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CLINICAL VIGNETTE

Investigating Female Hypogonadotropic Hypogonadism

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A 23-year-old female presented to the Endocrine department for evaluation and management of amenorrhea and osteopenia. She had her first period when she was around 17 or 18 years old. Since that time, she had only spontaneous menstruation, 2 to 3 periods which lasted for about 3 weeks, with a brownish discharge over a period of 3 years. She was subsequently started on Depo-Provera at age 20 to 22 and had one period during the progesterone therapy. She has always been slender, with a BMI between 18 to 19. Usually her weight is around 85 to 87 pounds. She gained some weight with Depo-Provera and lost weight when she changed to a progesterone implant. Her highest weight was 98 pounds when she was on Depo-Provera. She was a competitive gymnast until age 14, training at least 20 hours a week. She started gymnastics at age 2 to 4 years. She currently rows and goes to the gym to do elliptical 3 to 4 days a week for 1 hour. She provides no history of anorexia or bulimia. She had acne while on Depo-Provera and used spironolactone for 4 to 5 years. No facial hair. No scalp hair loss. She was previously evaluated by Pediatric Endocrinology including normal karyotyping, 46XX, and normal labs including, FSH, LH, and testosterone levels, prolactin and thyroid testing. She was also evaluated for short stature and no secondary cause was identified. She tried oral contraceptives and transdermal estrogen. However, she had severe migraines as well as acne.

Laboratory evaluation demonstrated an undetectable low LH, FSH, and estradiol. Testosterone, DHEA sulfate, TSH, and prolactin levels were normal. MRI of the pituitary gland was normal. She was also shown to have osteopenia on bone density. Pelvic ultrasound was normal.

The presumed diagnosis is functional hypothalamic amenorrhea. The patient was aggressively counseled in nutrition and moderating exercise. She was also counseled to increase dietary calcium and maintain vitamin D levels in normal range. She subsequently gained weight reaching a BMI of 21. Approximately one year after weight gain, the patient spontaneously resumed menstrual cycles.

Discussion

Functional hypothalamic amenorrhea is typically due to decreased caloric intake and/or increased energy expenditure. It is a form of chronic anovulation due to altered GnRH function leading to reduced LH and FSH production. This subsequently leads to lower estradiol concentrations. It is commonly seen in female athletes and military personnel. Other etiologies need to be ruled out including thyroid dysfunction, hyperprolactinemia,

hyperandrogenism, and pregnancy.¹ After pregnancy is ruled out, a progestin challenge can be administered to rule out abnormalities of the outflow tract. Finally, it is recommended to obtain a baseline bone density.

Treatment is aimed at optimized the energy balance.² This involves decreased exercise and increased caloric consumption as well as mental health support. It is advisable not to use OCPs to induce menses or improve bone mineral density as it may mask an ongoing nutritional deficiency leading to further bone loss.³ It is reasonable to consider short term use of transdermal estradiol (100 mcg) with oral progesterone in patients with ongoing amenorrhea in the setting of attempted behavioral changes.⁴

In terms of bone loss, patient should be advised to take 1200 to 1500 mg of calcium through diet and supplementation and maintain vitamin D levels between 30 to 50 ng/ml. Osteoporosis therapy such as teriparatide is not advised unless the patient is suffering recurrent fractures.¹

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