

A patient with two thyroid papillary carcinomas demonstrating hot and cold lesions on ^{123}I thyroid scintigraphy

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A 44-year-old euthyroid woman had two palpable nodules in the thyroid gland. ^{123}I thyroid scintigraphy showed a hot nodule in the right lobe and a cold one in the left lobe. Total thyroidectomy was performed, and histopathologic examination revealed that both tumors contained papillary carcinoma. Thus, hot nodules on a thyroid scintigram with ^{123}I do not necessarily preclude malignancy.

Key words: thyroid carcinoma, ^{123}I scintigraphy, hot nodule

INTRODUCTION

THYROID CARCINOMA generally shows a cold lesion on a thyroid scintigram whether with ^{123}I or with $^{99\text{m}}\text{Tc}$ -pertechnetate. It has been proposed that a hot nodule seen on a thyroid scintigram is highly suggestive of a benign one, but there have been several cases reported of thyroid carcinoma with scintigraphic hot or warm lesions.^{2–13} We report a rare case in which a hot nodule in the right lobe and a cold nodule in the left lobe, both contained thyroid carcinoma. The mechanism of such a unique scintigraphic appearance is also discussed in this case report.

CASE REPORT

A 44-year-old woman visited our hospital because she had occasionally been suffering from nephrolithiasis for the past 20 years. It was pointed out by her chief urologist that she had anterior neck swelling. She did not present any other symptoms or signs, and had no major diseases except nephrolithiasis in her past history. She had no history of radiation exposure or family history of thyroid

disease. On physical examination, an elastic hard 3.2×2.6 cm nodule was palpable in the lower half of the right lobe and a stony hard 2.4×2.0 cm nodule was palpable in the lower part of the left lobe of the thyroid gland. Both nodules were movable, had a smooth surface and no tenderness. No cervical lymph node was palpable. Serum levels of TSH, T_3 , T_4 , free T_3 , free T_4 and thyroglobulin were $0.54 \mu\text{U/ml}$ (RIANOST tTSH; CIS Diagnostics, Chiba, Japan, normal: $0.30\text{--}3.90 \mu\text{U/ml}$), 100 ng/dl (T_3 RIABEAD; Dinabot, Tokyo, Japan, normal: $90\text{--}170 \text{ ng/dl}$), $7.8 \mu\text{g/dl}$ (SPAC T_4 RIA; Daiichi Radioisotope Laboratories, Tokyo, Japan, normal: $5\text{--}11 \mu\text{g/dl}$), 3.4 pg/ml , 1.16 ng/dl (Amerlex MAB; Ortho Clinical Diagnostics, Tokyo, Japan, normal: free T_3 ; $2.2\text{--}5.0 \text{ pg/ml}$, free T_4 ; $0.99\text{--}1.92 \text{ ng/dl}$) and $<10.0 \text{ ng/ml}$ (Thyroglobulin-IRMA; Daiichi Radioisotope Laboratories, Tokyo, Japan, normal: $<45 \text{ ng/ml}$), respectively. Antithyroglobulin and antimicrosomal antibody titers were negative when determined by the hemagglutination assays (SERODIA-ATG and SERODIA-AMC, Fuji Rebio, Tokyo, Japan). Other blood test results were all normal. Both ^{123}I and ^{201}Tl scans were taken with the same gamma camera (Gamma View-F RC-IC-1635LF, Hitachi Medical Corporation, Chiba, Japan) equipped with a high-resolution parallel hole collimator. The former image was acquired 3 hours after oral administration of $7.4 \text{ MBq Na}^{123}\text{I}$ and the uptake value was determined 3 and 24 hours later. The latter image was acquired 10 minutes (early scan) and 3 hours (late scan) after intravenous administration of 74 MBq

