

Accumulation of thallium-201 in medullary thyroid cancer with negative serum calcitonin and carcinoembryonic antigens: A case report

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Thallium-201 (^{201}Tl) scintigraphy has been used in the evaluation of thyroid neoplasm. Even though several authors have shown the usefulness of ^{201}Tl scintigraphy in evaluating recurrent tumor of medullary thyroid cancer, the number of reports on primary thyroid cancer is limited. We presented a case of medullary thyroid cancer which showed ^{201}Tl uptake in both early and delayed scans. This case had normal serum levels of calcitonin and carcinoembryonic antigen.

Key words: thallium-201 scan, medullary thyroid cancer

INTRODUCTION

SINCE THE INTRODUCTION of thallium-201 (^{201}Tl) scintigraphy,^{1,2} several authors have reported the results of ^{201}Tl scintigraphy in medullary thyroid cancer (MTC). Most of the reports deal with the recurrence of MTC, and a high detection rate was reported.³⁻⁵ However, concerning only a few cases of primary MTC were the results of ^{201}Tl scintigraphy described in the literature.^{2,6-8} And there was no report which showed ^{201}Tl accumulation in MTC in a delayed scan. Calcitonin and carcinoembryonic antigen (CEA) are the well-known markers for MTC. The serum calcitonin level in particular is reported to be positive almost in all MTC cases.⁹ In the present report, we describe a MTC patient with normal serum calcitonin and CEA, who showed positive ^{201}Tl uptake both in early and delayed scans.

CASE REPORT

A 59-year-old female with two thyroid nodules, one on the right and the other on the left, was referred to our hospital. On palpation, the right nodule was found to be soft and movable, and measured 2 cm

in diameter; and the left nodule was hard and fixed, and measured about 2 cm in diameter. Her complete blood counts and biochemistry data were all within normal limits on admission. A thyroid function test also showed euthyroid with T₄; 9.5 $\mu\text{g/dl}$ (normal range, 5-13), T₃; 1.2 ng/dl (normal range, 0.8-1.2) and TSH; 2.7 $\mu\text{U/dl}$ (normal range, below 9). Thyroid test and microsome test results were negative. Furthermore, the serum CEA level was below 1 ng/dl (normal range, below 2.5) and serum calcitonin level was 38 pg/dl (normal range, below 100). The serum calcitonin level was measured with a RIA kit manufactured by Mitsubishi-Petrochemical Co., Ltd. and detected on an intact form of calcitonin. She had no familial history of thyroid disease or other endocrinological disease. Ultrasonography and computed tomography showed a calcification in the wall of the left thyroid nodule (Figs. 1 and 2). Technetium-99m ($^{99\text{m}}\text{Tc}$) pertechnetate thyroid scan delineated two cold palpable thyroid nodules (Fig. 3). ^{201}Tl scan was performed to characterize the nature of the tumor, and positive uptake in both early and delayed scans was shown in the left nodule and there was a cold spot in the right nodule (Fig. 4). Intense ^{201}Tl uptake was noted in an early scan (Fig. 4A). Even though the degree of ^{201}Tl uptake was decreased, definite uptake was shown in a delayed scan (Fig. 4B). Fine needle aspiration showed class V in the left nodule and class I in the right nodule. Total thyroidectomy was performed with a malignant thyroid nodule definitely suspected.

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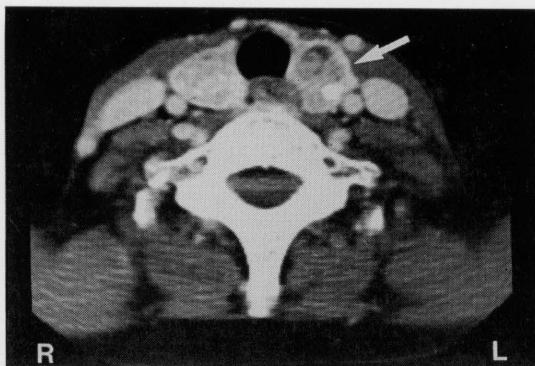


Fig. 1 Computed tomography of the thyroid gland with contrast enhancement showing a solid mass with calcification and a cystic component in the left thyroid gland. Arrow indicates the MTC.

