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SAT-LB38

Objectives: Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare condition of Cushing's syndrome (CS) characterized by benign bilateral enlarged adrenal masses. The aim of this study is to analyze clinical features, individualized treatment and prognosis of PBMAH.

Methods: Clinical data of 46 patients with PBMAH were retrospectively analyzed compared with 205 patients with unilateral adrenal cortisol-secreting adenoma (UAA), including general information, cortisol evaluations, treatments and prognosis.

Results: PBMAH were more frequently found in male, the average age at diagnosis was (52.1±8.7) years; most patients visited hospital due to incidentally findings of bilateral adrenal lesions; had a higher proportion of subclinical CS. The PBMAH cases showed significantly lower levels of basal cortisol, LDDST suppressed cortisol, and HDDST suppressed cortisol than the UAA cases (452.6 ± 183.3 vs. 578.7 ± 166.4 nmol/L, P = 0.003; 394.5 ± 298.9 vs. 549.2 ± 217.7 nmol/L, P= 0.002; 397.3 ± 282.3 vs. 544.3 ± 187.6 nmol/L, P =0.003). Similarly, the PBMAH cases had significantly lower levels of basal 24-h UFC, LDDST suppressed 24-h UFC, and HDDST suppressed 24-h UFC than the UAA patients (1144.4 ± 1048.1 vs. 1674.9 ± 1520.4 nmol/24h, P = 0.032; 1157.3 ± 1483.5 vs. 1940.1 ± 1360.9 nmol/24h, P = 0.003; 1256.4 ± 1767.0 vs. 1969.9 ± 1361.7 nmol/24h, P = 0.011). Compared PBMAH group with UAA group, there were statistically significant differences in the percentage change of cortisol (absolute value after suppressed over the basal value) during LDDST (73.01% ± 39.33% vs. 96.13% ± 31.59%, P =0.001) and during HDDST (73.90% ± 38.53% vs. 96.58% ± 28.79%, P=0.001); and there were statistically significant differences in the percentage change of 24-h UFC during LDDST (90.11% ± 79.60% vs. 134.47% ± 131.26%,P =0.045) and during HDDST (100.05% ± 89.59% vs. 143.75% ± 98.12%, P =0.017). The 24-hour continuous plasma ACTH and cortisol monitoring directly and thoroughly revealed the heterogeneity of hormone secretion of PBMAH cases. Among the 18 PBMAH cases with subclinical CS, 11 only received drug symptomatic treatment; 6 underwent unilateral adrenalectomy on the larger side; 1 not relieved well after unilateral adrenalectomy, then received resection of the contra-side. Among the 28 PBMAH cases with CS, 6 refused surgery because of economic reasons and just received symptomatic drugs treatment with bad prognosis; 15 underwent unilateral adrenalectomy on the larger side; 7 not relieved well after unilateral adrenalectomy, then
conducted resection of the contra-side, and at last treated with glucocorticoid replacement obtained good prognosis.

Conclusions: PBMAH is often associated with a relatively low degree of cortisol autonomous secretion. It is necessary to choose a specific therapy plan to alleviate the high cortisol state according to the individualized hypercortisolemia condition.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS I

Extreme Insulin Resistance: The Diagnostic Challenges When Cost Is a Limitation.

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SAT-LB116

Introduction: Insulin resistance occurs most commonly in association with obesity but may result from multiple causes, e.g. medications, lipodystrophy, or antibodies to insulin or insulin receptors. We review a case of an unusual presentation of insulin resistance. We highlight challenges of diagnostic testing and treatment when there are cost limitations. **Clinical Case:**A 41 year old Hispanic male with T2DM and a history of well-controlled BPD on quetiapine only presents for management of diabetes. His current treatment is metformin and a TDD of 170 U human insulin; A1C is 12.2%. He was diagnosed at age 32 via routine lab tests. At diagnosis BW was 96.4 kg, BMI 29, BP 100/70, CHOL 152, TG 247, HDL 35, LDL 68. Physical exam was unremarkable without acanthosis or lipodystrophy. Anti-GAD, anti-islet cell antibodies, insulin and C-peptide levels were ordered, but not obtained due to cost. He was managed with lifestyle modification for 2 years with maintenance of A1C <7%. At age 35 he developed symptomatic hyperglycemia with A1C 9.4% and was started on metformin and glyburide. At age 36 A1C was >11%, with no change in BW. Glargine 5 U was added, and glyburide was changed to glipizide. Glargine was increased to 40 U without changes in glycemia. At age 37 glipizide was stopped, and he could not afford glargine. He was switched to 70/30 human insulin. Insulin dosages were progressively increased to 220 U a day with no change in glycemia. Liraglutide was tried but not continued due to cost, and quetiapine was switched to trazodone without improvement in A1C. LFTs, CBC, HIV, Hepatitis C and B have been negative. The patient has had multiple visits for education with documented adequate disease understanding and performance of injections. Nonadherence was suspected; for its evaluation, the patient was observed in clinic self-injecting 30 U of regular insulin (brought from home); fasting was confirmed for 3hrs post-injection. BG was 327mg/dL pre-injection and 326mg/dL 3hrs post-injection. Insulin antibodies were requested but not obtained due to cost. Insulin receptor antibodies are not commercially available in the US. Potential empiric strategies, e.g. the NIH protocol for insulin type B resistance (rituximab + dexamethasone + cyclophosphamide) was considered but cost is a limitation. We discussed steroids or methotrexate for possible antibody mediated insulin resistance versus a trial of thiazolidinedione, which has been reported to decrease severe insulin resistance in patients with lipodystrophy. The patient opted to initially try a thiazolidinedione. **Conclusion:**Although poor adherence has not been excluded, the patient appears to

have no response to high doses of injected human insulin, suggesting extreme insulin resistance. Cost limitations preclude optimal diagnostic evaluation. Empiric treatment with low cost options potentially may provide diagnostic information as well as efficacious treatment.

