

Reproductive Endocrinology

REPRODUCTIVE HEALTH CASE REPORTS

A Case of Autoimmune Polyglandular Syndrome Type 3b Initially Presenting as Generalized Weakness in an Elderly Patient

Hazem Ayesah, MD, MPH¹, Cameron Burmeister, MD, MS¹, Ahmed Abdelrahman, MD¹, Azizullah. Beran, MD¹, Pooja Suri, MD².

¹UNIVERSITY OF TOLEDO, Toledo, OH, USA, ²Promedica Toledo Hospital, Toledo, OH, USA.

Introduction: Autoimmune polyglandular syndrome (APS) is a multiorgan genetic autoimmune disease. APS-3B subtype is autoimmune thyroiditis with pernicious anemia. In this case, we will discuss an elderly female patient diagnosed with APS-3B.

Case Presentation: A 69-year-old Caucasian female patient with a past medical history of autoimmune thyroiditis presented to the emergency department with a two-month history of generalized weakness and nausea. Associated symptoms included shortness of breath and diarrhea. Review of systems was otherwise unremarkable. Physical exam was positive for depigmented skin macules over the upper extremities. Lab results showed hemoglobin 8.2 [11.7 - 15.5 g/dL], MCV 121 [80 - 100 fL], platelets 144,000 [150 - 450 X10E9/L], WBC 1.9 [4.0 - 11.0 X10E9/L], LDH 1153 [100 - 235 U/L], TSH 0.28 [0.49 - 4.67 uIU/mL], free T4 1.7 [0.61 - 1.60 ng/dL], direct Coombs test negative. Iron saturation 55%, vitamin B12 level <50 [180 - 914 pg/mL], folate >25 [5.8 ng/mL], total bilirubin 2.3 [0.3 - 1.2 mg/dL], haptoglobin <30 [32 - 228 mg/dL], AST 43 [0 - 41 U/L], reticulocyte 1.4%. Blood smear showed absolute neutropenia with flow cytometry unremarkable. Chest x-ray and urinalysis were negative. Immunofixation showed low IgM 44 [45 - 281 mg/dL], low IgG 619 [635 - 1,741 mg/dL]. Intrinsic factor antibodies (IF-Ab) were positive. Hematology reported that hemolytic anemia is less likely given Coombs test was negative. About 1.5% of Vitamin B12 deficiency present with a hemolytic picture due to ineffective erythropoiesis while Coombs test help to differentiate it from autoimmune hemolytic anemia. Diagnosis of pernicious anemia was made and the patient started on vitamin B12 injections. The combination of pernicious anemia, autoimmune thyroiditis, and vitiligo supported the diagnosis of autoimmune APS-3B. There was a normalization of vitamin B12 level and symptomatic improvement on a one-week follow-up.

Discussion: The patient was diagnosed with autoimmune thyroiditis in 2014 with positive anti-TPO antibodies and elevated TSH; she required levothyroxine supplementation since diagnosis. Hypothyroidism causes macrocytic anemia, which may delay pernicious anemia diagnosis. APS-3B is associated with HLA-B8 and/or DR3 and DR5. Many studies reported that autoantibodies can be detected before developing symptoms of organ involvement. Thorough family history provides support for autoantibody testing to detect cases of APS-3B earlier. Active surveillance and early diagnosis will help minimize invasive testing such as bone marrow biopsy, so proper history taking is a key factor to early diagnose these conditions.

Conclusion: APS-3B is a rare disorder. Diagnosis is difficult hypothyroidism causes macrocytic anemia. Early

detection of APS-3B may help to prevent complications that increase the risk of mortality and morbidity, particularly in the elderly population.

Reproductive Endocrinology

REPRODUCTIVE HEALTH CASE REPORTS

A Case of Hyperreactio Luteinalis Complicated With Biochemical Hyperandrogenism, Symptomatic Hyperthyroidism and Preeclampsia

KY Wong, MRCP, MWH Mak, MRCP, KM Lee, MRCP, KF Lee, FRCP.

Kwong Wah Hospital, Hong Kong, Hong Kong.