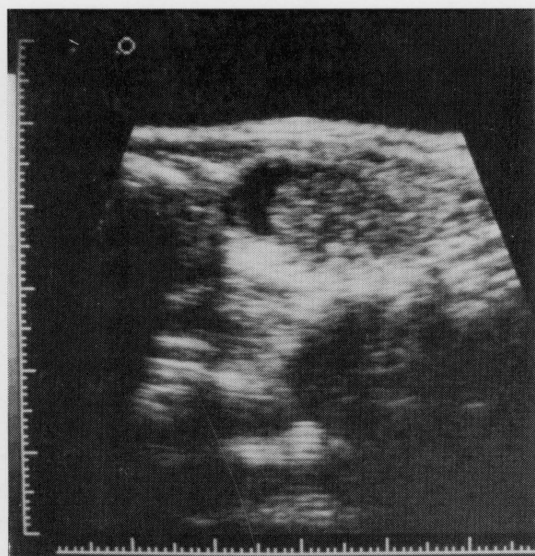


Fig. 2 Ultrasonography of the left thyroid gland showing a solid mass with calcification.

Pathological findings revealed that the right nodule was an adenomatous goiter $2.5 \times 2.0 \times 1.5$ cm in size and the left mass was a MTC $2.0 \times 2.0 \times 1.5$ cm in size. The left mass was encapsulated and constructed of non-follicular solid trabecular cells which were positive for Grimelius stain (Fig. 5). There were also several small adenomatous goiter nodules measuring less than 1 cm in diameter scattered throughout the entire the thyroid. No lymph node involvement was detectable, and the postoperative clinical course was good and there was no evidence of recurrence.

DISCUSSION

MTC has been shown to account for 3.5–11.9% of all thyroid malignancies. About 90% of cases occur sporadically, while in about 10% the disease is inherited as an autosomal dominant trait with half of the offspring affected.

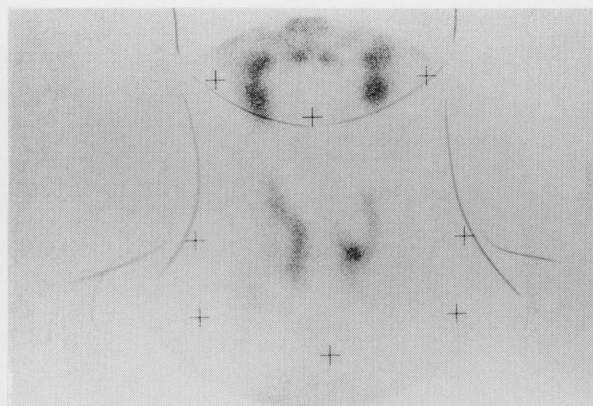


Fig. 3 ^{99m}Tc pertechnetate thyroid scintigraphy showing two cold areas in bilateral lobes with a hot spot adjacent to or just caudal to left thyroid cold lesion.

It has been shown that MTC originates in C cells which arise from the neural crest. The tumor cells are uniform and solidly arranged with a high percentage of amyloid present in the stroma, and secrete various bioactive substances such as calcitonin, histaminase, prostaglandins, CEA, serotonin, etc. And in most MTC cases there is an increase in serum calcitonin and CEA. Hypersecretion of calcitonin was reported to be present in almost all patients with MTC, while CEA production was not recognized in some patients.⁹ In our case, serum calcitonin and CEA levels were within normal limits. It was difficult to predict that the thyroid nodule was a MTC from the laboratory data.

Many methods such as computed tomography, ultrasonography, magnetic resonance imaging, nuclear medicine techniques, and fine needle aspirations are used in evaluating thyroid nodules. Specific diagnosis of MTC by computed tomography, ultrasonography and magnetic resonance imaging is difficult.

There are many nuclear medicine techniques for the detection of thyroid nodules. Iodine and ^{99m}Tc pertechnetate usually do not accumulate in MTC, even though a report described accumulation of ^{131}I and ^{99m}Tc pertechnetate in recurrent MTC masses.³ The case presented in this report showed a cold area in ^{99m}Tc pertechnetate scintigraphy.

^{131}I metaiodobenzyl-guanidine (^{131}I MIBG) was reported to accumulate in MTC.¹⁰ However, cumulative reported data on the diagnostic use of ^{131}I MIBG indicate that 25–30% of MTCs are positive for ^{131}I MIBG, showing preponderance of familial MTC cases.¹¹ Another radionuclide for MTC is ^{99m}Tc (V) DMS. Four MTC patients were successfully imaged, but all 12 patients with other histological types of thyroid cancer were negative.¹² Clarke et al. studied 5 patients with MTC with 4 positive and one equivocal ^{99m}Tc (V)DMS results.¹³ Hildlitch et al.

