DURVALUMAB-INDUCED GRAVE'S DISEASE

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Objective

Immune checkpoint inhibitors (ICIs) used to treat advanced cancers are commonly associated with autoimmune thyroid endocrinopathies. Destructive thyroiditis and hypothyroidism are the more frequent types of thyroid dysfunction, while Grave's disease (GD) is rarely reported. Similar to other ICIs, durvalumab is an anti-programmed cell death-ligand 1 (PD-L1) monoclonal antibody that can induce thyroid dysfunction. We report a unique case involving a patient who developed hyperthyroidism due to GD after initiation of durvalumab for non-small cell lung cancer.

Case Presentation

A 56 year old woman with a past medical history of stage III lung adenocarcinoma presented with asymptomatic sinus tachycardia, with a heart rate of 150 bpm. Labs showed an undetectable TSH < 0.01 IU/mL and an elevated FT4 of 6.9 ng/dL. Three weeks prior to her presentation she had been started on durvalumab 611 mg IV for her locally advanced lung cancer and had received a total of 2 doses. Thyroid function tests (TFTs) prior to the initiation of durvalumab were consist with subclinical hyperthyroidism as TSH was suppressed to 0.054 IU/mL and FT4 was normal at 1.75 ng/dL. Furthermore, her mother had a history of GD. A radioactive iodine uptake (RAIU) scan was not performed since she had undergone imaging with iodinated contrast to assess for pulmonary embolism, which was negative. Due to evidence of subclinical hyperthyroidism prior to the ICI and her family history, she was started on methimazole 15 mg daily for presumed GD and metoprolol 100 mg twice a day.

Methimazole was initiated at a lower dose because of a low absolute neutrophil count of 640/uL. A thyroid ultrasound demonstrating diffuse increased vascularity supported a diagnosis of GD, but thyroid stimulating immunoglobulin (TSI) was absent. Durvalumab was held until FT4 normalized to 0.82 ng/dL. Methimazole and metoprolol continue to be reduced based on monthly TFTs and heart rate.

Relevant Figure

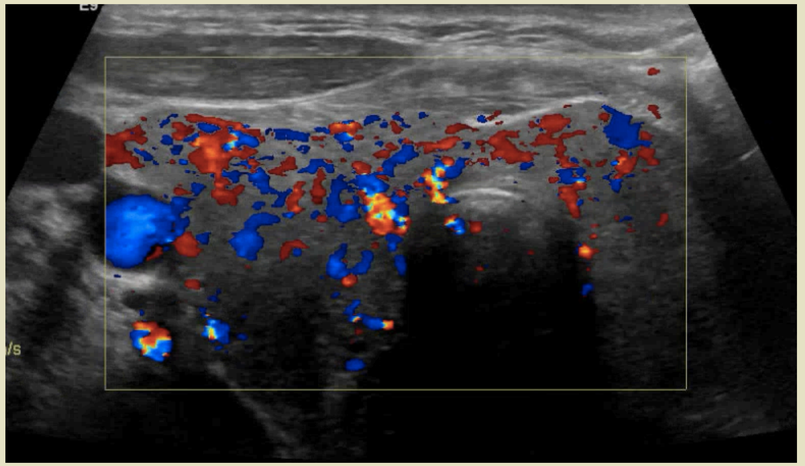

Figure 1: Right thyroid lobe transverse ulltrasound with increased vascularity

References

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Discussion

ICIs have become popular therapies for advanced cancers, but they can prompt autoimmune endocrine disorders, including GD, by virtue of how they function to stimulate the immune system. Features favoring GD include the presence of thyroid autoantibodies, diffuse increased vascularity on thyroid ultrasound, diffuse increased uptake on RAIU scan, Grave's ophthalmopathy, and/or family history of GD. In our case, not only did our patient have a thyroid ultrasound consistent with GD and a positive family history, but she also had labs consistent with subclinical hyperthyroidism prior to the initiation of the ICI durvalumab. In addition, the tachycardia and hyperthyroidism that developed after durvalumab was started significantly improved with methimazole. These features highlight that such patients with subclinical hyperthyroidism should be evaluated for GD and may require anti-thyroidal therapy before the initiation of ICIs to avoid symptoms of thyrotoxicosis. Another important point to note from our case is that the absence of TSI antibodies does not rule out GD. Based on guidelines, the patient's ICI was held to allow normalization of TFTs. Once TFTs were WNL, durvalumab was restarted and methimazole was continued.

Conclusion

Although rare, hyperthyroidism due to GD may be induced by ICIs, such as anti-PD-L1 monoclonal antibodies, as shown in our case. Therefore, physicians caring for patients who develop thyrotoxicosis while on ICIs should have the ability to distinguish between GD and destructive thyroiditis. Furthermore, the presence of subclinical hyperthyroidism prior to the initiation of ICIs should prompt the evaluation of GD and consideration of anti-thyroidal therapy to prevent the development of thyrotoxicosis.