFP**



**Hormone therapy and supplemental calcium and vitamin D are recommended for women with primary ovarian insufficiency to help prevent loss of bone density and other negative effects of low estrogen.**

## References

1. Welt CK. Primary ovarian insufficiency: a more accurate term for premature ovarian failure. *Clin Endocrinol (Oxf)*. 2008;68:499-509.
2. Betterle C, Rossi A, Dalla Pria S, et al. Premature ovarian failure: autoimmunity and natural history. *Clin Endocrinol (Oxf)*. 1993;39:35-43.
3. Fox H. The pathology of premature ovarian failure. *J Pathol*. 1992;167:357-363.
4. Panay N, Kalu E. Management of premature ovarian failure. *Best Practice & Research Clinical Obstetrics and Gynaecology*. 2009;23:129-140.
5. Braunstein GD. False-positive serum human chorionic gonad-

otropin results: causes, characteristics, and recognition. *Am J Obstet Gynecol.* 2002;187:217-224.

6. Levisky ME, Handler JA, Suarez RD, et al. False-positive urine beta-HCG in a woman with a tubo-ovarian abscess. *J Emerg Med.* 2001;21:407-409.
7. Er TK, Chiang CH, Cheng BH, et al. False-positive urine pregnancy test in a woman with adenomyosis. *Am J Emerg Med.* 2009;27:1019.e5-7.
8. Rajabi B, Khoury J, Brewer C, et al. Urothelial bladder carcinoma with choriocarcinomatous differentiation presenting with a false-positive pregnancy test. *Am J Med Sci.* 2013;346:256-258.

9. Marcillac I, Troalen F, Bidart JM, et al. Free human chorionic gonadotropin beta subunit in gonadal and nongonadal neoplasms. *Cancer Res.* 1992;52:3901-3907.

10. Kountz DS, Kolander SA, Rozovsky A. False positive urinary pregnancy test in the nephrotic syndrome. *N Engl J Med.* 1989;321:1416.
11. National Institute of Health, National Institute of Child Health and Human Development. What are the treatments for POI? National Institute of Child Health and Human Development Web site. Available at: <https://www.nichd.nih.gov/health/topics/poi/conditioninfo/Pages/treatments.aspx>. Accessed August 5, 2015.

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