Conclusion: HNF4A gene encodes hepatocyte nuclear factor-4-alpha that regulates hepatic gluconeogenesis and lipid metabolism. Dominant inactivating variants in HNF4A gene associated with familial HI, are typically associated with increased size for gestational age, mild diazoxide-responsive hypoglycemia (which may be transient) and monogenic diabetes during adolescence. HNF4A mutations were described as one of the most common genetic cause of diazoxide-responsive congenital hyperinsulinism and are associated with MODY1. It is important to consider genetic evaluation in diazoxide responsive HI cases. Identifying children with HNF4A variant early on will impact their long-term follow-up leading to earlier diagnosis and treatment of MODY-1 and potentially improve long-term outcomes.

Thyroid

THYROID NEOPLASIA AND CANCER

Influence of Lymphocytic Thyroiditis at Histology and Serum Thyroglobulin Autoantibodies on the Course of Papillary Thyroid Carcinoma

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PURPOSE Papillary thyroid carcinoma (PTC) is frequently associated with diffuse lymphocytic thyoiditis (LT) at histology and serum autoantibodies to thyroglobulin (TgAb) and to thyroperoxidase (TPOAb). The influence of LT and thyroid autoantibodies on the prognosis of PTC is debated. We evaluated the clinical course of a large group of PTC patients according to the presence or absence of LT (LT+ and LT-) and thyroid autoantibodies. METHODS We evaluated 194 consecutive and non-selected PTC patients treated with total thyroidectomy plus ^{131}I ablation between 2007 and 2009, followed for 7.2 years (mean). 72 patients had follicular variant of PTC, 97 classic, 16 tall cells and the remaining 9 others variants (solid or oxyphilic cells). LT was diagnosed in presence of >10 lymphocytes/field (40x). At the time of ablation, all patients underwent measurement of Tg, TgAb and TPOAb, neck ultrasound and whole body scan. After ablation, patients underwent Tg (Beckman Coulter), TgAb and TPOAb (Tosoh) measurement and neck ultrasound (associated with other imaging if required) every 6-12 months. PTC was considered in remission according to the following criteria: un-stimulated Tg <0.2 ng/mL or stimulated Tg <1 ng/mL with TgAb <8 IU/mL and no evidence of structural disease. PTC was considered as persistent when un-stimulated Tg was ≥0.2 ng/mL or stimulated Tg was ≥1 ng/mL, or when TgAb were ≥8 IU/mL, or there was evidence of structural disease. RESULTS LT was found in 47% of patients, with a F/M ratio of 6.6/1, and was associated with a hypoechoic pattern at thyroid ultrasound (p = 0.05). At the end of follow-up 44/194 (22.7%) had persistent disease. Among them, 17/72 (23.6%) were follicular, 19/97 (19.6%) classic, 6/16 (37.5%) tall cells and 2/9 (22.2%) other variants. The time to remission was longer in the LT+ compared to the LT- patients (19.5 vs 7.5 months) (median) (p <0.001), in TgAb positive compared to TgAb negative patients (28.5 vs 7.5 months) (p <0.001) and in TPOAb positive compared to TPOAb negative patients (28.0 vs 8.0 months) (p = 0.005). At multivariate analysis TgAb were the only independent factor influencing the time to remission (0.54; 0.35-0.83; HR and confidence interval) (p = 0.001). However, evaluating only the 111 TgAb negative patients, the time to remission (undetectable un-stimulated or stimulated Tg and no evidence of structural disease) was similar in the LT+ and LT- groups (8.0 months for both). At variance, in 83 TgAb positive patients the time to remission was longer in LT+ than in LT- patients (29.3 vs 13.0 months) (p=0.01). CONCLUSIONS The time to remission is longer in LT+ compared to LT- PTC patients treated with total thyroidectomy plus ^{131}I ablation. This is due to the frequent association of LT with TgAb, because undetectable TgAb is required to define the remission of PTC. Indeed, coexistent LT does not influence the time to remission when the analysis is restricted to TgAb negative patients.

Thyroid

THYROID NEOPLASIA AND CANCER

Polygenic Susceptibility to Papillary Thyroid Cancer in Italian Subjects

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Polygenic Susceptibility to Papillary Thyroid Cancer in Italian Subjects

INTRODUCTION AND AIM. Thyroid cancer is the most common endocrine neoplasia, with an estimated age-standardized incidence rate of 6.7 per 100000 worldwide in 2018 [1]. This rate is rapidly increasing and papillary thyroid carcinoma (PTC) is the main histotype. PTC susceptibility is the result of genetic predisposition, environmental factors and lifestyle. We studied the genetic combination that characterizes PTC affected subjects, differentiating them from healthy controls.

METHODS AND RESULTS. We considered the genetic variants (SNPs) significantly associated with PTC on the PubMed database. 184 informative SNPs were selected, considering linkage disequilibrium. Then, SNPs data were extracted from the online 1000 Genomes database,