Progressive loss of the thyroid tissue integrity visualised by serial CT scans

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SUMMARY
A man in his 70s developed thyrotoxicosis due to painless thyroiditis after starting nivolumab, which was subsequently followed by severe hypothyroidism. We diagnosed him as chronic thyroiditis, initiated levothyroxine supplementation and treated appropriately. Retrospective CT images of the thyroid gland during the clinical course revealed that the CT attenuation value was high at first but gradually decreased. The high-density signal of the normal thyroid tissues reflects its function of concentrating inorganic iodine, and the progressive decrease of the CT density in the present case can be viewed as a reflection of the thyroid destruction and progressive loss of iodine during the clinical course of the development of chronic thyroiditis. Considering the high incidence rate of functional thyroid disease in patients treated with immune checkpoint inhibitors, CT density of the thyroid gland needs to be paid attention to as the first sign of thyroiditis in this patient population.

DESCRIPTION
Case presentation
A man in his 70s without any history of thyroid disease underwent partial resection of gastric and rectal double cancer 3 years before. As a third-line chemotherapy, nivolumab was initiated.

Fifty-six days after nivolumab initiation, thyrotoxicosis was first noted by a regular blood test. Absence of fever, acute swelling or neck pain along with negative antithyrotropin receptor autoantibody has led us to the diagnosis of painless thyroiditis. During the follow-up, his serum-free thyroxine and triiodothyronine levels were subsequently decreased. Since both antithyroidperoxidase and antithyroglobulin autoantibodies were positive, we diagnosed him as chronic thyroiditis potentially as a manifestation of immune-related adverse event. Therefore, levothyroxine supplementation was initiated on day 108 and the patient became euthyroid at the daily dose of 100 µg levothyroxine on day 260.

Since serial CT scans were performed to see any signs of cancer progression, we retrospectively looked at the thyroid gland during the clinical course. On the first day of nivolumab administration, the thyroid gland could easily be identified with a high attenuation with the CT density of 88.2 HU (figure 1A). However, on day 56 when the patient was diagnosed as painless thyroiditis, the CT density was decreased down to 64.1 HU (figure 1B). On day 108 and when he was diagnosed as hypothyroid, the density eventually dropped as low as 44.0 HU and became almost indistinguishable from the surrounding neck muscles (figure 1C).

Figure 1 Image studies of the thyroid gland. Thyroid gland on both sides (orange arrowhead) are shown by CT scans (A–C) or by ultrasonography (D). CT scans are performed serially on day 0 (A), day 56 (B) and day 108 (C) of the nivolumab therapy, showing the time-dependent loss of the high-density signal of the gland suggestive of inflammation and destruction. Ultrasonography is performed on day 56, on the same day as (B).

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DISCUSSION

We experienced a case of immune checkpoint inhibitor-associated chronic thyroiditis whose progressive loss of the thyroid tissue integrity was visualised by serial CT scans.

The normal thyroid gland generally gives a high-density signal of 80–100 HU in CT scans and thus can easily be distinguished from the surrounding organs such as neck muscles or vasculature. The high-density signal of the normal thyroid tissues reflects its function of concentrating inorganic iodine, whose local concentration reaches almost 100 times higher than that in the serum. In painless thyroiditis, as the inflammatory cells infiltrate and follicular cells are rapidly destroyed, the iodine storage is depleted and the CT density is reported to be decreased. Although no histological evidence of inflammation or follicle destruction was available, the progressive decrease of the CT density in the present case can be viewed as a reflection of the thyroid destruction and progressive loss of iodine during the clinical course of the development of Hashimoto thyroiditis.

Although CT scan is not generally accepted as the basic diagnostic tool for functional thyroid diseases, our case illustrates a potential effectiveness of its use in some cases. CT scans may particularly be beneficial in cases treated with immune checkpoint inhibitors, whose cancer is followed up by serial CT scans. More importantly, with a desperately high incidence rate of approximately 10% of functional thyroid disease in patients treated with immune checkpoint inhibitors, CT density of the thyroid gland needs to be paid attention to as the first sign of thyroiditis in this patient population.

CONTRIBUTORS
HK is the attending physician in charge of treating thyroid disease and drafting the article. RH is giving advice to HK. HS played a central role in the treatment of this patient’s cancer. TT is the head of our department. We gather everyone together and argue about the patient to achieve a correct diagnosis and treatment. He also had final approval of the article to be published.

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REFERENCES

LEARNING POINTS
- The high-density signal of the thyroid tissues in CT scans reflects the integrity of the gland, which concentrates inorganic iodine.
- Loss of the signal is potentially useful in the early detection of Hashimoto thyroiditis.
- In patients treated with immune checkpoint inhibitors, CT images taken for cancer follow-up should be screened for any change of the thyroid density to watch for the onset of thyroiditis.