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Thyroid cancer biology is extremely diverse. While some cases never progress clinically or do so indolently, others evolve aggressively and may even lead to death. Cell adhesion molecules are glycoproteins present in the cell membrane and play an important role in inflammatory and neoplastic diseases by recruiting immune cells to these sites. The aim of the present study was to investigate the role of mRNA expression of SELL, ICAM1 and ITGAL in thyroid tumors and their relationship with lymphocyte infiltration. We evaluated by RT-qPCR technique 191 thyroid nodules including 97 benign (79 females, 17 males; 49.8±12.5 years old) and 94 malignant (71 females, 23 males; 48.3±15.5 years old) cases. Clinical and pathology data were obtained from 47 goiters; 50 follicular adenomas (FA); 74 papillary thyroid carcinomas (PTC), including: 29 classic papillary thyroid carcinomas (CPTC), 21 follicular variant of PTC (FVPTC), 12oxifilic variant of PTC (OVPTC), 12 tall cell papillary thyroid carcinomas (TCPTC); and 20 follicular thyroid carcinomas (FTC). All patients were managed according to a standard protocol based on current guidelines and followed-up for 78.7±54.2 months. SELL was more expressed in malignant (0.85±1.54 UA) than in benign (0.54±0.71 UA, p=0.0027) nodules. The same occurred with ICAM1 (0.99±1.41 vs. 0.46±0.85, p=0.0001), but not with ITGAL gene expression (1.04±1.63 vs. 0.76±1.21, p=0.2131). In addition, the expression of SELL was different when we compared PTC with FA (0.94±1.62 UA vs. 0.47±0.72 UA, p=0.0018) and FTC with FA (0.82±2.38 UA vs. 0.47±0.72 UA, p=0.0078). ICAM1 expression was lower in goiters (0.46±0.90 UA) when compared with PTC (0.93±1.22 UA, p=0.0030) and FTC (1.03 \pm 3.30 UA, p=0.0207). Higher expression of *ICAM1* $(1.16\pm3.04~{\rm UA~vs.}~0.52\pm0.96~{\rm UA},~{\rm p=}0.0064)$ and ITGAL(1.17±1.54 UA vs. 0.49±1.39 UA, p=0.0244) was observed in tumors with lymphocyte infiltrate. Also, ITGAL gene expression was higher in tumors that had distant metastasis at diagnosis (1.53±2.18 UA vs. 0.57±1.10 UA, p=0.0217). We were not able to demonstrate any association between any of the investigated molecules and patients' outcome. In conclusion, our data suggest that cell adhesion molecules may play an important role in neoplastic thyroid cells proliferation. In addition, our findings show that gene expression of SELL and ICAM1 may assist in the histological characterization of follicular patterned thyroid nodules.

Reproductive Endocrinology

SEX DETERMINATION AND REPRODUCTIVE AXIS DEVELOPMENT

Discordant Serum 17-hydroxyprogesterone and Androstenedione in the Management of Congenital Adrenal Hyperplasia: Are 11-oxygenated Androgens Useful?

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Background 21-hydroxylase-deficiency (210HD) accounts for more than 95% of CAH cases. Serum 17-hydroxyprogesteron (170HP) and androstenedione (A4) are traditional biomarkers for monitoring therapy. While generally there is good linear correlation between 17OHP and A4, physicians are likely to encounter scenarios where 170HP is within "acceptable range" while A4 is elevated and vice versa. Mildly elevated 170HP is considered acceptable, as normalization of 170HP is likely to result in overtreatment. 11-ketotestosterone (11KT) is a potent agonist of the androgen receptor with androgenic activity equivalent to testosterone. We hypothesized that patients with high 170HP would be more likely than those with high A4 to be in good disease control. We speculated that A4 would correlate more strongly with 11-oxygenated C₁₉ steroids (11oxyandrogens) than 17OHP and that patients in poor clinical control would have higher median fold-elevation of 11oxyandrogens, especially 11-KT, compared to controls. **Methods** We performed retrospective analysis of patients seen at NIH from 2006 to 2019 and identified discordant 17OHP and A4 (17-OHP ≥1200 ng/dL with A4 normal for age/sex or tanner stage and vice-versa). Good or poor clinical control was based on abnormal growth, precocious puberty. irregular menses, hypogonadotrophic hypogonadism and A4/T. Quantitation of 15 steroids in stored peripheral sera was performed by LC-MS/MS and compared to age- and sexmatched controls. Data between groups were compared using t-tests or non-parametric Wilcoxon rank sum tests. Correlation analyses utilized the Pearson and Spearman's rho. Results We identified 122 of 789 (15%) discordant laboratory assessments among adults [84 with high 170HP (69%)] and 347 of 1,949 (18%) among children [319 with high 170HP (92%)]. Of these, 50 patients with available serum samples were identified (44 with high 17OHP). Twenty-five patients (50%) appeared to have good disease control. There was no difference in the frequency of patients in good or poor control between patients with high 17OHP or those with high A4 (p=0.7). Median fold elevation of 11KT relative to controls was higher in patients in poor control (2.87 fold, IQR 1.87-5.42, range 0.31-10.69) but with wide ranges and substantial overlap compared to those in good control (1.71 fold, IQR 1.06-2.92, range 0.35-16.59, p=0.068). 17OHP correlated with 21-deoxycortisol (r =0.67, p<.001) while A4 correlated strongly with 11oxyandrogens (r range 0.42-0.71, p<.003 for all). However, we did not find any substantial difference in the level of 11oxyandrogens between patients with high 170HP and those with high A4. Conclusion: Discordance between 17OHP and A4 is common in the management of CAH and patients with elevation of either of these biomarkers are equally likely to have poor disease control. Limited evidence suggests a role for 11KT, as a discriminator for disease control.

Pediatric Endocrinology

SEXUAL AND GENDER DEVELOPMENT IN THE PEDIATRIC POPULATION

Gain in Near Adult Height Using the Combination of an LHRH Analogue and an Aromatase Inhibitor in Early Maturing Girls with Compromised Growth. The "Gail" Study ISRCTN11469487

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