Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Metabolic Parameters in Cancer Patients with and Without Diabetes Mellitus

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MON-116

Background: We have previously examined the link between diabetes mellitus (DM) and malignancy with respect to mortality, but little is known about how the cancer affects glycemic control. Therefore, the aim of this study was to evaluate metabolic parameters in patients with cancer with and without DM. **Methods:** We selected 1404 patients with newly diagnosed prostate, breast, lung, colorectal, and pancreatic cancer from the institutional cancer registry from 2010–2015. Records were selected and matched 2:1 cancer without DM (n=936) and cancer and concurrent DM patients (n=468). Patients were matched by year of diagnosis, age, gender, and cancer type. Metabolic parameters during the year after cancer diagnosis were examined using linear mixed models with fixed effects for time, cancer type, DM status and individual-specific random effect allowing each patient to have a different intercept. **Results:** Prostate cancer accounted for the majority of cases (n=199), followed by lung cancer (n=91), breast cancer (n=71), colorectal cancer (n=54), and pancreas cancer (n=53). Mean overall hemoglobin A1c (HbA1c) was 6.9 (1.2)%. Pancreas cancer patients had higher HbA1c overall (p=0.02). There was no change in HbA1c one year post cancer diagnosis (p=0.28). Mean glucose in non-DM was 108(18) mg/dL and 146 (45) mg/dL in DM pts. Lung and pancreas cancer patients had higher glucose values overall (p<0.001). Time (p<0.001), DM (p<0.001) and time * DM (p=0.02) were significant in a mixed model. A decrease in glucose over the year was observed in DM patients across all cancer types. **Conclusions:** A diagnosis of malignancy does not worsen glycemic control within the first year of cancer diagnosis. This should be reassuring to endocrinologists and oncologists who treat patients with DM and cancer. Longer term studies, and analysis in larger and more diverse patients groups are needed.

Thyroid

THYROID DISORDERS CASE REPORTS II

Acute GI Bleed Associated with Myxedemic Coma: Yes It Still Exists!

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SAT-496

Introduction: Myxedemic coma is a life-threatening medical emergency. It needs to be treated emergently & carries very high mortality. It involves multi-organ failure at cellular level due to severe thyroid hormone deficiency. Most common clinical presentation involves CVS. With advancement in health care it is now uncommon to see myxedemic coma especially associated with GI Bleed. Here in we present an interesting case of GI bleed associated with myxedemic coma. ***Case***: 84 years old male was discovered in home, minimally responsive. EMS intubated & brought him to ED with agonal respirations, hypotensive & unresponsive, He was admitted to ICU. Past medical history was significant for smoking & hypertension. Physical Exam was significant for dryness of skin, obtundation, hypothermia, tachypnea & BMI >30. Initial Labs revealed anemia with Hemoglobin of 5.1mg/dL, Hematocrit 17.5%, Hyponatremia-134meq/L, Hyperkalemia-K+ levels 5.3meq/L, BUN-84mg/dL & creatinine-4.1mg/dL, His serum TSH levels were 352 mIU/ml with low free T4 and T3 levels at 0.15ng/dl and 1.99pg/ml, respectively. Stool was positive with Blood. IV fluids were given.GI was consulted. He underwent emergent upper GI endoscopy, which found the Dieulafoy's lesion at cardiac end of stomach & treated with a combination of epinephrine injection, argon laser, & 3 hemo-clips. He had 6 PRBCs transfused. He was started on IV Thyroxine, Liothyronine and Hydrocortisone. His mental status improved, & hemoglobin remained relatively stable. Later on, he decided to move to palliative care & was discharged to hospice. ***Discussion***: Myxedemic coma is a term generally used to denote most severe decompensated hypothyroidism. The typical progression is lethargy evolving into a stupor & eventually into a coma with respiratory failure and hypothermia. It can lead to volume depletion, hyponatremia, & AKI, which can worsen to ATN if prolonged ischemia remains.GI bleed is a rare manifestation of myxedemic coma. Pathophysiology of GI bleed in these patients involves mucosal edema & mucopolysaccharide infiltration. Also, myxedemic coma is associated with neurological changes resulting in slow peristalsis & GI atony. This coupled with coagulopathy associated with decompensated hypothyroidism results in increased risk of bleeding. Dieulfoy's lesion are rare cause of GI bleed. Stress & ischemic changes are one of the inciting factors for these lesions. These lesions are more common in elderly males & are associated with severe systemic illness similar to our patient. Treatment is usually supportive with goal of identifying the lesions, stopping the bleed & aggressively managing myxedemic coma. We present an interesting case of GI bleed associated with myxedemic coma now relatively uncommon with advancement in healthcare. It provides an excellent learning opportunity for clinicians to consider while managing these patients.

Thyroid

THYROID NEOPLASIA AND CANCER

An Open-Label, Single-Arm, Multicenter, Phase 2 Trial of Lenvatinib (LEN) for the Treatment of Anaplastic Thyroid Cancer (ATC)

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MON-521

Background: ATC is aggressive, with a low 5-year patient (pt)-survival rate. Apart from recent advances in treating ATCs in pts with *BRAF* mutations, systemic treatments have limited efficacy and duration of response is short. In a small, phase 2 study conducted in Japan, 24% of pts with ATC achieved a partial response (PR) with LEN (Study 208 [Takahashi, *Future Oncol.* 2019]). This study (NCT02657369 [Study 213]) aimed to further evaluate the efficacy and safety of LEN in a broader population of pts with ATC.

