mutation. Three months after, her acne and frontal hair loss were better, and a trial of spironolactone 50 mg daily, was prescribed. For her sister and mother was suggested to consult endocrinology, due to possible same disease.

Conclusion: this case highlights the importance of recognizing NCCAH as a cause of hyperandrogenism. Molecular genetic analysis should be offered with genetic counseling to patients, since they can carry a severe allele which can affect their progeny. Clinicians should be aware of the importance of family history when diagnosing NCCAH on their patients; for detection, treatment and genetic counseling of NCCAH on family members as well, as found in this case.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

Rare Case of Ectopic Cushing Syndrome Caused by ACTH Secreting Thymic Neuroendocrine Tumor in a Patient with Multiple Endocrine Neoplasia Type 1.

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Introduction

Cushing syndrome (CS) represents an uncommon manifestation of MEN1 and can be caused by both ACTH dependent or independent etiologies. Among them, ectopic ACTH secretion from a Thymic neuroendocrine tumor (TNET) in MEN1 is rare, with very few cases reported so far in literature. We report a case of Ectopic Cushing syndrome (ECS) in a MEN1 patient (pt) with multiple tumors, secondary to ACTH-secreting TNET.

Case description:

A 44 year old male presented to our institution for nausea, vomiting, dizziness. He had initial workup which revealed multiple tumors (papillary thyroid cancer, thymic mass, parathyroid adenomas, bilateral adrenal nodules, macroprolactinoma, peripancreatic nodules). Given concern for MEN 1, genetic testing was performed which was confirmative. Hormonal workup at this time for adrenal nodules was negative including low dose dexamethasone suppression test(DST). The immobile thymic mass was found to be poorly differentiated NET on biopsy with Ki-67 >50% with vascular invasion and adhesions to lung/chest wall on VATS, not amenable to surgery. The pt declined chemotherapy and radiotherapy due to poor social support. Six months later, he presented with complaints of shortness of breath, proximal muscle weakness, anasarca. Evaluation revealed AM cortisol >60 ug/dL(range 6.7-22), high-dose DST Cortisol >60 ug/dL, 24hr urine free cortisol: 8511mcg (range 4-50) and ACTH level: 278pg/mL(range 6-50) confirming ACTH-dependent CS. Special stains from the previous TNET biopsy demonstrated positive staining for ACTH confirming ectopic ACTH secretion. Ketoconazole and chemotherapy with Etoposide and Carboplatin was started, however he clinically deteriorated and expired a few weeks after diagnosed of ECS.

Discussion:

TNET in MEN 1 is rare, with a prevalence of 3-8%. TNET are unusual neoplasms that account for 2% to 7% of all mediastinal tumors. TNET in MEN1 rarely secrete functional hormones with very few reported Ectopic ACTH secretion. MEN1 associated ECS from TNET is an aggressive disease with local invasion of adjacent mediastinal structures or metastasis being common, resulting in poor prognosis as demonstrated in few case reports including our case. Radical surgery of involved adjacent structures and adjuvant local RT can provide local disease control.

Conclusion:

Our pt is a rare case of ECS from TNET in MEN1 with poor prognosis. A special feature of this case is that the patient had initial negative evaluation for hypercortisolemia, however 6 months later he presented with signs and symptoms of severe hypercortisolism, with evaluation confirming transformation into ACTH producing TNET. This conversion is very rarely found in literature and adds to the unique presentation of the case.

Diabetes Mellitus and Glucose Metabolism

METABOLIC INTERACTIONS IN DIABETES

Metabolic and Functional Regulation of T Cells by Insulin and Insulin like Growth Factor 1

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Obesity leads to altered immunity characterized by increased risk of autoimmunity, poor response to infection, and impaired vaccine response. T cells play an important role in this obesity-associated immune response; however, the mechanisms by which T cells are altered in obesity remain unknown. Our goal is to identify nutritionally regulated hormones and cytokines that link whole body nutrition and immunity, and to understand the mechanisms by which such factors can alter T cell response in obesity. To that end, we have identified the hormones insulin and insulin-like growth factor-1 (IGF-1) as potential links between nutritional status and T cell metabolism and function. Insulin is secreted from pancreatic beta cells in response to increasing blood glucose levels, and circulating insulin levels are elevated in obesity due to insulin resistance in metabolic tissues. IGF-1 levels are influenced by protein intake and nutrition status, and free (bioactive) levels of IGF-1 are elevated in obesity. To study the role of insulin and IGF-1 on T cell function and metabolism, we treated activated CD4 T cells with physiologic levels of insulin or IGF-1 in vitro for 24 hours. Treatment of CD4 T cells with insulin or IGF-1 increased glucose uptake, glycolytic metabolism, and mitochondrial metabolism while altering inflammatory cytokine production. In particular, both insulin and IGF-1 decreased IFN-γ production, whereas IGF-1 specifically increased IL-17 production from both bulk activated CD4 T cells and T cells skewed toward a T helper 17 (Th17) phenotype. Using a T cell-specific insulin receptor (IR) conditional knockout mouse, we found that loss of IR signaling decreased glucose uptake and mitochondrial metabolism and increased IFN-γ production by activated T cells. Moreover, IR appears to be required for both insulin and IGF-1 effects on T cells.