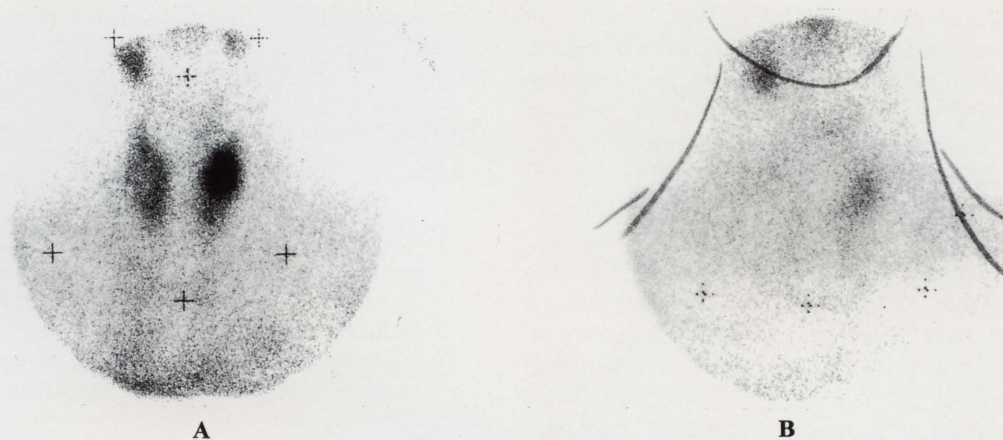


Fig. 4 Thallium-201 scintigraphy of early (A) and delayed (B) scans are shown. Intense uptake is seen in the left thyroid gland and a cold area is noted in the right on early scan (B). Faint but definite ^{201}Tl uptake remains in the left mass lesion.

