associated to hyperinsulinism in the context of gestational diabetes. Micropenis was noted on physical exam. As part of the study for hypotonia, serial thyroid function tests were obtained revealing central hypothyroidism. A low dose ACTH stimulation test was performed which revealed adrenal insufficiency. The patient was started on cortisol and thyroid hormone replacement. Brain MRI showed an ectopic neurohypophysis located along the floor of the hypothalamus, a small anterior pituitary gland, and a partially absent infundibulum, findings consistent with pituitary stalk interruption syndrome. The patient received testosterone injections for micropenis and is being followed for development of other pituitary hormone deficiencies. PSIS is a rare congenital condition that is increasingly recognized in neonates manifesting with signs of hypopituitarism.

Neuroendocrinology and Pituitary PITUITARY TUMORS II

Cancer Incidence in 1,296 Patients with Acromegaly Is Not Increased: A Nationwide Population-Based Study
Daniela Esposito, MD1, Oskar Ragnarsson, MD, PhD2, Gudmundur Johannsson, MD, PhD2, Daniel S. Olsson, MD, PhD2.
1Sahlgrenska University Hospital, Gothenburg, Sweden, 2Sahlgrenska University Hospital, Gothenburg, Italy.

MON-330

Background: Single- and multi-center studies have shown an increased incidence of malignancies in patients with acromegaly. These findings may be affected by selection bias. Our aim was therefore to investigate the incidence of malignancies in a nationwide unselected cohort of patients with acromegaly.

Methods: Adult patients diagnosed with acromegaly due to a pituitary tumor between 1987 and 2017 were identified in the Swedish National Patient Registry. All malignancies following the diagnosis of acromegaly were identified in the Swedish Cancer Registry that has a coverage of over 96%. Standardized incidence ratios (SIRs) for malignancies, with 95% confidence intervals (CI), were calculated by using the Swedish general population as a reference. Incidence of malignancies was also analyzed in sub-groups of patients treated with radiotherapy and in those having diabetes mellitus and hypopituitarism.

Results: A total of 1,296 patients with acromegaly were included (621 men, 675 women). The mean age (±SD) at diagnosis was 51.6±14.7 years. The mean follow-up was 12.7±8.3 years, with a total of 16,395 person years at risk. Results: The diagnosis was 51.6±14.7 years. The mean follow-up was 12.7±8.3 years, with a total of 16,395 person years at risk. Pituitary surgery was performed in 842 (65%) patients and radiation therapy in 152 (12%) patients. The diagnosis of hypopituitarism and diabetes mellitus was recorded in 29% and 16% of patients, respectively. Overall, 186 malignancies were identified in patients with acromegaly as compared to 179 expected malignancies in the general population (SIR 1.04; 95% CI 0.90-1.20). Incidence of malignancies was similar in men and women [SIR 1.08 (95% CI 0.88-1.32) vs 1.00 (95% CI 0.80-1.23)]. Incidence of colorectal cancer (SIR 1.12; 95% CI 0.75-1.62) or malignancies of the respiratory system (SIR 1.22; 95% CI 0.76-1.84) was not increased. Incidence of kidney and ureter cancer (n=17) was, however, increased (SIR 3.81; 95% CI 2.22-6.11). In the entire study cohort, only three cases of thyroid cancer were recorded. SIR for malignancies in patients treated with radiotherapy (1.12; 95% CI 0.56-2.01) and in patients with hypopituitarism (SIR 0.91; 95% CI 0.68-1.18) or diabetes (SIR 1.08; 95% CI 0.78-1.45) did not differ from the general population.

Conclusions: This large nationwide population-based study showed that the overall incidence of malignancies in patients with acromegaly was not different from the general population. In particular, incidence of colorectal and thyroid cancer was not increased. Incidence of malignancies of the urinary tract was, however, increased.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Cholesterol Uptake as a Critical Vulnerability in Triple Negative Breast Cancer
Kathleen O’Neill, BS.
University of Colorado - Anschutz, Aurora, CO, USA.

