Thyroid

THYROID NEOPLASIA AND CANCER

Local Lymph Node Metastasis Is Less Common in RAS- Mutated Thyroid Cancer Compared to BRAFV600E- Mutated Thyroid Cancer

Mayumi Endo, MD, Fadi Nabhan, MD, Pamela Brock, MS, Katie Roll, MS, Jennifer Anne Sipos, MD, Matthew David Ringel, MD.
Ohio State University, Columbus, OH, USA.

MON-530

Introduction: Somatic mutations of *RAS*- and *BRAFV600E*- are the most common driver mutation in thyroid cancer (TC) and in the majority of cases, these are mutually exclusive[1,2]. Clinical characteristics of TC with either *RAS* or *BRAFV600E* mutation is not systemically studied.

Methods: This is a retrospective study at the Ohio State University (OSU) from 1/2000 to 12/2018. Data were extracted from OSU Endocrine Neoplasia Repository (ENR). Medullary thyroid cancer was excluded. The treating physician determined patient management. Statistical analysis was performed with the chi-square test for categorical values and Mann-Whitney U test for continuous unpaired values. Two-sided P values of less than 0.05 were considered statistically significant.

Results: Out of 320 patients, 152 patients had a positive mutational profile. Of these, 128 patients had a *BRAFV600E* mutation and 14 had a *RAS* mutation. Details of *RAS* mutation were as follows; *NRASQ61K* (n=2), *NRASQ61R* (n=1), *HRASQ61R* (n=1), *HRASQ61K* (n=1), *NRAS* without further details (n=9). Local lymph node metastasis was significantly less in *RAS* mutated cancer (58% vs 16%, p<0.05). Lymph node metastasis was limited to N1a in all *RAS* group, whereas 38% of *BRAFV600E* had N1b status. The number of positive lymph nodes were significantly fewer in the *RAS* group (mean 0.42 vs. 9.1, p=0.003). None of the patients in *RAS* group developed subsequent local neck recurrence, whereas 19% of *BRAFV600E* group developed a recurrence (p=0.05). Bone metastasis was more common in *RAS* compared to *BRAF*V600E group (21% vs 6%, p=0.04) but there were no differences in other distant metastases. Presence of extrathyroidal extension was significantly higher in *BRAFV600E* compared to *RAS* group (58 % vs 8%; p=0.04). Classic variant papillary thyroid cancer was the most common histologic diagnosis with both mutations, however, follicular-variant papillary thyroid cancer was more common in *RAS* than *BRAFV600E* group (29% vs 8%, p=0.04) and follicular thyroid cancer was only seen in the *RAS* group (25% vs 0%, p<0.05). There was no difference in gender, age at diagnosis, disease status after initial therapy, RAI treatment, RAI dosage, and mortality between the groups.

Conclusion: Thyroid cancer associated with a *RAS*-mutation has less tendency to metastasize locally and has a higher incidence of bone metastasis compared to thyroid cancer with *BRAFV600E*-mutation. Individualized clinical follow up may be indicated depends on their mutational profile.

References:

1. Cancer Genome Atlas Research N. Integrated genomic characterization of papillary thyroid carcinoma. *Cell*. 2014;159(3):676-690.

2. Nikiforova MN, Lynch RA, Biddinger PW, et al. RAS point mutations and PAX8-PPAR gamma rearrangement in thyroid tumors: evidence for distinct molecular pathways in thyroid follicular carcinoma. *J Clin Endocrinol Metab*. 2003;88(5):2318-2326.

Steroid Hormones and Receptors

STEROID AND NUCLEAR RECEPTORS

Low-Dose Dihydrotestosterone Lowers Lipogenic Master Regulator in Liver and Adipose Tissue from Female Mice

Tina Seidu, MHS, Stanley Andrisse, Ph.D.
Howard University College of Medicine, Washington, DC, USA.

SUN-740

Hyperandrogenemia (HA) and insulin resistance (IR) are hallmarks of polycystic ovary syndrome (PCOS), a common endocrine disorder that affects 1 in 10 women. These hallmarks are also integral elements of non-alcoholic liver disease (NALFD), a disorder that is common in women with PCOS. Administering low dose dihydrotestosterone (DHT) induced a lean female mouse model with a PCOS-like phenotype, displaying IR and NAFLD. The molecular mechanism of HA-induced NAFLD has not been determined. We hypothesized that low dose DHT would interrupt hepatic lipid metabolism leading to NAFLD. To investigate the role of androgens on the master regulator of lipogenesis, sterol regulatory element-binding protein 1 (SREBP1), we extracted white adipose tissue (WAT), liver, and skeletal muscle from wild-type, control and low dose DHT female mice; and performed Western blot and real-time quantitative PCR (qRT-PCR) analysis of lipogenic intermediates of the tissue homogenates. Low-dose DHT lowered the active form of cytosolic SREBP1 in the liver and WAT compared to controls. Additionally, low dose DHT lowered inactive SREBP1 in the liver. However, the condition did not alter the levels of the active and inactive forms of SREBP2 in the liver and WAT, though the active form was lowered in skeletal muscle. Further, p-ACC levels were unaltered in liver and WAT. FAS levels were unchanged in WAT and skeletal muscle. Taken together, our findings support the hypothesis that cytosolic SREBP1 decreased due to its translocation to the nucleus, where it regulates lipogenic protein levels. We speculate that low-dose DHT promotes the translocation of SREBP1 from the cytosol to the nucleus to influence lipogenic gene expression leading to increased lipogenesis contributing to NAFLD.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL GLUCOSE METABOLISM AND DIABETES

Effect of Whole Body Vibration on Glycemic Control in Adults with Type 2 Diabetes

Manuela de Lucca Michels, MD, Ana Clara d'Acampora, MD, Camila Sartor Spivakoski, MD, Priscila Nobre Dantas Mattje, MD, Bruna da Silva Réus, MD, Débora Monteiro dos Santos Alves, MD, Karine Pilletti, MD, Marcelo Fernando Ronsoni, MD, PhD, Alexandre Hohl, MD, MSc, PhD, Simone van de Sande-Lee, MD, PhD.