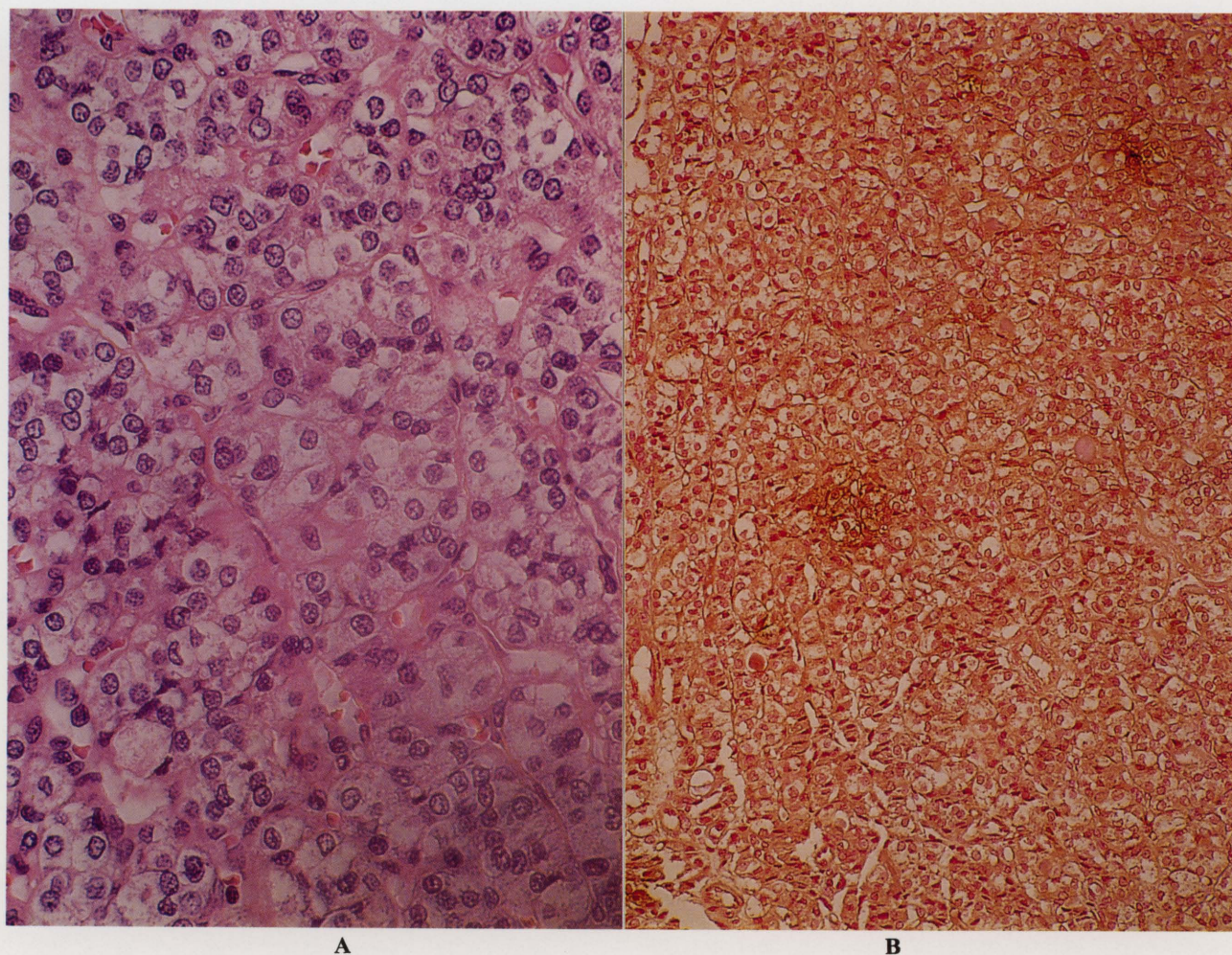


Fig. 5 Hematoxylin-eosine staining (A) ($\times 400$) and Grimelius staining (B) ($\times 200$) are shown. Tumor cells are clear and granular with a round nucleus (A). Brown staining is seen in the cytoplasm (B).

reported unsuccessful $^{99m}\text{Tc}(\text{V})\text{DMA}$ results in MTC.¹⁴ Hoefnagel reported that 2 of 3 were positive with $^{99m}\text{Tc}(\text{V})\text{DMA}$.¹¹ Judging from these reports, the sensitivity of $^{99m}\text{Tc}(\text{V})\text{DMA}$ is high but not 100%. This radiopharmaceutical is promising for the diagnosis of MTC. It is regrettable that ^{131}I MIBG and $^{99m}\text{Tc}(\text{V})\text{DMS}$ were not performed in the case reported here.

^{201}Tl accumulation in recurrent MTC has been reported by many authors.³⁻⁵ However, few reports on primary MTC are available now. Senga et al. reported first positive ^{201}Tl uptake in one case,⁶ whereas Ochi et al. reported a ^{201}Tl negative MTC case.² Bleichrodt et al. reported one MTC case who showed positive ^{201}Tl uptake in an early scan and negative in a delayed scan.⁷ Yobbagy et al. reported a positive MTC case of multiple endocrine neoplasia type-2b.⁸ Furthermore, these positive cases were demonstrated only in early ^{201}Tl scans. Two cases were reported in whom both early and delayed scans were performed: one case was reported by Ochi² with negative early and delayed scans and the other case was reported by Bleichrodt et al.⁷ with a positive early scan and a negative delayed scan. The present case showed positive ^{201}Tl uptake in both early and delayed scans, even though the uptake was faded in the delayed scan. Judging from the ^{201}Tl uptake patterns of reported cases and our case, ^{201}Tl often accumulates in MTC in an early scan and the clearance from MTC is likely to be as fast as that from normal thyroid tissue. This rapid clearance from MTC is different from other types of differentiated thyroid cancers (papillary and follicular cancers) which often show positive ^{201}Tl uptake in an early scan and persistent accumulation in a delayed scan.

^{201}Tl scintigraphy is not specific for MTC even with early and delayed scans, and it should be emphasized that various ^{201}Tl patterns may be seen in primary MTC. Bunsnardo et al. reported that CEA was positive in MTC patients who had advanced disease.⁹ The negative CEA result in our case should be due to the limited spread of the disease. However, the reason for the negative or base-line level of serum calcitonin is unknown. The small size of the tumor and/or the encapsulated nature of the tumor might be the reason for the base-line level of the serum calcitonin in our case.

With increase in calcitonin and/or CEA, it should be easy to interpret the ^{201}Tl scintigraphic results and combination with other radiopharmaceutical such as $^{99m}\text{Tc}(\text{V})\text{DMS}$ scan should increase the accuracy of the diagnosis. However, it is difficult to diagnose with ^{201}Tl scintigraphy without an increase in calcitonin and CEA. Our case is unique in that the patient had negative serum calcitonin and CEA levels and her MTC accumulated ^{201}Tl not only in

an early scan but also in a delayed scan.

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