Background: Hyperreactio luteinalis (HL) describes the development of multiple large ovarian cysts during pregnancy, which regress post-partum. We report a case of HL complicated with preeclampsia, biochemical hyperandrogenism and hyperthyroidism. **Clinical Case:** A 31-year-old non-obese Chinese woman presented at 14-week gestation for lower abdominal pain. USG showed a single fetus, multiple ovarian cysts with largest measured 39.5ml. She complained of hand tremor, palpitation but no vomiting. She had no goiter, orbitopathy or family history of thyroid disease. fT4 was 23.1pmol/L (normal: 9.8-19.8pmol/L) and TSH was <0.01mIU/L. Anti-TG, anti-TPO and anti-TSHR antibodies were negative. She had history of silent miscarriage at 6-week gestation in her first pregnancy 2 years ago, USG showed normal ovaries at that time. Carbimazole was started at 16-week gestation for fT4 26.6pmol/L (normal: 9.4-18.5pmol/L). The largest ovarian cyst increased to 130ml at 19-week gestation. Serum β -hCG was 251926IU/L (normal: 4060-165400IU/L). HL with hCG-mediated hyperthyroidism was suspected. Serum total testosterone was 22.9nmol/L (normal: 2.2-10.7nmol/L) and serum androstenedione was 70.5nmol/L (normal: 0.28-9.81nmol/L). Ferriham Gallwey score was 4. fT4 fell to 13.8pmol/L (normal: 8.8-17.0pmol/L) but TSH remained suppressed. Carbimazole was stopped at 22-week gestation with no rebound in fT4 level. She developed preeclampsia and GDM at 27-week gestation. IUGR was evident despite decreasing β -hCG level and ovarian cyst shrinkage. She had emergency LSCS for severe preeclampsia at 33-week gestation. A 1510g female baby with normal genitalia was delivered. Placenta pathology was normal. 2 days after delivery, β -hCG fell to 7081IU/L; fT4 was 9.9pmol/L (normal: 9-19pmol/L) and TSH was 0.25mIU/L (normal: 0.35-4.5mIU/L). **Clinical Lessons:** 1) hCG stimulates growth of ovarian stroma and androgen secretion, results in virilization in 30% of HL patients. However, only 5% of patients had hyperthyroidism. LH and hCG are structurally similar and bind to the same receptor. In contrast, hCG is a weak agonist of TSH receptor: a hCG level of more than 100000IU/L is required to cause clinical thyrotoxicosis. Since 30% of HL patients have normal hCG level, this may explain the lower incidence of hyperthyroidism than hyperandrogenism. 2) Degree of maternal virilization does not correlate with testosterone level. Study by Condic et al. found significant overlap of testosterone levels in women with (13.7-197.5nmol/l) and without (6.2-37.3nmol/l) virilization. Genetic polymorphism of androgen receptor may account for the different clinical manifestation. Fetal

virilization is rare, due to protective role of placental aromatase. 3) Elevated hCG in apparently “normal” singleton pregnancy may be due to poor placentation in early gestation and is a risk factor for preeclampsia and IUGR in HL patients.

Reproductive Endocrinology REPRODUCTIVE HEALTH CASE REPORTS

A Rare Case of Autoimmune Progesterone Disease

Preethi Padmanaban, MBBS MD.

Hamilton Medical Center, Dalton, GA, USA.

Background: Autoimmune progesterone disease is a rare disease, with fewer than 200 reported cases. Unfortunately, there are no published estimates of incidence or prevalence.

Clinical Case: A 24 year-old woman with no significant past medical history presented with sudden and new onset swelling of the lips which was unresponsive to Benadryl and prednisone. Swelling eventually progressed into blistering over the lips, oral, pharyngeal mucosa and tongue. She was admitted to the hospital for suspicion of Steven Johnson syndrome and was discharged after resolution of skin and oral lesions following treatment. She presented again in 3 months with full body rash and blisters now involving oral and vaginal mucosa. She underwent biopsy of these lesions during this admission and findings were suspicious for drug eruption vs erythema multiforme. Unfortunately, inciting drug or event could not be associated even with pathological diagnosis. She continued to have mucocutaneous flare every month for the next 8 months with multiple hospitalizations and was treated with antibiotics during these admissions. Over the course of her evaluation, it was noted that her symptoms seemed to coincide with her menstrual cycles. Her IUD was removed and she was started on OCPs but her symptoms persisted without any improvement. She underwent intradermal progesterone challenge test at tertiary center for ongoing cyclical dermatitis and tested positive for progesterone sensitivity. She was diagnosed with Autoimmune Progesterone dermatitis. She had to ultimately undergo total abdominal hysterectomy and bilateral salphingo-oophorectomy as she failed OCPs and had adverse effects to progesterone desensitization including full body rash and blisters. Post operatively, she has been started on IM depot injections of estrogen and vaginal estrogen cream.

