1/1,000,000 and highly variable prognosis dependent on subclassification as seminomatous or non-seminomatous. Non-seminomatous germ cell tumors can cause significant enough elevations in hCG to induce thyrotoxicosis via structural homology allowing for cross-reactivity with the TSH-receptor. Limited cases involving EGCTs inducing thyrotoxicosis have been studied.

Case: A 27-year-old male presented to the emergency department with intractable abdominal and back pain. He reported night sweats, nausea, dizziness, and a 10 lb weight loss in 1 week. He was resting comfortably and only complaining of pain. He was moderately tachycardic, tachypneic and hypertensive, with a physical exam only remarkable for tenderness to palpation of the abdomen. Abdominal CT revealed mesenteric and retroperitoneal lymphadenopathy, bilateral adrenal enlargement, a mass in the head of the pancreas, as well as gallbladder and common bile duct distention. Lymph node biopsy was conducted for a suspected lymphoma; however, pathology found a poorly differentiated carcinoma. A diagnosis of a non-seminomatous EGCT was made when ultrasound of the testes was negative for masses and labs revealed elevations in hCG (74842 mIU/ml), and LDH (1421 U/L) with normal AFP (6.98 ng/mL). Further workup showed a slightly elevated T4 Free Thyroxine (1.55 ng/dl) with normal TSH (0.555 mIU/L); thus his thyrotoxicosis was secondary to the high HCG. Treatment for thyrotoxicosis was deferred with the expectation that symptoms would resolve when the tumor burden was decreased. Our patient had numerous other complications requiring management from nephrology, GI and urology teams in addition to endocrinology and hematology-oncology. Bleomycin, Etoposide and Cisplatin (BEP) combination chemotherapy was initiated after recovery from acute complications. Further pathology evaluation suggested tumor susceptibility to the biologics nivolumab and pembrolizumab.

Conclusion: Patients with thyrotoxicosis secondary to metastatic non-seminomatous germ cell tumors often present with widespread metastasis and relatively few symptoms of thyrotoxicosis that resolve as the hCG levels decrease with chemotherapy without specific antithyroid medication. This case highlights the importance of considering clinically occult thyrotoxicosis in patients who have elevated hCG secondary to germ cell tumors. Early detection of germ cell tumor and recurrence is crucial for chemotherapeutic success. Thus, patients should be closely followed for thyrotoxicosis relapse which could potentially herald a carcinoma relapse and aid in early diagnosis.

Thyroid

THYROID CANCER CASE REPORTS II

The Case of a Rare Anaplastic Thyroid Cancer Variant with Rhabdoid Features

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Introduction: We present a very rare case of a variant of anaplastic carcinoma, a high-grade thyroid carcinoma with rhabdoid features. Less than 15 cases have been reported in English literature over the last 20 years. The prognosis of thyroid cancer with this variant phenotype is unfortunately very poor with a mean survival time of only 6 months after diagnosis. Treatment includes surgery, often a total thyroidectomy due to the rapid rate of growth of this tumor type. The benefits of chemotherapy and radiation are not yet apparent.

Case presentation: A 49 year old female with history of breast cancer status-post recent chemoradiation therapy presented to the emergency department for a rapidly enlarging, right-sided neck mass. The mass had been present for approximately one month, but it was estimated to have grown from 3cm to 5cm within the two weeks prior. The patient was being followed by her ENT specialist and had a recent outpatient CT scan done. The results of the CT revealed a large thyroid tumor partially obstructing the esophagus and given the rapid progression of symptoms, she was instructed to go straight to the ED for emergent admission. Upon arrival, the patient reported not having consumed any solids or liquids for the past day due to concerns of aspiration and increasing neck pain. She had complaints of worsening dysphagia. Initial lab work revealed low thyroglobulin (1.4 ng/mL), elevated T4 (15.42 nmol/L) presumably due to Tamoxifen exposure, and elevated PTH (96.9 pg/mL), likely primary hyperparathyroidism. She was admitted and endocrine was consulted for further evaluation. The patient underwent a fine-needle aspiration biopsy showing high-grade anaplastic carcinoma with extensive necrosis and rhabdoid features. The tumor was eventually classified as stage 4B with gross extra thyroidal extension to the adventitial layers of the esophagus, thus it was determined to be unresectable. It was recommended at that time she have a percutaneous tracheostomy and feeding tube to protect her airway. However, the patient requested to be discharged so that she could obtain a second opinion regarding treatment options and prognosis. She subsequently underwent a total thyroidectomy at another hospital.

Conclusion: It remains unclear whether this patient's history of breast cancer treated with chemoradiation therapy played a role in the development of this rare thyroid carcinoma. Some cases of the rhabdoid phenotype are documented to have transformed from papillary thyroid carcinoma, for which radiation therapy is a well-known risk factor. Future studies should use molecular markers, such as BRAF V600E mutations common to papillary and anaplastic thyroid carcinomas, to help differentiate between types of thyroid cancers and avoid delayed treatment options for rapidly metastasizing thyroid tumors.

