Case Report: This is a retrospective analysis of four cases of Insulinoma diagnosed between
Sep 2016 and Mar 2019. All the patients were males and aged 36, 22, 63 and 15 years respectively. Baseline characteristics, duration to diagnosis of Insulinoma, diagnosis and treatment
given before definitive diagnosis and post-surgery outcomes were analyzed. All the four patients had relatively long latency to diagnosis despite frequent, spontaneous hypoglycemic
episodes, longest being ten years. The patients had a neurological and/or psychiatric diagnosis prior to definitive diagnosis. The symptoms improved with consumption of food. One of the
four patients was on antipsychotics for episodic abnormal behavior before the diagnosis of
Insulinoma. Two of them were on anti-epileptic medications for seizures. All the insulinomas
were localized with CECT without requirement for additional localization techniques. All our
patients responded well to surgical resection of the tumor. All insulinomas were benign grade
1 tumors. Acanthosis nigricans regressed in all the patients post-surgery. In addition, all the
patients had significant weight loss post-surgery. Two of the four patients developed diabetes
mellitus and were on insulin therapy.
Conclusion: A strong index of suspicion of Insulinoma is warranted while dealing with patients
presenting with seizure disorders, behavioral abnormalities and neurological symptoms because the spectrum of symptoms is wide and non-specific. Seeking diagnosis is of utmost importance because of implications on treatment and prognosis.
Reference:
Valente LG, Antwi K, Nicolas GP, Wild D, Christ E. Clinical presentation of 54 patients with endogenous hyperinsulinaemic hypoglycaemia: a neurological chameleon (observational study).
Swiss Med Wkly. 2018 Nov 18;148:w14682.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS II

Autonomous Cortisol Secretion Coexisting with Pancreatic Neuroendocrine Tumor: A Rare Presentation

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MON-921

Introduction: neuroendocrine tumors (NET) are a very rare and heterogeneous group of malignancies that can be associated with adrenocortical tumors in approximately 20% of the cases, mostly bilateral and non-functioning. Autonomous cortisol secretion occurs in less than 10% of adrenal incidentalomas and the coexistence of pancreatic neuroendocrine neoplasms and autonomous cortisol secretion is not well-described.
Clinical case: a 54-year-old man with previous history of systemic hypertension and type 2 diabetes mellitus, presented with left hypochondrium pain in the last 18 months, associated with abdominal distension, constipation and nausea. Physical examination without abnormalities. Abdominal tomography demonstrated dilatated pancreatic duct and a solid heterogeneous nodule in left adrenal, measuring about 2.7 cm. Ecoendoscopy revealed a heterogeneous, hypoechoic and oval nodular lesion, located at the transition of pancreatic head and uncinate process, measuring 1.5x1.1cm. Biopsy was performed, showing a pattern of neuroendocrine neoplasia, with chromogranin and synaptophysin +, Ki67 1%. Gallium-68 dotatate PET revealed two pancreatic nodular formations, one in proximal neck/body (1.5 cm) and the other in pancreatic tail (1 cm), presenting SUV of 20.4 and 21, respectively. Adrenal nodule presented minimal increase in radiopharmaceutical concentration. To exclude the hypothesis of metastasis, PET FDG was performed, showing physiological uptake in adrenal nodule. Pituitary MRI had no abnormalities.
Chromogranin A and gastrin values were normal. Pheochromocytoma and primary hyperaldosteronism were excluded. Hypercortisolism investigation presented the following results: 23h salivary cortisol 167ng/dl (NR < 100), 24-hour free urinary cortisol 42.1 mcg/24h (NR 4.2-60), post-1mg and 2mg dexamethasone serum cortisol of 10.8 mcg/dl and 3.8 respectively (serum dexamethasone levels of 193 and 780 ng/dl; NR > 130), ACTH 13 and 11 pg/ml.
By these results, coexistence of non-functioning pancreatic neuroendocrine tumor and autonomous cortisol secretion was confirmed. A total pancreatectomy with partial gastrectomy and bileodigestive anastomosis was performed. Pathological anatomical evidence demonstrated a well-differentiated neuroendocrine tumor (NET G1) and immunohistochemistry analyses showed positive chromogranine A, synaptophysine, Ki67 1% and negative ACTH. Clinical follow-up of the adrenal adenoma was preferred.
Conclusion: although most adrenocortical tumors associated with NET are nonfunctional, hypercortisolism should be considered. Adrenal metastasis and ectopic ACTH secretion are differential diagnosis. Clinical follow-up is an option when patient is asymptomatic and comorbidities are well-controlled.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

