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Background: Complete androgen insensitivity syndrome (CAIS) is a rare disorder of sex development and primary amenorrhea results in an XY karyotype but female phenotype. Patients with this syndrome have lower bone mineral density (BMD) when compared to age matched controls.
Clinical Case: A 44-year-old phenotypic woman with a history of complete androgen insensitivity syndrome presented for follow-up. She was previously on hormone replacement therapy (HRT) at various doses from the age of 12 until her early 30s when her therapy became sporadic. At age 40, she was prescribed transdermal estrogen therapy but discontinued soon after a dermatologic reaction and had not been on any form of hormone replacement since that time. Past medical history was significant for karyotype 46 XY, osteochondritis dissecans of right ankle and bilateral orchiectomy at age 4. She was single with one adopted child. Physical examination showed a height 75 inches, weight 244 lbs and a normal heart, lung, and abdominal examinations. Laboratory results showed estradiol 12.3pg/mL(7.63-42.6), total testosterone 12.0 ng/dL(7-40), FSH 109.6 mIU/mL(25.8-134.8), LH 42.49 mIU/mL(7.7-58.5), anti-mullerian hormone < 0.015 ng/mL (0.26-5.81), inhibin B <7.0 pg/mL(<17), androstenedione 48 ng/dL(41-262), dihydrotestosterone 2.7 ng/dL(4-22) and dehydroepiandrosterone sulfate 209 ng/dL(31-701). A baseline DXA showed low bone density for age with T-score (Z-score) of -2.0 (-1.6) lumbar-spine; -1.6 (-1.2) femoral neck, -1.1 (-0.8) total hip and -2.5 (-2.0) forearm.
Discussion:CAIS is caused by a mutation in the androgen receptor (AR) located on the X-chromosome causing complete unresponsiveness to androgen hormone. Karyotype is XY but feminization occurs due to aromatization of androgen to estrogen. Gonadectomy for testicular malignancy prevention is controversial as testicular tumors in CAIS is generally low and gonadal resection subjects individuals to lifelong hormone replacement. These patients also have lower BMD when compared to female or male age matched controls. This is even more apparent in those with removed gonads. Low BMD is exacerbated by poor compliance, inadequate dose or inappropriate HRT. Whether or not fracture risk is higher has yet to be elucidated. Currently, there is no guideline on how to manage low BMD including osteoporosis in this patient population. It is important to counsel patients with CAIS on BMD loss and to ensure optimization of factors that affect bone health including compliance with HRT, vitamin D/calcium intake and exercise.
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Reproductive Endocrinology
REPRODUCTIVE HEALTH CASE REPORTS

Cyclical Premenstrual Psychosis - Sometimes It Is Your Hormones

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Background: Menstrual psychosis is a broad term used to describe a number of disorders characterized by the acute onset of psychotic symptoms with brief duration, complete resolution of symptoms between episodes, with timing related to menses. This entity was first described in the 18th century, with only 27 confirmed cases using strict diagnostic criteria. While research into causation is limited, estrogen withdrawal is thought to precipitate psychotic symptoms. We describe a case of premenstrual psychosis successfully treated with use of transdermal hormonal contraception and extended menstrual cycling. **Clinical Case:** A 25-year-old non-binary biologic female (they/them/theirs) with bipolar disorder, anxiety, and psychogenic non-epileptiform seizures was referred to endocrinology for evaluation of recurrent psychotic symptoms associated with menses. They endorsed stable mental health symptoms on aripiprazole except during the seven days prior to their menstrual cycle. During this time they reported persistent auditory hallucinations along with dysmenorrhea, with symptoms resolving at the onset of menses. Timing of menarche was uncertain, however they reported oligomenorrhea until beginning oral contraceptives at age nineteen, after which they developed regular monthly cycles accompanied by psychotic symptoms. Pituitary and ovarian hormone levels were unable to be assessed due to hormonal contraception. Prolactin was 8.3 ng/mL (3-30 ng/mL). In order to limit hormonal fluctuations from daily oral contraceptive pills and monthly withdrawal, the decision was made to transition to transdermal norelgestromin and ethinyl estradiol patches changed weekly, with extended cycling to allow one menstrual cycle every three months. At follow-up visit nine months later they reported resolution of auditory hallucinations on this regimen, with symptoms recurring only during extreme stress. **Conclusions:** While the etiology of menstrual psychosis is unclear, described treatments include a combination of neuroleptics and hormonal therapy, including estrogen, progesterone, and GnRH agonists. As symptoms did not resolve until suppression of monthly menstrual cycles, this case supports the estrogen withdrawal hypothesis. Our case adds to the literature both in that transdermal, rather than oral or injectable therapy was used, and treatment was successful in alleviating the patient's psychotic symptoms, improving their mental health and quality of life. **References:** (1) Brockington, I. Menstrual Psychosis. World Psychiatry 2005;4(1):9-17. (2) Reilly, T.J., Sagnay de la Bastida, V.C., Joyce, D.W., Cullen, A.E., McGuire, P. Exacerbation of Psychosis During the Perimenstrual Phase of the Menstrual Cycle: Systematic Review and Meta-analysis. Schizophrenia Bulletin 2020;46(1):78-90.

