Reproductive Endocrinology

REPRODUCTIVE HEALTH CASE REPORTS

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

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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.

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

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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