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CASE REPORTS

RARE AETIOLOGY FOR AMENORRHEA IN A 14-YEAR-OLD ADOLESCENT GIRL

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ABSTRACT

Secondary amenorrhea involves a thorough investigation into hypothalamic, pituitary, ovarian and uterine factors. The epidemiology of secondary amenorrhea encompasses common causes such as pregnancy, polycystic ovary syndrome and mental health-related factors, alongside the infrequent yet impactful occurrence of premature ovarian insufficiency (POI). POI, affecting around 1% of women under 40, stems from various causes, including autoimmune mechanisms, genetic abnormalities and ovarian injury. A presented case involves a 14-year-old with regular menses until age 13, presenting with six months of amenorrhea. The multidisciplinary evaluation ruled out common causes, leading to an in-depth investigation revealing elevated FSH levels indicative of POI. The discussion emphasizes the importance of family history, thorough. Psychological support, addressing estrogen deficiency-related concerns and managing infertility become integral components. Hormone replacement therapy and fertility preservation methods offer potential interventions. Additionally, encouraging a lifestyle conducive to bone and cardiovascular health becomes paramount. This study aims to heighten awareness among healthcare practitioners regarding rare conditions like POI in adolescents with amenorrhea, facilitating early diagnosis and comprehensive patient care.

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Amenorrhea, Secondary amenorrhea, Premature ovarian insufficiency.

Introduction

Menarche is arguably the biggest physical change that occurs during puberty in females. Age at menarche is viewed as an evolutionary adaptive mechanism that finds a balance between early reproduction, thus lowering the risk of death before reproduction and large body size increasing fertility and lowering offspring mortality.[1] From 15 to 16 years during the 19th century to 12 to 13 years by the middle of the 20th century, these range of variation is explained by improvements of living conditions, nutrition and health care.[1] In Portugal one recent study demonstrated that the onset of female maturation in Portuguese women continues to decline, with no hint of an imminent slow-down toward a plateau.[1] The absence of menses in a woman of reproductive age is defined as amenorrhea and is divided into primary and secondary types. Secondary amenorrhea is defined as the absence of menses for 6 months in females with previously irregular menstrual pattern, or the absence of menses for more than three months in females who previously had regular menstrual cycles.[2]

A number of conditions should be taken into account when determining its aetiology. Anatomically we can divide the approach into: hypothalamus, pituitary, ovary and uterus. Ruling out pregnancy being the first step, measurement of serum beta subunit of human chorionic gonadotropin (hCG) is the most sensitive test to accomplish that. The next step should include a detailed clinical history addressing: drugs, stress, changes in weight, recent exercise habits, diets, history of mental illness/ eating disorder, systemic illness, hirsutism, acne, headaches, visual field defects, hot flashes, vaginal dryness, poor sleep and decreased libido. Physical examination is essential and should look for signs of hyperandrogenism, thyroid disease, galactorrhea and body mass index. Finally initial laboratorial tests are essential to determine and locate any disturbances on the hypothalamic-pituitary-ovarian axis: follicle-stimulating hormone (FSH), serum prolactin (PRL), serum estradiol (E2) and thyroid-stimulating hormone (TSH).

Epidemiologically, the most frequent causes for secondary amenorrhea are: pregnancy, polycystic ovary syndrome, stress and factors related to mental health, weight loss, excessive physical exercise, thyroid pathology and hyperprolactinemia.[2,3] Additionally, a rare but life-changing cause of secondary amenorrhea can occur, premature ovarian insufficiency (POI). POI has previously been referred to as premature ovarian failure, but due the grade of ovarian impairment fluctuation over time, this terminology has fallen out. The prevalence of POI in women under 40 years old is estimated at 1% in the general population.[2,4] Data

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regarding its prevalence in adolescent females was not found in literature.

POI can arise from multiple causes that can be divided in disorders that cause ovarian follicle dysfunction or follicle depletion.[5,6] Mutations on the receptor of either Follicle-stimulating-hormone or Luteinising-hormone elicit a signalling defect that ultimately produce ovarian follicle dysfunction. Autoimmunity is another mechanism that is linked to follicle dysfunction, with over 20% of the patients having an associated autoimmune disease, the most common being autoimmune thyroiditis.[2] Adrenal and thyroid autoimmunity syndromes, adding to lymphocytic oophoritis are some examples and the reason why adrenal-cell antibodies (21-hydroxylase autoantibodies), thyroid peroxidase antibodies, antithyroglobulin antibodies and ovarian antibodies should be tested.[5] Follicle deletion occur in women with structural and numerical abnormalities of the X chromosome, Turner Syndrome is one example between others like Autosomal or X translocations or X Trisomy or polysomy. Other causes of POI include ovarian injury due to surgery, chemotherapy or irradiation. It is important to notice that approximately 90% of all diagnosed cases of spontaneous POI do not have a determined underlying etiology.[7]

The three main signs/symptoms of POI are amenorrhea for at least four months, insufficient sex hormone and two measurements of serum FSH concentrations of more than 40 IU/L at least one month apart in a woman under 40 years old (>2 Standard Deviation below the mean menopausal age).[5,8] Clinically, adding to amenorrhea, POI may manifest with symptoms of estrogen deficiency such as hot flashes, night sweats, sleep disturbance and dyspareunia. It is important to notice that not all patients have profound estrogen deficiency, consequently vaginal examination can be normal.[6]

