Hyperthyroidism secondary to disseminated differentiated thyroid cancer on \(^{99m}\text{TcO}_4\) scan

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To the Editor: A 53-year-old woman was admitted to the Zhongshan Hospital, Fudan University because of pain and suspected lobectomy of right thyroid, but no cancer was found pathologically. In recent 1 year, the patient developed hyperthyroidism, but no treatment was given because of leukocyte depletion induced by methimazole. She had typical symptom of hyperthyroidism and was supported by her laboratory test results as follows: free triiodothyronine, 12.3 pmol/L (reference 2.8–7.1 pmol/L); free tetraiodothyronine, 46.7 pmol/L (reference 12.0–22.0 pmol/L); thyroglobulin (Tg), >5000.0 ng/mL (reference 1.4–78.0 pmol/L); thyroid-stimulating hormone, <0.005 μIU/mL (reference 0.270–4.200 μIU/mL); anti-Tg antibodies, 163.2 IU/mL (reference <115.0 IU/mL); and thyroid peroxidase antibody, 15.5 IU/mL (reference <34.0 IU/mL). Multiple nodules in the left lobe of the thyroid which were suspected as adenomas were disclosed by ultrasonography. Family history of thyroid disease was denied.

On \(^{99m}\text{TcO}_4\) scintigraphy, mild radioactivity accumulation (lower than the nasal mucosa) in area of right iliac bone. Eight years ago, she underwent lobectomy of right thyroid, but no cancer was found pathologically. In recent 1 year, the patient developed hyperthyroidism, but no treatment was given because of leukocyte depletion induced by methimazole. She had typical symptom of hyperthyroidism and was supported by her laboratory test results as follows: free triiodothyronine, 12.3 pmol/L (reference 2.8–7.1 pmol/L); free tetraiodothyronine, 46.7 pmol/L (reference 12.0–22.0 pmol/L); thyroglobulin (Tg), >5000.0 ng/mL (reference 1.4–78.0 pmol/L); thyroid-stimulating hormone, <0.005 μIU/mL (reference 0.270–4.200 μIU/mL); anti-Tg antibodies, 163.2 IU/mL (reference <115.0 IU/mL); and thyroid peroxidase antibody, 15.5 IU/mL (reference <34.0 IU/mL). Multiple nodules in the left lobe of the thyroid which were suspected as adenomas were disclosed by ultrasonography. Family history of thyroid disease was denied.

On \(^{99m}\text{TcO}_4\) scintigraphy, mild radioactivity accumulation (lower than the nasal mucosa) in area of neck. In addition, multiple lesions with radioactivity accumulation could be found in the thorax [Figure 1A]. Therefore, the patient received \(^{99m}\text{TcO}_4\) whole-body planar imaging, which revealed intense tracer accumulation in the thorax and multiple bones [Figure 1B]. Percutaneous CT-guided biopsy was performed and follicular epithelium was found, pathologically [Figure 1E]. Immunohistochemically, the tumor tissue was positive for Tg and thyroid transforming factor-1 [Figure 1F and 1G]. Left thyroid lobectomy was conducted with the post-operative pathology prone to be follicular adenoma. The uptake of \(^{99m}\text{TcO}_4\) in residual thyroid was mild, but the thyroid hormone was high. This indicated secondary hyperthyroidism which might be caused by the hormone secreted from the metastatic lesions.\(^{[1]}\) Extensive lung and bone metastases were visualized on \(^{99m}\text{TcO}_4\) imaging, which could not explain the diagnosis of follicular adenoma in situ, but were consistent with follicular carcinoma. Therefore, empirical treatment of radioactive \(^{131}\text{I}\) at a dose of 3700 MBq (100 mCi) was given to her. Post-therapy whole-body \(^{131}\text{I}\) planar imaging [Figure 1C and 1D] revealed multiple lesions with intense radioiodine uptake in the thorax and bones, consistent with lung and bone metastases, respectively.

Four months after treatment, the serum level of T3, T4, and Tg decreased gradually to 3.2, 12.7 pmol/L, and 430.9 ng/mL, respectively. Therefore, the patient was treated with radioactive \(^{131}\text{I}\) again. One year after, the level of T3, T4, and Tg dropped to 4.3, 29.1 pmol/L, and 3.2 ng/mL, respectively.

Thyroid carcinoma may occur concomitantly with thyrotoxicosis in one patient. It has been proposed previously that hyperthyroidism may be due to overproduction of thyroid hormone by a malignant tumor.\(^{[1]}\) However, hyperthyroidism secondary to disseminated differentiated thyroid cancer is rare and its molecular mechanism has not been clarified so far. The pre-treatment diagnostic \(^{131}\text{I}\) whole-body scan to detect residual thyroid and metastatic foci is still controversial in clinic because of \(^{131}\text{I}\)-induced thyroid stunning.\(^{[2]}\) \(^{99m}\text{TcO}_4\) is a substrate for the sodium-iodide symporter protein which can be accumulated in the membrane of thyroidal cells. The \(^{99m}\text{TcO}_4\) whole-body scan has been widely applied in assessment of thyroid diseases.\(^{[2,3]}\) However, it is not as sensitive as \(^{131}\text{I}\) whole-body scan, and negative false result is common in \(^{99m}\text{TcO}_4\) whole-body scan.

A rational treatment should take the clinical symptoms, laboratory results, and imaging findings into consideration. \(^{99m}\text{TcO}_4\) whole-body imaging can provide additional...
The possibility of secondary hyperthyroidism induced by metastases from differentiated thyroid carcinoma should be considered when uptake of $^{99m}$TcO$_4^{-}$ in residual thyroid was lower than that of the nasal mucosa on $^{99m}$TcO$_4^{-}$ scintigraphy, especially in condition of elevated serum Tg.

**Declaration of patient consent**

The authors certify that they have obtained written informed consent from the patient. The patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

None.

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