Characterization of an Ovarian Steroid Cell Tumor in a VHL Patient

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SUN-931

Most ovarian steroid cell tumors arise sporadically. However, they can also be observed as a rare manifestation of von Hippel Lindau disease. Here, we present a clinical, pathological and molecular characterization of a steroid cell tumor in a VHL patient. A 14 year old girl with molecularly confirmed diagnosis of VHL developed hirsutism and amenorrhea. Initial clinical hormonal evaluation was notable for elevated 17-OHP of 406ng/dl, androstenedione 275ng/dl, and testosterone 102ng/dl. In order to exclude congenital adrenal hyperplasia as a common cause of hirsutism in adolescents, ACTH stimulation was performed, but no increase in 17-OHP was observed. Anti Muellerian hormone, inhibin (INH) A and INH B were normal. Imaging revealed a bilobed 6cm left adnexal mass. The mass was resected en bloc via a left oophorectomy. Pathological evaluation showed multinodular steroid cell tumor with clear cytoplasm and delicate vascular meshwork. Immunoprofiling demonstrated positivity for inhibin and calretinin; while renal cell carcinoma markers were negative. All laboratory values normalized post-surgery. In addition to clinical measurements pre- and post-surgery, steroid profiles were evaluated by LC-MS/MS. Quantitative RT-PCR analysis showed robust tumor expression of enzymes facilitating the production of androgens, but not estrogens. Further preliminary analysis by exome sequencing confirmed the known germline pathogenic variant in VHL, but no additional obvious somatic driver mutations were identified. Interestingly, the NGS analysis of different specimens from the same tumor revealed multiple different single base pair variants in the VHL gene as a second hit. In summary, hirsutism in VHL patients should raise the suspicion for unusual ovarian tumors. In contrary to the usual theory of a monoclonal expansion after loss of the wt VHL allele, this tumor appeared to be oligoclonal as evidenced by different somatic VHL mutations. This could be either explained by initial parallel occurrence of several clones or that the VHL second hit is not an initial event, but the mutation instead supports tumor expansion following initial steps of tumorigenesis.

Reproductive Endocrinology

SEX, GENDER, AND HORMONES

11-oxygenated C19 Steroids in Normal Weight, Overweight, and Hyperandrogenic Girls

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OR27-07

Hyperandrogenism (HA) often begins during puberty and may be a forerunner to polycystic ovary syndrome (PCOS). PCOS women have elevated 11-oxygenated androgens (O'Reilly MW et al, JCEM 2017), but the contribution of these androgens to HA in peri-pubertal girls is unknown. To address this uncertainty, we assessed classical and 11-oxygenated steroid levels at baseline and in response to both ACTH and recombinant human chorionic gonadotropin (r-hCG) administration in peri-pubertal girls. Girls (n=35) were studied in the mid-follicular phase (as relevant): age 13.1±3.1 (7.3-18.8) y (mean ± SD [range]); BMIz 1.1±1.1 (-1.08 to +2.65); Tanner breast 3.8±1.4 (1-5); bone age 14.1±3.1 (7.3-18) y. Of pre-menarcheal (PRE) girls, 4 were normal weight (NW, BMI% 5-84) and 7 overweight (OW, BMI% ≥ 85). Of post-menarcheal (POST) girls, 10 were NW, 6 OW, and 8 HA (3 NW, 5 OW). Blood was drawn at baseline (8 am, no meds); post-ACTH (60 m after 250 mcg IV, 10 h after dexamethasone [DEX, 1 mg PO]); and post-r-hCG (24 h after 50 mcg IV, 10 h after second dose DEX). Serum concentrations of classic (dehydroepiandrosterone [DHEA], androstenedione [A4], testosterone [T], dihydrotestosterone [DHT]) and 11-oxygenated androgens (11OHA4, 11KA4, 11OHT, and 11KT) were measured by liquid chromatography-tandem mass spectrometry. Wilcoxon Rank Sum and simple Spearman correlations were used for comparisons. Unless stated otherwise, $p \leq 0.05$ for all results reported below. At baseline, 11KT was 3-fold higher than T in PRE girls (1.2±0.6 vs. 0.4±0.2 nmol/L), while they did not differ in non-HA POST girls (1.4±0.6 vs. 1.1±0.5 nmol/L). The ratio of A4/T was 6.6±2.7 and 6.0±1.6 in PRE and non-HA POST girls, respectively, while 11KA4/11KT was 3.8±1.8 and 3.7±2.9, respectively; this suggests more efficient activation of 11-oxygenated androgens. Compared to NW POST girls, OW POST girls had higher T at baseline (1.9±0.9 vs. 1.2±0.8 nmol/L) and higher A4 post-ACTH (10.0±4.3 vs. 6.6±1.5 nmol/L). Compared to non-HA POST girls, HA girls had higher T at baseline (2.2±1.1 vs. 1.1±0.5 nmol/L) and higher DHEA, A4, and T post-r-hCG (DHEA: 8.8±2.7 vs. 5.6±2.2; A4: 11.3±4.1 vs. 7.3±2.8; T: 3.4±2.9 vs. 1.2±0.6 nmol/L). 11-oxygenated androgens were not elevated in OW or HA girls. In the entire cohort, HA status correlated with DHEA, A4, and T (r=0.40, 0.54, 0.63), while hirsutism correlated with A4 and T (r=0.47, 0.57). No androgen correlated with BMIz, but T correlated with fasting insulin and HOMA-IR (r=0.37, 0.38). The ratio of classic (DHEA, A4, T) to 11-oxygenated (11OHA4, 11KA4, 11OHT, 11KT) androgens trended higher in non-HA POST girls vs. PRE girls (58%:42% vs. 44%:56%, p=0.056). From early to late puberty, there appears to be a shift away from the 11-oxygenated pathway. Most androgens in HA girls derive from the classic androgen pathway. The mechanisms of the later switch to 11-oxygenated androgen pathway predominance in adult PCOS remain to be elucidated.

Neuroendocrinology and Pituitary

CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY II

Axenfeld Rieger Syndrome: An Uncommon Cause of Growth Hormone Deficiency

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