As to imaging, it is vital to obtain analyse the patient's reproductive tract, generally with the use of transvaginal ultrasound, in order to determine any abnormalities. Pelvic ultrasound or magnetic resonance can provide information regarding the volume of the ovaries as well as antral follicle count within each ovary. Ovarian volume is anticipated to be low with few to no antral follicles visualized in POI.[7] An additional laboratorial test can help the diagnosis by being a marker for ovarian reserve, antimullerian hormone (AMH), with most women diagnosed with POI having levels under 1 ng/mL.[9]

Case Report

A 14-year-old adolescent, who experienced menarche at the age of 10 and had regular menses until the age of 13, presented with a six-month history of amenorrhea. She had no significant past medical history, including no prior surgeries, chemotherapy, or pelvic traumas and was not on any regular medications. Upon referral to the pediatric endocrinology clinic, an evaluation was performed. During the evaluation, the patient denied recent weight loss, excessive stress, excessive physical activity, or any known systemic diseases, particularly of autoimmune nature. Her Body Mass Index (BMI) was measured at 22 kg/m2. On physical examination, her height was within the 40th percentile for her age, no aberrant dysmorphic features and there were no signs of androgen excess such as hirsutism or significant acne. Initial laboratory test were performed and results were as follows: Pregnancy test (beta subunit of human chorionic gonadotropin) was negative; Estradiol: 13 pg/ml, FSH: 96.95 mUI/ml; LH (Luteinizing Hormone): 27 mUI/ml; TSH and prolactin levels were within the normal range for her age. Subsequently supplementary exams were performed including dosing of thyroid, ovarian and adrenal antibodies, dosing of Antimullerian hormone, genetic profile including karyotype and pelvic ultrasound.

Discussion

Detailed family history, careful physical examination and laboratorial tests focused on the hypothalamic-pituitary-ovarian axis are essential when assessing secondary amenorrhea. The diagnosis of POI can be made definitively in women younger than 40 years with irregular menses in association with follicle-stimulating hormone (FSH) concentrations in the menopausal range levels, as defined by the testing laboratory. As women's whole health, including bone density, neurological and cardiovascular systems, well-being and sexual health, is affected by primary ovarian insufficiency, a multidisciplinary approach should be addressed in the management of adolescents with POI. It is vital to provide the patient and her family with psychological support, address issues related to estrogen deficiency (osteoporotic fractures) and manage the ensuing infertility. Hormone replacement therapy and fertility preservation methods like cryopreservation of eggs or embryos or preservation of ovarian tissue are available as treatments for primary ovarian insufficiency. Also, women diagnosed with POI should be motivated to lead a lifestyle that enhances their bone and cardiovascular well-being. This involves participating in regular weight-bearing physical activities, ensuring sufficient daily intake of calcium (at least 1200 mg) and vitamin D (a minimum of 800 IU), adopting a balanced diet to prevent obesity and undergoing screenings for cardiovascular risk factors. Any identified risk factors should be treated accordingly.

Compliance with Ethical Standards

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Conflict of Interest : None

References:

1. Queiroga, A. C., Silva, R. S., Santos, A. C., Maia, I., & Barros, H. (2020). Secular trend in age at menarche in women in Portugal born between 1920 and 1992: Results from three population-based studies. American Journal of Human Biology. doi:10.1002/ajhb.23392.
2. Deligeoroglou E, Athanasopoulos N, Tsimaris P, et al. Evaluation and management of adolescent amenorrhea. Ann N Y Acad Sci 2010; 1205:23.
3. Diaz, A., M.R. Laufer & L.L. Breech. 2006. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Pediatrics 118: 2245-2250.
4. Rudnicka E, Kruszewska J, Klicka K, Kowalczyk J, Grymowicz M, Skórska J, Pięta W, Smolarczyk R. Premature ovarian insufficiency - aetiopathology, epidemiology and diagnostic evaluation. Prz Menopauzalny. 2018 Sep;17(3):105-108. doi: 10.5114/pm.2018.78550. Epub 2018 Sep 30. PMID: 30357004; PMCID: PMC6196779.

5. De Vos M, Devroey P, Fauser BC. Primary ovarian insufficiency. Lancet. 2010 Sep 11;376(9744):911-21. doi: 10.1016/S0140-6736(10)60355-8. Epub 2010 Aug 11. PMID: 20708256.
6. Nelson LM. Clinical practice. Primary ovarian insufficiency. N Engl J Med. 2009;360(6):606-614. doi:10.1056/NEJMcp0808697.
7. Sullivan SD, Sarrel PM, Nelson LM. Hormone replacement therapy in young women with primary ovarian insufficiency and early menopause. Fertil Steril. 2016 Dec;106(7):1588-1599.
8. Natalia Sopiarz; Paul B. Sparzak, Primary Ovarian Insufficiency, StatPearls Publishing; 2023 Jan.
9. Lambrinoudaki I, Paschou SA, Lumsden MA, Faubion S, Makrakis E, Kalantaridou S, Panay N. Premature ovarian insufficiency: A toolkit for the primary care physician. Maturitas. 2021 May;147:53-63.