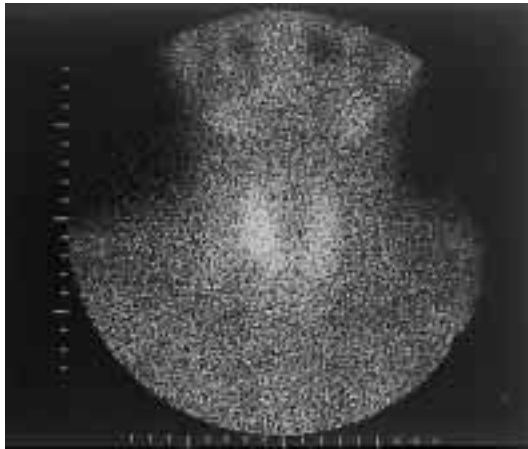
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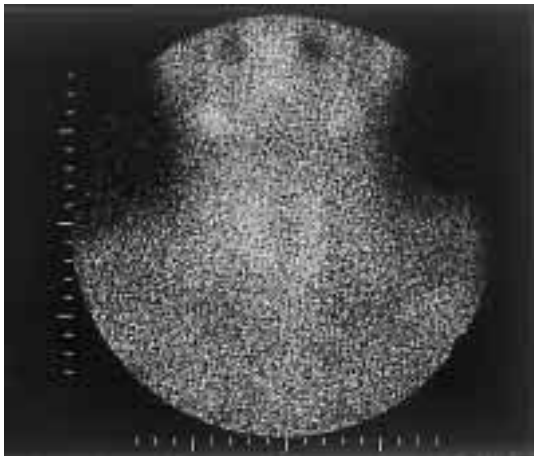
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Fig. 1 The palpable nodule in the right lobe is hot (*white arrow*), whereas that in the left lobe is cold (*white arrowhead*) on ^{123}I thyroid scintigram.



A



B

Fig. 2 ^{201}Tl scintigraphy shows accumulation of the radionuclide in the two palpable nodules on both early (A) and late (B) scans. The initial uptake in these nodules is not increased compared to the extranodular tissue and has been partly washed out on the late scan.

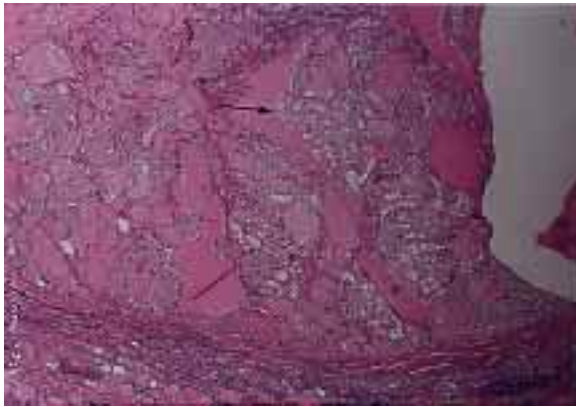


A

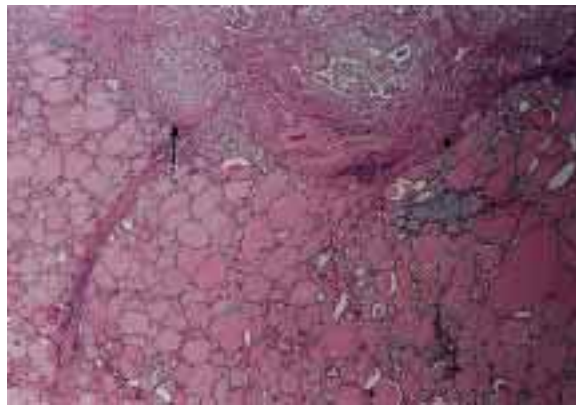


B

Fig. 3 Ultrasonography shows that the right nodule is isoechoic with a small amount of cystic components (A), and that the left nodule is slightly hypoechoic with intranodular patchy and more hypoechoic area which can not be recognized as cystic change (B). No calcification is seen in any of the nodules.



A



B

Fig. 4 On postoperative histopathologic examination, well-differentiated papillary carcinoma cells occupy the whole left nodule and approximately 10% of the right nodule. In the right nodule, the cancer cells exist predominantly in the lower part of the right nodule, forming island-like lesions (*black arrow*) within the adenomatous tissues (A, B).

