CLINICAL VIGNETTE

Premature Ovarian Insufficiency

Evelyn Curls, MD, MBA

Introduction

Primary ovarian insufficiency (POI) is a condition in which women under the age of 40 experience ovarian dysfunction secondary to premature exhaustion of the pool of primordial follicles.[1] Age related incidence of spontaneous POI is 1 in 250 by age 35 and 1 in 100 by age 40.[2] While natural menopause occurs on average at age 51.4, women affected by POI experience menopausal symptoms including oligomenorrhea or amenorrhea prior to age 40. The main symptom of POI is a reflection of the lack of the sex steroid hormone, estrogen. Prolonged amenorrhea is the most common reason for patients to seek medical attention. POI can occur as a result of many different conditions including Turner's syndrome, FMR1 premutation, exposure to cytoxic drugs, and/or prior irradiation. POI also occurs spontaneously. Presented here is a case of a 35 year old women who complained of symptoms suggestive of spontaneous POI.

Case Report

The patient is a 35-year-old female with past medical history of intermittent asthma who presented to her Primary Care Physician with a 3 month history of amenorrhea. In regards to menstrual and pregnancy history, the patient was G4P202. She had one medical termination, a spontaneous miscarriage at 8 weeks, and two normal spontaneous vaginal deliveries. She denied prior history of irregular menses preceding her last pregnancy. She stated that she had lactation amenorrhea for eight months following the birth of her second child. She reported that upon return of menstruation, she had irregular menses, with cycles occurring every two months after cessation of lactation.

The lack of menstruation for three consecutive months prompted her presentation to her PCP. Initial evaluation included FSH and estradiol, which returned abnormal at 85 and <12, respectively. The patient returned for follow up and upon further questioning reported intermittent hot flashes and new vaginal dryness. She was referred to gynecology for initiation of hormone replacement therapy for treatment of premature ovarian insufficiency. She was started on 0.1mg estrogen patch and oral prometrium then transitioned to estrogen patch and levonorgestral IUD. She reported vaginal bleeding after initiation of hormonal therapy. She noted resolution of hot flashes and improvement in vaginal dryness after 2 weeks of treatment.

Discussion

Primary ovarian insufficiency (POI) is defined as amenorrhea for 4 months, low serum estradiol levels, and two measurements of an elevated Follicle-stimulating Hormone (FSH) above 40IU/L obtained one month apart in a woman under 40 years old.[3] In addition to menstrual irregularity, women with POI present with symptoms typical of menopause including vaginal dryness, subsequent atrophic vaginitis and dyspareunia, as well as hot flashes. In this patient population menstrual irregularities and vasomotor symptoms can be masked by use or oral contraceptive pills, thereby delaying diagnosis. It is not until the oral contraceptive pills are stopped and menses fail to return that patients become aware of the condition. Others notice lack of return of menses after pregnancy. Ovarian insufficiency occurs on a spectrum and FSH levels can fluctuate leading to intermittent ovarian function early in the disorder. Nearly 5-10% of women can become pregnant after diagnosis secondary to fluctuating ovarian function.[1,4]

Diagnosing POI requires exclusion of other disorders, namely pregnancy, hyperprolactinemia, primary adrenal insufficiency, and hypothyroidism. After the diagnosis has been made prompt treatment should be initiated as the premature deficiency of estrogen puts patients with POI at risk. Estrogen deficiency leads to bone loss and a higher incidence of osteoporotic fractures. POI also places patient at increased risk for cardiovascular disease and increased all-cause mortality.[5] Because of lack of estrogen, patients with POI may also be at increased risk of ischemic stroke.[6] Additionally prolonged estrogen deficiency can result in impaired cognition and diminished emotional and sexual well-being.[5]

Conclusion

The aforementioned patient presented with typical symptoms of POI including secondary amenorrhea, hot flashes and vaginal dryness. The American College of Gynecology recommends prompt HRT for treatment of POI. Because of the increased risk of cardiovascular disease and osteoporosis, patients with POI should be treated with HRT until the median age of menopause, which is 50-51.[5,7] This patient was treated with estrogen and progesterone in the form of patch and IUD respectively. Vaginal delivery or transdermal delivery of estrogen offers the most physiologic replacement of sex steroid hormones, and carries the lowest risk of DVT.[7] Progesterone replacement is necessary for any patient with an intact uterus. Progesterone can be delivered subdermally, IUD or oral supplementation.

Care should be taken to address the emotional impact of the diagnosis of POI. Most women report that the diagnosis is emotionally traumatic as they must forgo plans for raising a family. This emotional trauma can lead to the development of depression and anxiety, diagnoses that should be routinely screened for in follow up visits and treated by a therapist with experience in treating women with POI.[5] Longitudinal care includes additional routine screenings. Patients with spontaneous premature ovarian insufficiency have higher rates of hypothyroidism, and subsequently should be tested with annual TSH with reflex. POI carries significant long term emotional, sexual, cardiovascular and bone health consequences. It is important to identify patients with POI early in the disease course to help mitigate these risks. Any woman who presents with amenorrhea over 3 months should receive prompt testing including but not limited to measurement of FSH and estradiol levels. Patients with POI have an average of 3 physician encounters prior to obtaining a diagnosis. It is important to thoroughly investigate any complaints of amenorrhea to avoid delayed or misdiagnosis.

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