Thyroid

NO LONGER A PAIN IN THE NECK — RECENT INSIGHT INTO THYROID GROWTH, DEVELOPMENT, AND PATHOLOGY

Approaching Indeterminate Thyroid Nodules in the Absence of Molecular Markers. "The BETH-TR Score"

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OR28-05

Context: Given the lack of easy access to molecular markers, for indeterminate thyroid nodules (Bethesda (BETH) category III, IV), the clinician can either decide to get a second opinion from an expert high volume thyroid cytopatholgist, re-do the FNAC after a period of 3-6 months or send the patient for a diagnostic hemithyroidectomy. Reviewing the sonographic risk features is also one way of triaging these nodules. The ACR-TIRADS (TR) is an objective method of sonographic risk assessment and is superior to other forms of sonographic classification. **Aim**: We propose combining the scoring of TR category and BETH category (both expressed as numerical value and summated) and look at the score which could potentially guide the clinician in deciding whom to send for surgery. **Settings and Design**: Observational Prospective collection of consecutive patient data from Thyroid FNAC clinic. **Statistical analysis used**: The BETH categories were represented numerically and summated with the TR category. The categorical outcome variables of Benign and Malignant nodules and the summated score was analysed using Kruskal-Wallis test. **Results**: We analysed 450 FNAC data, out of which 403 were thyroid nodule aspirates. Out of these nodules, 96 of them underwent surgery and 64% of these nodules were malignant on final histopathology (Malignant=62 and Benign=34). The mean (sd) size of the benign nodules was 3.6 (2.2)cm compared to 2.8 (1.8)cm of the malignant nodules. After excluding those with BETH 1 (n=4), the mean BETH-TR score for benign nodules was 6(1.4) and malignant nodules 9.4(2.1) ($p<0.0001$). The BETH-TR score progressively increased from 7.3(0.92) in Follicular thyroid cancers (FTC) to 8.6(1.4) in Follicular variant Papillary thyroid cancer (FVPTC) to 10(1.3) in classic Papillary thyroid cancers (PTC). Among the indeterminate nodules (BETH III & IV; n=40), the BETH-TR score of benign nodules was 6.75(1) and malignant nodules was 7.5(0.72) (p value=0.01). A BETH-TR score >=7 gave a sensitivity of 92% specificity of 74% and correctly identified malignant nodules in 86% of cases (Likelihood ratio 3.5; ROC area: 0.8841; CI 0.79-0.94). **Conclusion**: A combined sonocytological BETH-TR score is one way to triage management of indeterminate thyroid nodules. A BETH-TR score >=7 gave a sensitivity of 92% specificity of 74% and correctly identified malignant nodules in 86% of cases.

Thyroid

NO LONGER A PAIN IN THE NECK — RECENT INSIGHT INTO THYROID GROWTH, DEVELOPMENT, AND PATHOLOGY

Constitutive Activation of NRF2 Antioxidant Response Leads to Age-Dependent Goiter and Compensated Hypothyroidism in Male Mice.

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OR28-01

Background: Familial non-toxic multinodular goiter (MNG) is a rare disease. *KEAP1* gene (Kelch-like ECH-associated protein 1) that encodes the main inhibitor of nuclear factor erythroid 2-related transcription factor 2 (Nrf2), a central mediator of antioxidant responses, has been found to be one of the mutated genes that lead to familial MNG. The proposed association of *KEAP1* with familial MNG is based on only two loss-of-function mutations in respective Japanese families, only one of which included proper phenotyping and demonstration of co-segregation of phenotype and mutation. To date, there is no experimental evidence from model organisms to support that decreased Keap1 levels can cause goiter. **Hypothesis:** We hypothesized that enhanced Nrf2 signaling induced by loss of Keap1 function in mice can lead to goiter. **Methods:** To this end, male Keap1 hypomorphic C57BL/6J mice that express ~80% less Keap1 in their tissues (Keap1 knockdown mice:"Keap1KD") were studied at 3 and 12 months of age and compared to wild-type mice (WT). Plasma, thyroids and pituitary glands were collected for assessment of thyroid function by radioimmunoassays and for histology as well as gene and protein expression by quantitative PCR and immunoblotting respectively. **Results:** Keap1KD showed diffuse goiter that began to develop in early adult life and became highly prominent at the age of 12 months when the thyroids of Keap1KD were 6-fold heavier than WT. Histomorphometry assessment of thyroids showed that Keap1KD had ~3-fold larger follicle