$^{201}\text{TlCl}$. ^{123}I thyroid scintigraphy revealed that the palpable nodule in the right lobe was hot, whereas that in the left lobe was cold (Fig. 1). The uptake value at 24 h was 17.8% (normal range: 7–35%). ^{201}Tl accumulated in the two palpable nodules on both early and late scans, although the initial uptake in these nodules was partly washed out on the late scan (Fig. 2A, B). Ultrasonography revealed an isoechoic nodule with a maximal diameter of 2.0 cm in the right lobe and a hypoechoic nodule with a maximal diameter of 2.2 cm on the left lobe. Both lobes were slightly enlarged, containing a few tiny cysts in the extranodular tissue. The right nodule contained a small amount of cystic components, surrounded by a marginal hypoechoic zone, which was somewhat irregular in width. The left nodule appeared extremely inhomogeneous, containing more hypoechoic areas and tiny high-echo spots (Fig. 3A, B). A part of the extranodular tissue in the right lobe was felt as a nodular lesion, which might explain the difference in the diameter of right nodule determined by palpation and US. Subsequent fine needle aspiration biop-

sies (FNA) revealed that both nodules contained papillary carcinoma cells (Papanicolaou class V). Total thyroidectomy with bilateral local neck dissection was performed. On postoperative histopathologic examination, well-differentiated papillary carcinoma cells occupied the whole left nodule and approximately 10% of the right nodule, predominantly the lower part. Papillary carcinoma cells in both lobes appeared similar to each other histopathologically. In the right nodule, the cancer cells existed within adenomatous nodular tissues, forming island-like lesions (Fig. 4A, B). The extranodular area consisted of normal thyroid tissue and tiny cysts in both lobes. Bilateral paratracheal lymph node metastases were also identified.

DISCUSSION

Approximately 85% of all thyroid nodules are cold, 10% are warm, and 5% are hot on thyroid scintigraphy with ^{123}I or $^{99\text{m}}\text{Tc}$ pertechnetate.¹ Approximately 15% of cold nodules undergoing thyroid surgical resection have been reported to be malignant.¹ Thyroid cancer is known to be depicted as a cold lesion on thyroid scintigraphy, and one concentrating these radionuclides is generally considered to be rare, but there have been several reports of thyroid carcinoma with scintigraphic hot or warm lesions.^{2–13}

Scintigraphic hot or warm lesions in thyroid cancer patients could be explained by the following 3 mechanisms. First, cancer cells themselves are functioning. To the best of our knowledge, such cases are extremely rare, only 20 having been reported.⁹ There are only two well-documented reports in which specimen autoradiography showed a high radioiodine concentration in an area of histopathologic thyroid carcinoma.^{4,8} Second, non-functioning cancer cells coexist with functioning non-cancer cells, and due to relative insufficiency of the non-functioning cells the nodule appears hot or warm on a scintigram. We assume that most of the previously reported cases represent the coexistence of occult malignancy or a small amount of malignant lesions in or close to the benign functioning tissue, providing no adequate data to confirm that the malignancy itself was the hot source.^{10–13} We could not prove that carcinomatous lesions in the right nodule themselves were the hot source through histopathologic analysis of the resected specimen by autoradiography, but we assume that the present case probably belongs to this category, considering that the presence of functioning and nonfunctioning cancer cells in separate lobes seems unlikely. Third, ^{123}I or $^{99\text{m}}\text{Tc}$ pertechnetate accumulates in the cystic lesion of the non-functioning carcinoma as reported by Kusic et al.¹⁴ In the present case, the cystic lesion was too small to explain the scintigraphic appearance.

FNA is the most reliable means in the clinical work-up of thyroid nodules for differentiating malignancy from benignancy, leading to total thyroidectomy. According to

Liel et al. benign thyroid FNA results provide a high level of long-term assurance and repeating FNA is warranted in patients with predisposing risk factors for thyroid malignancy or with morphological changes in the thyroid nodule over time.¹⁵ Nevertheless, we should keep in mind that FNA may occasionally fail to detect cancer cells when they exist within functional tissues forming island-like lesions, but fortunately we could detect cancer cells in this case.

²⁰¹Tl scintigraphy, especially delayed scanning and assessment of the washout ratio, has been used widely to differentiate malignancy from benignancy of the nodules,¹⁶ but the clinical usefulness of ²⁰¹Tl scanning for this purpose is still controversial.¹⁷ In this case, the radionuclide accumulation in the two nodules was visually similar to each other and also to that in the extranodular tissues, indicating no important roles in the differential diagnosis.

Our patient showed an unique clinical picture, having two papillary carcinomas, the one in the right lobe being hot and the other in the left lobe being cold on ¹²³I scintigraphy. In conclusion, scintigraphic hot lesions that are considered mostly benign, do not necessarily preclude malignancy, and careful clinical management including histopathologic examination is required.

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