Thyroid Function Before, During and After COVID-19

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Context: The effects of COVID-19 on the thyroid axis remain uncertain. Recent evidence has been conflicting, with both thyrotoxicosis and suppression of thyroid function reported. **Objective:** We aimed to detail the acute effects of COVID-19 on thyroid function and determine if these effects persisted upon recovery from COVID-19. **Design:** Cohort observational study. **Participants and Setting:** Adult patients admitted to Imperial College Healthcare National Health Service Trust, London, UK with suspected COVID-19 between March 9 to April 22, 2020 were included, excluding those with pre-existing thyroid disease and those missing either free thyroxine (FT4) or TSH measurements. Of 456 patients, 334 had COVID-19 and 122 did not. **Main Outcome Measures:** TSH and FT4 measurements at admission, and where available, those taken in 2019 and at COVID-19 follow-up. **Results:** Most patients (86·6%) presenting with COVID-19 were euthyroid, with none presenting with overt thyrotoxicosis. Patients with COVID-19 had a lower admission TSH and FT4 compared to those without COVID-19. In the COVID-19 patients with matching baseline thyroid function tests from 2019 (n=185 for TSH and 104 for FT4), both TSH and FT4 were reduced at admission compared to baseline. In a complete cases analysis of COVID-19 patients with TSH measurements at follow-up, admission and baseline (n=55), TSH was seen to recover to baseline at follow-up. **Conclusions:** Most patients with COVID-19 present with euthyroidism. We observed mild reductions in TSH and FT4 in keeping with a non-thyroidal illness syndrome. Furthermore, in survivors of COVID-19, thyroid function tests at follow-up returned to baseline.

Thyroid

THYROID AUTOIMMUNITY, COVID-19 & THYROID DISEASE

Thyroid Immune-Related Adverse Events Among Cancer Patients Treated With Combination of Anti-PD1 and Anti-CTLA4 Immune-Checkpoint Inhibitors: Clinical Course and Outcomes

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Introduction: Thyroid immune-related adverse events (irAEs) have been reported to have prognostic significance among cancer patients treated with anti-PD1 and anti-PDL1 monotherapies. There are scanty data in the literature thus far about the clinical course and prognostic significance of thyroid irAEs in the routine clinical use of combination anti-PD1/anti-CTLA4 treatment in advanced cancer patients. We evaluated the clinical course and predictors of thyroid irAEs, in relation to outcomes of advanced cancer patients treated with combination anti-PD1/anti-CTLA4. **Method:** We conducted a territory-wide study and identified advanced cancer patients who received ≥1 cycle of combination anti-PD1/anti-CTLA4 between 2015 and 2019 in Hong Kong. Patients were excluded if (i) they had a history of thyroid disorder or thyroid cancer, (ii) immune checkpoint inhibitor-related endocrinopathies occurred before the commencement of combination anti-PD1/anti-CTLA4, (iii) they were on concurrent tyrosine kinase inhibitor (TKI), (iv) baseline thyroid function tests (TFTs) were absent or abnormal, and (v) the duration of follow-up was <30 days. TFTs were monitored every three weeks. Thyroid irAE was defined by ≥2 abnormal TFTs after initiation of combination anti-PD1/anti-CTLA4 in the absence of other causes. The initial presentation was classified into hypothyroidism (overt if TSH >4.8 mIU/L and fT4 <12 pmol/L; subclinical if TSH >4.8 mIU/L and fT4 12-23 pmol/L) and thyrotoxicosis (overt if TSH <0.35 mIU/L and fT4 >23 pmol/L; subclinical if TSH <0.35 mIU/L and fT4 12-23 pmol/L). **Results:** One hundred and three patients were included (median age: 59 years; 71.8% men). Around half of patients had hepatocellular carcinoma. About 45% had prior anti-PD1 exposure. Upon median follow-up of 6.8 months, 17 patients (16.5%) developed thyroid irAEs, where 6 initially presented with thyrotoxicosis (overt, n=4; subclinical, n=2), and 11 with hypothyroidism (overt, n=2; subclinical, n=9). Eventually, 10 patients (58.8%) required continuous thyroxine replacement. Systemic steroid was not required in all cases. Prior anti-PD1 exposure (OR 3.67, 95% CI 1.19-11.4, p=0.024) independently predicted thyroid irAEs. Multivariable Cox regression analysis revealed that occurrence of thyroid irAEs was associated with better overall survival (adjusted hazard ratio 0.39, 95% CI 0.19-0.79, p=0.009), independent of prior exposure to anti-PD1 (p=0.386) and prior TKI exposure (p=0.155). **Conclusion:** Thyroid irAEs are common in routine clinical practice among advanced cancer patients treated with combination anti-PD1/anti-CTLA4, and might have potential prognostic significance. Regular TFT monitoring is advised for timely treatment of thyroid irAEs to prevent potential morbidities.

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Thyroid Immune-Related Adverse Events Are Associated With Improved Survival in Cancer Patients

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