Conclusion: Autoimmune progesterone disease also known as progesterone dermatitis or progesterone hypersensitivity is not associated with other autoimmune diseases and usually affects women of reproductive age. It is a rare disorder with variable presentation and often overlaps with other forms of dermatosis. It is commonly underdiagnosed or misdiagnosed and appropriate treatment is often delayed. High clinical suspicion for symptoms of cyclical nature is necessary for making the diagnosis.

Reproductive Endocrinology REPRODUCTIVE HEALTH CASE REPORTS

Adult Onset Isolated Hypogonadotropic Hypogonadism- a Cause of Secondary Amenorrhea

Shailendra B. Patel, BM, ChB, DPhil¹, Srujana Kamala Yada, MD².

¹University of Cincinnati, Cincinnati, OH, USA, ²University of Cincinnati Medical Center/College of Medicine Endocrine Fellowship Program, Cincinnati, OH, USA.

A 23-year-old African American female was referred for secondary amenorrhea evaluation. She attained menarche at 12 years and had regular menses. At 18 years, she used OCPs for few months, and used plan B, after which her menses stopped. She had hot flashes and sweating. She was placed on progesterone, but never had withdrawal bleeding. Review of systems was positive for intentional weight loss after her menses stopped, hair loss and nipple discharge. She denied any loss of sensation of smell. She has a PMH of asthma, anxiety and OSA. Family history was not significant for any fertility issues. She smoked cannabis after menses stopped. On physical examination, vitals were stable, BMI of 35 kg/meter², well-developed secondary sexual characteristics, no thyromegaly, acne or hirsutism. Upon work up, CBC, CMP were normal, Urine pregnancy test was negative, gonadotropins were undetectable (FSH- <0.7mIU/ml, LH- <0.2mIU/ml), anti-mullerian hormone was 3.82ng/ml (WNL), Estradiol was also absent (<15pg/ml), with a low Total testosterone (11ng/dl), TSH was 1.17uIU/ml, Free T4 was 1.1ng/dl, ACTH was 9.58pg/ml, Cortisol was 14.8mcg/dl, and Prolactin was 1.5ng/ml. MRI brain was normal with normal pituitary gland, no focal lesion visualized. Pelvic ultrasound showed ovaries 5.9mL and 4.6mL with multiple follicles present bilaterally. Diagnosis of adult-onset isolated hypogonadotropic hypogonadism (IHH) was made. Patient was started on estradiol patches and progesterone. IHH is a genetic disorder of defective production or action of GnRH. IHH when associated with anosmia is called Kallmann syndrome. It was first described by German American geneticist Joseph Kallmann in 1944. GnRH is a decapeptide, produced in arcuate nucleus and pre-optic nucleus of hypothalamus. GnRH stimulates anterior pituitary to secrete FSH and LH. IHH is caused due to impaired migration of GnRH neurons to brain during embryogenesis. It is inherited as autosomal or X-linked dominant or recessive. Gene mutations associated are ANOS-1, FGFR, PROK-2. It is rare in females. IHH has a broad spectrum of clinical presentation from complete absence of sexual development to partial completion of puberty. It presents with micropallus, cryptorchidism, cleft lip/palate, syndactyly, renal aplasia. In childhood presents with anosmia, hearing deficits, dental agenesis, mirror movements, short stature. During puberty, absent pubertal growth spurt, amenorrhea, lack of virilization, no secondary sexual characteristics, infertility. In partial forms, known as Adult onset or acquired form of IHH, patients have slight testicular growth, thelarche, menarche. Goals of treatment are- pubertal induction, maintenance of sexual maturation and restoration of fertility. In females, pre-puberty only estrogen is given, after puberty both estrogen and progesterone are used, for fertility, pulsatile gonadotropins or GnRH analogues are used.

Reproductive Endocrinology REPRODUCTIVE HEALTH CASE REPORTS