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Diagnosis of Sertoli-Leydig Cell Tumor of the Ovary Complicated by the Pattern of Hyperandrogenemia and Results of Imaging

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Introduction: Virilization in a postmenopausal woman requires evaluation for an androgen-secreting tumor. The differential diagnosis includes adrenal carcinomas and adenomas and Sertoli-Leydig cell tumors, granulosa-theca cell tumors, and hilus-cell tumors of the ovaries. We present a case of virilization in a postmenopausal woman caused by a Sertoli-Leydig cell tumor (SLCT) in which evaluation was complicated by the pattern of androgen elevation, bilateral adrenal nodules, and absence of an adnexal mass. **Case:** A 64-year-old female was referred for evaluation of hyperandrogenism. Hirsutism, temporal hairline regression, and unusually deep voice were noted on examination. Two total testosterone levels obtained one month apart were 146 ng/dL (2-45), and measurements of dehydroepiandrosterone sulfate (DHEAS) and androstenedione were 299 mcg/dL (12-133) and 1.84 ng/mL (0.130-0.820), respectively. Abdominal CT revealed bilateral adrenal nodules - 2 cm and - 5 Hounsfield units (HU) on the left, and 1.5 cm and 5 HU on the right - but no ovarian masses. Transvaginal ultrasonography also failed to identify a discrete ovarian mass but showed endometrial hyperplasia. Virilization, magnitude of testosterone elevation, and results of imaging were felt to be most strongly indicative of ovarian hyperthecosis, and the patient underwent laparoscopic bilateral salpingo-oophorectomy and hysterectomy. The right ovary was 2.3 cm in largest diameter and approximately 90% replaced by an orange-red mass that showed Sertoli and Leydig cells on microscopy, immunohistochemical staining for the sex cord proteins inhibin and calretinin, and presence of the Leydig cell marker melan A. It was classified as well differentiated. Additional CT imaging and robotic assisted laparoscopy confirmed a stage IA tumor. One month after surgery, hyperandrogenemia had completely resolved (total testosterone < 10 ng/dL, androstenedione 0.379 ng/mL, and DHEAS 99 mcg/dL), and changes of virilization had mostly regressed at an eight months appointment. **Discussion:** SLCTs are a type of sex-cord stromal ovarian tumor. They constitute < 0.5% of ovarian tumors but account for approximately 75% of testosterone-secreting ovarian masses. This patient's case was unusual for multiple reasons: 1. Age - most SLCTs are diagnosed in the second or third decade, 2. Imaging - CT and ultrasonography usually show a solid or solid and cystic adnexal mass, and co-existing adrenal nodules are rare, likely due to typical young age of presentation, and 3. Pattern of androgen elevation - DHEAS was more than two-fold elevated, and usually < 10% of DHEA and DHEAS are produced by the ovaries. However, DHEAS fell significantly after oophorectomy. SLCTs are a potential etiology of virilization in postmenopausal women even in the absence of a detectable adnexal mass and when biochemistries and imaging raise the possibility of an adrenal source of androgen.

Reproductive Endocrinology

REPRODUCTIVE HEALTH CASE REPORTS

Effect of Omalizumab for Autoimmune Progesterone Dermatitis Refractory to Bilateral Oophorectomy: A Case Report

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Background: Autoimmune progesterone dermatitis (APD) is a rare skin condition caused by sensitivity to high levels of progesterone secreted during the luteal phase of the menstrual cycle. This may be due to various pathophysiological mechanisms including a Type I and Type IV hypersensitivity reaction, and potential cross-reactivity with other endogenous steroid hormones such as 17-α-hydroxyprogesterone. We present the case of a patient with APD who had her flare-up episodes controlled using omalizumab, after a bilateral oophorectomy failed to resolve her symptoms. **Clinical Case:** A 34-year-old female presented to our Endocrine Clinic with marked Cushingoid features secondary to high-dose oral prednisone prescribed for APD diagnosed six years earlier. She first developed a pruritic maculopapular rash on her arms and legs just after the birth of her second child in 2009. The rash was also associated with headaches and diffuse angioedema. It presented in a cyclical fashion, beginning one to two days before the start of her menstrual cycle, and ending shortly after it was complete. The severity of symptoms increased as time went on, and flare-ups began to also include dyspnea, nausea, vomiting and abdominal pain. After three years of persistent symptoms, the diagnosis of APD was confirmed by a progesterone skin test. Her symptoms were improved with oral prednisone use, however breakthrough episodes still occurred. After multiple failed treatment modalities, she elected bilateral oophorectomy in 2018. However, her symptoms of APD persisted and she still required high-dose oral prednisone. Her condition was further complicated by vasomotor menopausal symptoms and progressive iatrogenic Cushing's syndrome. She eventually was started on Omalizumab, which helped resolve her APD symptoms and allowed her to wean off prednisone. Vasomotor menopausal symptoms were resolved using conjugated estrogens with bazedoxifene. However, her symptoms of diffuse bony indeterminate bony pain and arthralgias which started whilst on prednisone have persisted in spite of discontinuing prednisone. **Conclusion:** To our knowledge, this is only the third case of APD which was successfully treated with Omalizumab and the first case where a bilateral oophorectomy failed to resolve symptoms of APD in the literature. Our case also demonstrates the complications of vasomotor menopause symptoms secondary to a bilateral oophorectomy, as well as the adverse effects of long-term glucocorticoid therapy.

Reproductive Endocrinology

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Euglycemic Diabetic Ketoacidosis in a Patient With Gestational Diabetes Mellitus and COVID-19 Infection

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