SAT-145

Triple Negative Breast Cancer (TNBC) is an aggressive subtype of cancer with poor prognosis due to high metastatic potential and lack of targeted therapies. Normal epithelial cells express the microRNA-200c (miR-200c), a potent suppressor of epithelial-to-mesenchymal transition (EMT). However, miR-200c is silenced or lost in TNBC, allowing a de-differentiated, non-epithelial phenotype and aberrant expression of genes conferring invasive and chemoresistant characteristics. Recent literature has demonstrated that EMT promotes altered tumor cell metabolism, creating novel vulnerabilities that can be exploited therapeutically. In addition to driving global metabolic changes, miR-200c-induced reversal of EMT alters key cholesterol metabolism genes that support the uptake of dietary cholesterol from the bloodstream. Intracellular cholesterol homeostasis is critical for cell survival and is carefully regulated, but how these homeostatic mechanisms adapt during tumor progression is poorly understood. Based on preliminary data, I hypothesize that TNBCs depend on exogenous cholesterol uptake and availability to maintain cell viability and an invasive phenotype. This work aims to identify novel cholesterol-related targets in breast cancer and delineate mechanisms regulating cholesterol homeostasis in normal and cancer physiology.Restoration of miR-200c in TNBC leads to alteration of the cholesterol uptake components low- and very-low-density-lipoprotein receptors LDLR and VLDLR, through direct and indirect mechanisms previously unexplored in cancer. miR-200c further inhibits Niemann-Pick Type C (NPC1), a lysosomal protein necessary for utilization of exogenous cholesterol. Interestingly, expression of NPC1 in TNBC correlates with a unique inability of cells to proliferate in the absence of exogenous LDL supply, suggesting defects in de novo cholesterol biosynthesis. Further, NPC1 inhibition leads to cell death in TNBC but not more epithelial-like breast cancers. Whether this cell death is due to disruption in critical cholesterol supply or due to defective lysosome dysfunction is currently being investigated. Overall, this work suggests a role of...
NPC1 in cancer cell metastasis that has not been previously explored, and identifies cholesterol uptake as a targetable dependency in TNBC.

Adrenal

ADRENAL - TUMORS

Increased Telomere Length in Adrenocortical Tumors Is Associated with Abnormal Expression of Chromatin Remodelling Factors

Monica F. Stecchini, MD1, Ana Carolina Bueno, PhD2, Leandra N Z Ramalho, MD, PhD2, Fernando S. Ramalho, MD, PhD2, Rodrigo T. Calado, MD, PhD2, Fernanda B. Coeli-Lacchini, PhD2, Mateus R. Campos, MD2, Davi C. Aragon, PhD2, Ayrton C. Moreira, MD, PhD1, Silvia R. Brandalise, MD, PhD2, Margaret Castro, MD, PhD1, Jose A. Yunes, PhD2, Sonir R. Antonini, MD, PhD2.

1Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, SP, Brazil, 2Boldrini Children’s Center, University of Campinas, Campinas, SP, Brazil.

SAT-179

Background: The pathogenesis of adrenocortical tumors (ACTs) in the pediatric population is partially known, and few prognostic factors have been identified in this age group. Recently, ATRX and DAXX have been implicated in the pathogenesis and prognosis of a variety of cancers. Their altered function has been shown to affect telomere length through a telomerase-independent mechanism.

Objective: To investigate ATRX and DAXX gene expression, ATRX and DAXX protein expression, and telomere length, as well as their clinical significance, in ACT samples from pediatric patients.

Methods: The records of 110 pediatric patients with available ACT samples were reviewed. ATRX, DAXX, TERT and TERC gene expression was assessed by qPCR (n = 100 ACTs; n = 12 normal adrenals). ATRX and DAXX protein expression was assessed by IHC (n = 45 ACTs). Telomere length was assessed by qPCR (n = 64 ACTs). For survival analysis, Kaplan-Meier curves were obtained. For association analysis, simple linear regression models were adjusted.