Methods: Study 213 was performed in collaboration with the International Thyroid Oncology Group and enrolled pts with ATC to receive LEN 24 mg/day. Key inclusion criteria were: histologic diagnosis of ATC, measurable disease per RECIST v1.1, ECOG score ≤1, and adequate organ function. Previous surgery, radiation, and neoadjuvant, adjuvant, or palliative chemotherapy for ATC were allowed. The primary end point (confirmed objective response rate [ORR]) was determined by investigator review per RECIST v1.1. Interim analysis was done after the first 20 evaluable pts completed ≥2 tumor assessments (baseline and 6-week scan) or discontinued treatment.

Results: The study was halted for futility when the minimum threshold for ORR (15%) was not met at the interim analysis. The full analysis set (FAS) included 34 pts because the protocol allowed enrollment until the interim analysis was complete. The median pt age was 66.5 years old and most were female (n=21/34), white (n=27/34), and had been treated with 1 or 2 prior anticancer regimens (n=20/34). Unconfirmed PR was experienced in 1/20 pts (ORR 5%; 95% CI 0.1–24.9%) in the interim analysis set. In the FAS, 1/34 pts had a confirmed PR (cPR) (ORR 3%; 95% CI 0.1–15.8%). In the interim and FAS, median progression-free survival (2.6 and 2.6 months, respectively) and median OS (2.9 and 3.2 months, respectively) were similar. In addition to the 1 cPR, 7 pts had 22–63% shrinkage in tumor measurements but did not meet the response criteria (FAS). Grade 3/4 treatment-emergent (TE) adverse events (AEs) occurred in 82.4% of pts, and 61.8% of pts experienced grade 3/4 treatment-related AEs (FAS). Grade 5 TEAEs occurred in 14/34 pts and there were 27 deaths by the time of data cut-off. There were no treatment-related deaths, and no major treatment-related bleeding events occurred.

Conclusion: In contrast to Study 208, Study 213 enrolled more pts with ATC (34 vs 17), more of whom had received prior chemotherapy (62% vs 41%). Additionally, in Study 208, all pts were Japanese and tumor assessments were conducted more frequently (4- vs 6-weekly). These differences may have contributed to the observed variation in results between the 2 studies. AEs observed were consistent with the safety profile of LEN or with ATC. Further investigation of LEN in combination with a checkpoint inhibitor may be warranted.

Pediatric Endocrinology

PEDIATRIC GROWTH AND ADRENAL DISORDERS

Evaluation of IGF-1 as a Biomarker to Inform Phase 3 Clinical Trial Design and Dose Selection in Patients Born Small for Gestational Age Who Fail to Demonstrate Catch-Up Growth by Age 2–4 Years

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SAT-094

Insulin-like growth factor-1 (IGF-1) is a key hormone in mediating the physiological response to endogenous and exogenous growth hormone (GH). Current clinical guidelines suggest use of IGF-1 for dose titration in adults with GH deficiency and for safety monitoring in adults and pediatric patients. Several GH drug development programs for pediatric indications have collected IGF-1, height standard deviation score (HSDS), and height velocity (HV), to support dose selection in Phase 3 clinical trials. In this analysis, patients born small for gestational age (SGA) who fail to demonstrate catch-up growth by age 2–4 years from different growth hormone product development programs were included. A total of 663 patients from 8 clinical trials were included in this analysis, with 7 placebo arms and 15 growth hormone treated arms. The growth hormone dosing regimen ranged from 33 ug/kg/day to 100 ug/kg/day. Both boys and girls throughout a wide range of ages (3 to 7 years old on average) were represented in this analysis. The average patient was 3 to 4 standard deviations below the age- and sex- adjusted mean height at baseline. IGF-1 was collected and standardized according to age and sex, so called the IGF-1 standard deviation score (IGF-1 SDS). At baseline, the average patient had normal IGF-1 (-1 to 0 on average). Based on preliminary findings, IGF-1 SDS change from baseline (CFB) at 6 months was correlated with HSDS CFB at 12 months. HSDS CFB at 3 months and 6 months were also correlated with HSDS CFB at 12 months, respectively. These findings were consistent across the three GH products included in the analysis, as well as age and gender. However, IGF-1 SDS CFB had much larger variability than HSDS CFB. Both HSDS CFB at 3 months and 6 months precisely and accurately predicted HSDS CFB at 12 months. IGF-1 SDS was more variable and did not add any further contribution in the prediction of HSDS at 12 months and therefore IGF-1 may not be sufficient in informing Phase 3 dose selection in such trials.

Reference: 1. Shoshana Yakar, Clifford J. Rosen, Wesley G. Beamer, et al. Circulating levels of IGF-1 directly regulate bone growth and density. J Clin Invest. 2002 Sep 15; 110(6): 771–781. 2. Locatelli V, Bianchi VE. Effect of GH/IGF-1 on Bone Metabolism and Osteoporosis. Int J Endocrinol. 2014;2014:235060 **Nothing to Disclose:** TL, JP, BC, MZ, JV, CS