sex-specific quartiles. To analyze the joint impact of insulin and IGF-1, we also categorized participants into four groups: Group I) IGF-1 <230 ng/mL & insulin ≥11 uIU/mL, II) IGF-1 <230 & insulin <11, III) IGF-1 ≥230 & insulin ≥11, and IV) IGF-1 ≥230 & insulin <11. Our primary outcome was all-cause mortality. We used survey design-adjusted Cox regression to estimate the risk of all-cause mortality, adjusting for confounders. Results: Among the 5,283 subjects, 2,214 (42%) had GI. Participants had a mean follow-up of 22.1 years, during which 1,835 (34%) of them died. Those with GI in the highest quartile of IGF-1 had an unadjusted 64% lower risk of all-cause mortality compared to the lowest quartile (GI = unadjusted OR [95% CI]: 0.37 [0.24,0.55]). This association, although protective, was significantly less protective than those with normal glucose tolerance (NGT) (unadjusted OR: 0.16 [0.12,0.23]). After adjusting for confounders, these associations became insignificant (GI = aOR: 1.02 [0.73,1.42], NGT = aOR: 1.04 [0.74,1.46]). When estimating risk of mortality among joint groups of insulin and IGF-1 levels, those in Group I with NGT had 20% increased adjusted odds of mortality (1.30 [1.01,1.71]), while in GI subjects, there was an insignificant increased odds of mortality (1.17 [0.84, 1.62]). Neither subgroup in Group 2 had significant adjusted odds of mortality relative to Group 4. Group 3 subjects with GI had an adjusted, insignificant 24% increased odds of mortality (1.24 [0.91, 1.70]) compared to 70% increased odds in NGT subjects (1.69 [1.18, 2.42]). Conclusion: The differences in odds of all-cause mortality across IGF-1 quartiles in glucose tolerant vs. intolerant individuals suggests that IGF-1 may play less of a protective role in Type II diabetes and prediabetes. Among those with normal glucose, higher insulin levels, regardless of IGF-1 levels, was associated with all-cause mortality. This association did not hold in those with glucose intolerance.

Adrenal

ADRENAL CASE REPORTS II

A Case of Ectopic Cushing’s Syndrome with Major Complications Leading to Treatment Dilemmas
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SUN-199

Background: Ectopic ACTH syndrome is an uncommon cause of Cushing’s syndrome and patients are at high risk for serious complications including infections, thromboses, cardiovascular and neuropsychiatric complications; therefore, swift diagnosis and treatment is needed. Clinical Case: A 63-year old woman presented with lower extremity edema and severe lower back pain. She also reported a 2 month history of polyuria, polydipsia, and headaches. Initial labs showed hypernatremia, hypokalemia, alkalosis and hyperglycemia and an 8AM cortisol of 367 pg/mL (N <25 mcg/dL). Imaging showed a right middle lobe lung mass and 3 vertebral body compression fractures. A failed attempt at biopsy of the lung mass resulted in pneumothorax, air embolism, stroke, and cardiac arrest with shock liver. She was then transferred to our tertiary care center. On arrival at our center, her examination was notable for hypertension, upper and lower extremity edema and 4/5 strength in her right shoulder and hip flexor. She had left hemiparesis and a depressed mood. No facial plethora, acanthosis, buffalo hump or striae were observed. Her 24-hour Urinary Free cortisol (UFC) was 1,176 mcg/dL (N 3.5-45 mcg/24H) and her SAM cortisol after 8 mg of dexa-methasone was 58.3 mcg/dL (N <1.8mcg/dL).

A pituitary MRI did not identify a lesion, and petrosal sinus sampling was considered too high-risk due to recent infarct and cerebral edema. A PET/CT-scan showed increased uptake in the right lung nodule, enlarged hyperactive adrenals, and a retroperitoneal lymph node. The patient’s course was further complicated by diffuse deep vein thromboses of her left leg and a subsequent retroperitoneal bleed while on anticoagulation, as well as an E.coli urinary tract infection. Interdisciplinary discussions regarding options for surgical management were ongoing, however given the patient’s fragile medical state, the endocrine team initiated medical therapy to treat her hypercortisolism while awaiting surgical decision. Initially, a continuous etomidate infusion was used that resulted in a 50% reduction in 24Hr UFC. When her liver function improved, she was transitioned to ketoconazole. She ultimately underwent a right middle lobectomy, revealing a 2.3cm typical carcinoid tumor with strongly diffusely positive ACTH staining on pathology. A day after surgery her ACTH level was 12 pg/mL, though cortisol was still elevated at 55.5 mcg/dL. Cortisol declined to 3.3 mcg/dL within one week. Her neuropsychiatric symptoms reversed almost entirely and she was discharged on a steroid taper.

Conclusion: Ectopic ACTH syndrome is a rare paraneoplastic syndrome with significant comorbidity. In many cases, surgical excision can induce profound and rapid reversal of many of the symptoms of cortisol excess; however, if surgery is delayed, prompt medical treatment is vital to prevent compounding complications.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

A Tough NUT (Midline Carcinoma) to Crack
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SAT-125

Introduction
NUT midline carcinoma (NMC) is a rare, highly aggressive cancer with poor prognosis. To date, there is no established therapeutic strategy; further studies are necessary to compare treatment modalities as well as investigate novel immunotherapeutic agents.