Results: Most patients were female (70.9%) and harbored germline TP53 mutations (90.2%). Median age at diagnosis was 21.1 months (2.1 – 199). Younger patients (< 3 years) had better survival (p < 0.01), while those with metastasis at diagnosis and carcinomas (classified by the Wieneke score) had worse survival (p < 0.01). ATRX gene expression was decreased (p < 0.01), while DAXX gene expression was increased (p < 0.01) in ACTs, compared to normal adrenals. ATRX gene expression was even lower in the context of the germline TP53 (R337H) mutation (p < 0.01). TERT expression was not detected in ACTs or normal adrenals, and TERC expression was not altered (p = 0.69). ATRX protein expression was lost in the majority of ACTs (95.6%), while DAXX was lost in a minority (21.1%). There was no association between gene or protein expression and disease-free or overall survival. There was a significant association between decreased ATRX and DAXX gene expression and increased telomere length (p < 0.01 and p = 0.03, respectively).

Conclusion: In pediatric ACTs, decreased ATRX and DAXX gene expression was associated with increased telomere length, independently of TERT or TERC expression. In these tumors, ATRX gene expression was decreased and ATRX protein expression was overall lost, while DAXX gene expression was increased and DAXX protein expression was overall retained. No significant association between these alterations and prognosis was found in this cohort. These findings suggest that ATRX and DAXX altered function may be more involved in the pathogenesis of pediatric ACTs than in the prognosis of the affected patients.

Thyroid

THYROID AUTOIMMUNITY AND BENIGN THYROID DISEASE

Thyroid Function Test Abnormalities Secondary to Immune-Checkpoint Inhibitors: A Marker of Survival?

Joana Lima Ferreira, MD1, Cláudia Fernandes Costa, MD2, Sofia Castro, MD2, Joana Oliveira, MD1, Ana Paula Santos, MD1, Inês Lucena Sampaio, MD1, Hugo Duarte, MD2, Isabel Torres, MD2.

1Hospital Pedro Hispano, Unidade Local de Saúde de Matosinhos, Portugal, 2Instituto Português de Oncologia, Porto, Portugal.

OR18-06

Immune-checkpoint inhibitors (ICI) are monoclonal antibodies which target molecules to enhance antitumor response. Several adverse events have been described and the major ICI-related endocrinopathies are thyroid dysfunction and hypophysitis. Its occurrence has been associated with increased survival.

A retrospective study of adult patients treated with ICI between March 2014 and September 2019 at an oncologic centre was performed to evaluate the impact of thyroid function test abnormalities (TFTA) in their prognosis. We excluded patients without regular monitoring of thyroid function, with previous thyroid or pituitary disease (including medical and surgical treatments), previous head/neck radiotherapy and who performed only one ICI cycle. Clinical data of all patients were examined independently by two Endocrinologists. Survival analysis was performed using the Kaplan-Meier method. Cox regression was used to evaluate associations between the occurrence of TFTA and the outcome of overall survival (OS). It was adjusted for sex, age, primary neoplasm, tumor staging and ICI. All analyses were performed using IBM-SPPS v.25 and a level of significance α=0.05 was noted.

We included 161 of 205 patients, with a median age of 65 years [Interquartile range (IQR) 15] and 67% male. Most patients had melanoma (52%) and lung cancer (43%). Globally, 86, 59 and 25 patients were under pembrolizumab, nivolumab and ipilimumab, respectively. Median duration of ICI treatment was 4.4 months (IQR 7.7) and median total follow-up was 11.4 months (IQR 11.2). New onset TFTA was diagnosed in 18% of patients, at median age of 65 years (IQR 20) and 55% male. Almost half (45%) had primary hypothyroidism, 28% had central hypothyroidism and 13.8% had biphasic thyroiditis and thyrotoxicosis,