Diabetes Mellitus and Glucose Metabolism

PREGNANCY, LIPIDS, AND CV RISK — IMPACT OF DIABETES ACROSS THE SPECTRUM

Differences in Advanced Lipoprotein Profile Between Rabson-Mendenhall Syndrome and Lipodystrophy

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Insulin resistance (IR) is associated with metabolic dyslipidemia (high triglycerides [TG] and low HDL) and increased cardiovascular disease (CVD) risk. In obesity-associated IR, dyslipidemia is thought to be caused by increased insulin-mediated stimulation of hepatic lipogenesis, whereas IR in glucoregulatory pathways leads to hyperglycemia. This dichotomy in insulin signaling pathways is termed selective insulin resistance. Rare human conditions exist in which there is extreme, non-selective, IR impairing all insulin signaling pathways (e.g. mutations of the insulin receptor, *INSR*) or extreme IR affecting only selected intracellular insulin signaling pathways analogous to obesity (e.g. lipodystrophy). Lipodystrophy leads to very high TG, low HDL, and increased CVD, while *INSR* mutation leads to low TG and high HDL, with unknown CVD risk. We sought to further characterize the lipid phenotype and atherogenicity in these conditions in order to understand effects of different insulin signaling pathways on CVD risk.

We studied 7 patients with *INSR* mutation (42% female; 5 homozygous; 2 heterozygous) and 21 with lipodystrophy (85% female; 5 generalized; 16 partial). Fasting lipoprotein profiles were assessed by NMR using the LP4 deconvolution algorithm. The major lipoprotein particle categories defined by this method are small, medium, and large HDL and LDL particles (HDLP and LDLP) and very small, small, medium, large, and very large TG rich lipoprotein particles (TRLP).

Very small TRLP (median 189.6 [68.7, 315.0] vs 4.5 [0.00, 9.4], p=0.0001), small LDLP (mean 1425.0 ± 636.2 vs 612.8 ± 233.9, p=0.003), small HDLP (mean 14.0 ± 4.7 vs 9.0 ± 3.2, p=0.014) were more elevated in patients with lipodystrophy vs *INSR* mutation. This lipoprotein profile has been associated with increased atherosclerotic coronary artery disease. GlycA, a marker of inflammation was also more elevated in lipodystrophy vs *INSR* mutation (435.9 ± 107.2 vs 315.7 ± 74.4, p=0.01). Insulin resistance assessed by HOMA-IR was higher in patients with *INSR* mutation vs lipodystrophy (mean 93.5 ± 94.4 vs 15.6 ± 14.7, p=0.00085).) Lipoprotein insulin resistance (LPIR), an index of IR based on lipoprotein particles, was lower in patients with *INSR* mutation (25.0 ± 19.0 vs 84.0 ± 9.0, $p < 0.0001$) despite their higher HOMA-IR.

In conclusion, severe, selective insulin resistance in patients with lipodystrophy was associated with a more atherogenic lipoprotein particle profile and increased inflammation compared to severe, non-selective insulin resistance caused by *INSR* mutations. Patients with *INSR* mutations had a striking discrepancy between a glucose/insulin-based index of insulin resistance (HOMA-IR) and a lipid-based marker of insulin resistance (LPIR). These findings point toward a key role of selective insulin resistance in the development of an atherogenic lipid profile, which should lead to increased CVD risk.

Diabetes Mellitus and Glucose Metabolism

TYPE 2 DIABETES MELLITUS

Should Vitamin B12 Status Monitoring Be Implemented for Patients Taking Metformin?

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Introduction: Cobalamin (vitamin B12) is used in multiple metabolic processes, functioning primarily as a coenzyme with Methylmalonyl-CoA mutase and Methionine synthase in humans. Without functioning enzyme, substrate levels build up which are neurotoxic, leading to neurological debilitation. Lack of enzyme also halts cellular replication processes causing severe anemia. Since numerous studies have found decreased cobalamin levels in patients who regularly take metformin1, then could regular monitoring of cobalamin levels in such patients prevent these outcomes?

Case Presentation: We present a 50-year-old female who reported to the ED with general weakness and shortness of breath after having a seizure. Her medical history included type 2 diabetes mellitus being treated with metformin and a history of seizures controlled by carbamazepine since childhood.

Neurological exam abnormalities consisted of DTRs that were 1/4 on all proximal and distal upper and lower extremities and absent fine sensory and vibratory sensation on ankles and feet bilaterally. Patient was also ataxic. Hgb A1c was 14%. Head CT, chest x-ray, EKG, and cardiac markers found no abnormalities. CBC found a profound pancytopenia with WBC 1.6, RBC 1.27, Hgb 5.2, MCV 119, MCH 40.9, MCHC 34.3, RDW 18.2, and platelets 113. Blood smear was normal. Bone marrow sample showed normochromic macrocytic cells with no other abnormalities. Folate level was normal and cobalamin was found to be low (61.5 pmol/L). Intrinsic factor antibodies were negative. Extensive autoimmune workup was also negative.

***Discussion*:** Our patient's neurological symptoms and pancytopenia were found to be due to multiple factors. R. Pawlak, found that metformin use had a 2.45 ($p < 0.0001$) times higher odds of developing B12 deficiency in comparison to non-metformin users1. This was also supported by a systemic review of the impact of metformin

Carbamazepine is known for its effects on decreasing the absorption of folate and has statistically been found to decrease cobalamin significantly as well.

There are several B12 assessment methods available to providers, including serum/plasma B12, Mean Corpuscular Volume (MCV), Homocysteine (Hcy), Holotranscobalamin II (holoTCII), and serum and urinary Methylmalonic Acid (MMA). Urinary MMA has been found to be the most specific and sensitive of these markers when adjusted by kidney function (through serum creatinine levels) and while fasting