

Introduction: Thyroid immune-related adverse events (irAEs) occur frequently after immune checkpoint inhibitor (ICI) cancer therapy, but their risk factors and potential influence on survival need further investigation. **Methods:** We performed a retrospective single-center cohort study of adult cancer patients who received ICIs including CTLA-4, PD-1, PD-L1 inhibitors from 12/1/2012-12/31/2019. Patients who developed thyroid irAEs after excluding surgical or ablative hypothyroidism were included. Survival analysis was performed by Kaplan-Meier curves and Cox-proportional hazards model. **Results:** Thyroid irAEs occurred in 145 (17.4%) of 834 ICI-treated patients (median age 64.9 y, 43.4% females) during a median follow-up of 11.6 mo. New-onset thyroid dysfunction occurred in 118 (14.2%), of which 55 presented with thyrotoxicosis (32 progressed to hypothyroidism, 22 returned to euthyroid state, 1 had Graves' disease). Worsening of pre-existing autoimmune hypothyroidism ($\geq 50\%$ increase in levothyroxine dose) occurred in 27 (3.2%). Of those with new-onset thyroid dysfunction, 79 (67%) required levothyroxine eventually. Patients with thyroid irAE had similar age, sex and cancer type as compared to those without but had higher median pre-treatment TSH [2.4 vs. 1.7 mIU/L ($p < 0.0001$); multivariable OR for TSH ≥ 2.4 mIU/L of 2 (95% CI 1.3, 3.2; $p = 0.004$)] and higher frequency of autoimmune disease history [26.9% vs. 14.8% ($p = 0.0009$); multivariable OR of 2 (95% CI 1.2, 3.5; $p = 0.013$)]. Thyroid irAEs occurred after a median of 2.4 mo from ICI, most frequently with PD-1/PD-L1 inhibitor. Thyroid irAEs were associated with better median overall survival [38.8 mo (95% CI 26.6, not reached) vs. 18.9 (95% CI 14.2, 24.8); $p < 0.0001$] which persisted on restricting to patients with new-onset thyroid dysfunction [40.1 mo (95% CI 26.6, not reached) vs. 18.8 (95% CI 13.6, 24.8); $p < 0.0001$]. On multivariable analysis, thyroid irAEs had HR for mortality of 0.51 (95% CI 0.37, 0.71; $p < 0.0001$), which persisted on restricting to new-onset thyroid dysfunction [HR 0.48 (95% CI 0.34, 0.69; $p < 0.0001$)]. **Conclusions:** Thyroid irAEs frequently occur after PD-1/PD-L1 inhibitor therapy, presenting as hypothyroidism or thyrotoxicosis usually progressing to hypothyroidism. Higher TSH even within normal range and autoimmune disease history may be risk factors for thyroid irAE. Improved survival with thyroid irAEs suggests these could be a marker for anti-tumor activity.

Thyroid

THYROID AUTOIMMUNITY, COVID-19 & THYROID DISEASE

What Are the Common Characteristics of Pediatric Patients With Antibody Negative Primary Hypothyroidism?

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Background: The most common cause of acquired primary hypothyroidism is autoimmune thyroiditis which is typically associated with positive anti-thyroid peroxidase and/or anti-thyroglobulin antibodies. However, some children present with primary hypothyroidism and negative antibodies. Whether there are differences between patients

with acquired primary hypothyroidism who have positive vs negative anti-thyroid antibodies has not been systematically examined. **Aim:** To define the characteristics of patients with primary hypothyroidism and negative antibodies. **Methods:** A retrospective chart review of patients with hypothyroidism seen in the pediatric endocrine clinic at Riley Hospital for Children in Indianapolis, Indiana from August 2016 until December 2019 was performed. Variables examined included age at diagnosis, signs and symptoms at presentation, height, weight, BMI, TSH, FT4, T4, thyroid peroxidase and anti-thyroglobulin antibodies, family history of thyroid disease, physical exam at diagnosis, and associated diseases. **Results:** Of 173 patients aged 10.6 ± 3.9 years, 128 (74%) had positive antibodies and 44 (26%) had negative antibodies. Of those with positive antibodies, 80% were female and 20% were male. Of those with negative antibodies, 53% were female and 47% were male. No differences were seen in the incidence of obesity or Down syndrome in patients with positive antibodies compared with those who had negative antibodies. A positive family history of thyroid disease was present in 45% of those with positive antibodies and in 22% of those with negative antibodies, $P = 0.006$. Fifty-eight patients (45%) with positive antibodies reported excessive fatigue and 40 (31%) had a goiter. In contrast, 10 (22.7%) who had negative antibodies reported mild intermittent fatigue, $P = 0.006$ and 7 (15.9%) had a goiter, $P = 0.04$. The average TSH in the antibody positive group was 129 ± 230 mcu/ml compared with 48 ± 131 mcu/ml in those with negative antibodies, $p = 0.04$. A trend was also noted for a lower FT4 in those with positive antibodies (0.68 ± 0.37 vs 0.85 ± 0.27 , $p = 0.050$). No other differences in baseline characteristics were seen between patients with negative vs positive antibodies. **Conclusion:** Patients with positive anti-thyroid antibodies had more severe hypothyroidism and were more likely to report extreme fatigue than those with negative antibodies. It is unknown why some children with acquired primary hypothyroidism presumed due to autoimmune thyroid disease have negative antibodies. Long-term follow-up will be needed to determine whether the natural history of thyroid disease in children with primary hypothyroidism is associated with antibody status.

Thyroid

THYROID BIOLOGY, HYPOTHALAMIC-PITUITARY-THYROID AXIS

Alert for TSH Measurement in High-Risk Pregnancies in Brazil

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Introduction: The hypothyroidism during pregnancy can lead to alterations in fetal neurological formation and has metabolic impact on pregnant women. If not diagnosed and treated it can cause complications during pregnancy and childbirth, besides causing changes in fetal formation. The