Case presentation
A 39-year-old female presented with a rapidly enlarging right neck mass and a recent 40-lb weight loss and was found to have a 5 cm poorly defined infiltrative hypoeptenuating mass on CT scan concerning initially for anaplastic thyroid malignancy. Endocrinology and ENT were consulted and the patient underwent thyroid biopsy, which was positive for NMC. PET scan demonstrated hypermetabolic
lymphadenopathy in the bilateral neck and mediastinum, but no distant metastases were identified. She then underwent total thyroidectomy with extensive dissection of the bilateral neck; pathology revealed one positive lymph node. On endobronchial biopsy, the mediastinal lymph nodes were benign. Immunohistochemistry revealed PD-L1 expression and gene assay showed an NSD3-NUTM1 fusion of the NUT gene. Oncology advised systemic treatment with carboplatin/taxol and considered Pembrolizimab, an anti-PD-L1 immunotherapy agent.

Discussion

The prognosis of NMC is less than 1 year and only 20-30 cases are reported per year in the USA. NMC is a poorly differentiated subtype of squamous carcinoma characterized by a chromosomal rearrangement of the NUT gene, involving molecular translocation with the BRD4 gene in 70% of cases. It remains challenging to treat NMC, as metastasis is present on diagnosis in most cases and there is currently no established approach. In a report of 40 patients from the NUT Midline Carcinoma Registry, surgical resection correlated with significantly improved survival in contrast to initial radiation or chemotherapy. Recently, BET domain inhibitors have emerged as a promising class of targeted agents for tumors with BRD4-NUT fusions. Their efficacy is unknown for other NUTM1 fusions. Both BET domain and histone deacetylase inhibitors are in clinical trials, and next-generation BET and CDK9 inhibitors have shown preclinical activity. Our patient likely benefited from early intervention with surgical therapy. Her PET scan findings suggest that re-sampling her mediastinal tissue would be prudent. Given her lack of BRD4-NUTM1 fusion, it is unknown if she would benefit from BET inhibitor.

Conclusion

NMC is an underrepresented cancer that warrants further investigation into treatment modalities and novel immunotherapies.

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Thyroid

THYROID DISORDERS CASE REPORTS II

Myxedema Coma: A Fatal Diagnosis in a Patient with No Known History of Hypothyroidism

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SAT-507

Myxedema coma is a rare yet commonly missed diagnosis. Early detection is key to management as this diagnosis carries a high mortality rate.

We report a case of a 108-year-old female with a past medical history of CKD stage 3, hypertension, CHF, and atrial fibrillation who was brought to the emergency department (ED) by her grandson for seizures. The patient has no history of seizures, hypothyroidism (previous TSH 6 years back was 2.29 micro IU/mL), diabetes, or previous radiation exposure. The family noticed the first seizure 8 hours prior to admission with eyes rolling backward, shaking for 1 minute and slurred speech upon awakening. She had 2 other seizure episodes prior to arrival to the ED. Vitals in the ED showed a temperature of 31.7°C, BP of 85/50, HR of 35, RR of 8, and SpO2 was 83% on room air. Given the patient’s age, code status was changed to DNR/DNI. Blood work in the ED revealed a sodium of 146 mEq/L (136-145), anion gap of 25, Creatinine of 2.67 mg/dL (last creatinine prior to this admission was 1.65 mg/dL), and a troponin of 0.04 ng/mL (<0.04). Thyroid function testing was not done in the ED. Home medications included Lasix, digoxin, isosorbide mononitrate, and atenolol. The patient was admitted to the medical floor for workup of bradycardia and was being worked up for beta-blocker/digoxin toxicity but continued to be bradycardic despite atropine. She became hypoglycemic to 37 mg/dL. The patient was admitted to the CCU at night on day 1 of admission and was started on dopamine and glucagon drips. Sulfonylurea screen was negative, and the patient did not have further hypoglycemic episodes. While in the CCU, blood work showed a lactic acid of 10 mEq/L (0.4-2.0), TSH of 21.03 micro IU/mL (0.45-5.33), free T4 of 0.61 ng/dL (0.70-1.70), and total T3 71 ng/dL (87-178). Myxedema score was >130. Digoxin level came back elevated at 4.5 ng/ml (0.9-2.0). Cosyntropin stimulation testing was negative for adrenal insufficiency and thus the patient was not started on steroids. Urinalysis revealed pyuria with blood, but no urine cultures were done. Blood cultures were negative. The patient was given levothyroxine 200 mcg IV in the AM on Day 2 of admission and was started on antibiotics with azithromycin, cefepime, vancomycin, and metronidazole given concern for sepsis. Hypoglycemia resolved and glucagon was discontinued. In the evening of Day 2 of admission, despite being on a dopamine drip, the patient became increasingly bradycardic, hypotensive, and short of breath. She was initially stabilized after a dose of bicarb, atropine, and ephedrine. However, her BP and respiratory status continued to decline, and the patient passed away.

In conclusion, myxedema coma should be suspected in patients presenting with typical symptoms and should be tested for on presentation even when no prior history of hypothyroidism exists.

Thyroid

THYROID DISORDERS CASE REPORTS I

Hyperthyroidism Induced Hepatic Apoptosis

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SUN-506

Background:

Graves’ disease is commonly associated with abnormal liver function tests, most frequently ALP, but the exact