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Metastasis of Colon Cancer to Medullary Thyroid Carcinoma: A Case Report

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Metastasis to the primary thyroid carcinoma is extremely rare. We report here a case of colonic adenocarcinoma metastasis to medullary thyroid carcinoma in a 53-yr old man with a history of colon cancer. He showed a nodular lesion, suggesting malignancy in the thyroid gland, in a follow-up examination after colon cancer surgery. Fine needle aspiration biopsy (FNAB) of the thyroid gland showed tumor cell clusters, which was suspected to be medullary thyroid carcinoma (MTC). The patient underwent a total thyroidectomy. Using several specific immunohistochemical stains, the patient was diagnosed with colonic adenocarcinoma metastasis to MTC. To the best of our knowledge, the present patient is the first case of colonic adenocarcinoma metastasizing to MTC. Although tumor-tumor metastasis to primary thyroid carcinoma is very rare, we still should consider metastasis to the thyroid gland, when a patient with a history of other malignancy presents with a new thyroid finding.

Keywords: Colorectal Neoplasms; Thyroid Neoplasms; Neoplasm Metastasis

INTRODUCTION

Although the prevalence of metastases to the thyroid gland is variable in previous reports, metastasis to the thyroid gland is known to be an uncommon condition. Moreover, metastasis to primary thyroid carcinoma is extremely rare. Fourteen cases of metastatic tumor to the primary thyroid carcinoma have been reported previously in the literature. The majority of reported primary thyroid carcinomas were papillary thyroid carcinoma (PTC), including follicular variant papillary thyroid carcinoma (FVPTC) (1-11). To our knowledge, there has been no reported case of a tumor metastasizing to medullary thyroid carcinoma (MTC). We report a case of tumor-to-tumor metastasis involving metastatic colonic adenocarcinoma and medullary thyroid carcinoma.

CASE DESCRIPTION

A 53-yr old man underwent an anterior resection of his cancerous sigmoid colon and adjuvant chemotherapy on November 14, 2005. About one year after surgery, a fluorine-18-fluorodeoxyglucose-positron emission tomography integrated with computed tomography (^{18}F-FDG PET/CT) scan showed focal hypermetabolism in the right lobe of the thyroid gland (standardized uptake value, [SUV] 4) and pulmonary nodules in the right lung, suggesting hematogenous metastatic lesions. He received chemotherapy as palliative treatment. Two years later, a PET scan still revealed a nodule, showing focal activity in the thyroid gland (SUV 2.5) (Fig. 1A). A thyroid gland ultrasonography showed a marked hypoechoic solid nodule with a lobulated margin and inner microcalcification in the right mid pole, suggesting malignancy (Fig. 1B). The patient underwent ultrasound-guided fine needle aspiration biopsy (FNAB) of the thyroid nodule. FNAB showed tumor cell clusters, which were suspected to be MTC. Serum calcitonin and carcinoembryonic antigen (CEA) levels were mildly elevated (17.3 pg/mL (reference range: 0-10 pg/mL) for calcitonin; 29.31 ng/mL (reference range: 0-4.7 ng/mL) for CEA. Thyroid stimulating hormone was 2.47 μIU/mL (0.25-4.0 μIU/mL), thyroglobulin antigens were 9.96 ng/mL (0-35 ng/mL), antithyroglobulin antibodies were 0.19 IU/mL (0-0.3 IU/mL). The serum level of intact parathyroid hormone was 40.83 pg/mL (15-65 pg/mL). The 24-hr urine cortisol/metanephrine/cathecholamin levels were within the normal range. Rearranged during transfection (RET) proto-oncogene mutations were not detected. Subsequently, the patient underwent a total thyroidectomy and bilateral central neck dissection.

On gross examination, the capsule of the right lobe of thyroid was intact, smooth, and the surface was irregularly bosselated.

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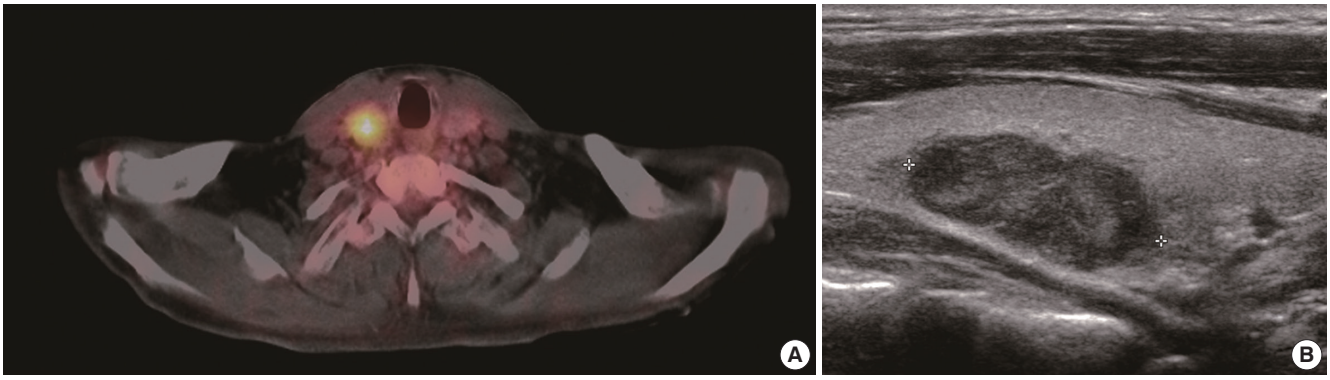

Fig. 1. PET scan and Ultrasound finding. (**A**) PET scan shows focal hypermetabolism in the right lobe of thyroid gland (SUV 2.5). (**B**) Ultrasonography shows marked hypoechoic solid nodule with lobulated margin with inner microcalcification, measured 1.6 × 1.0 × 2.5 cm (2.42 cm^3), in right mid pole.

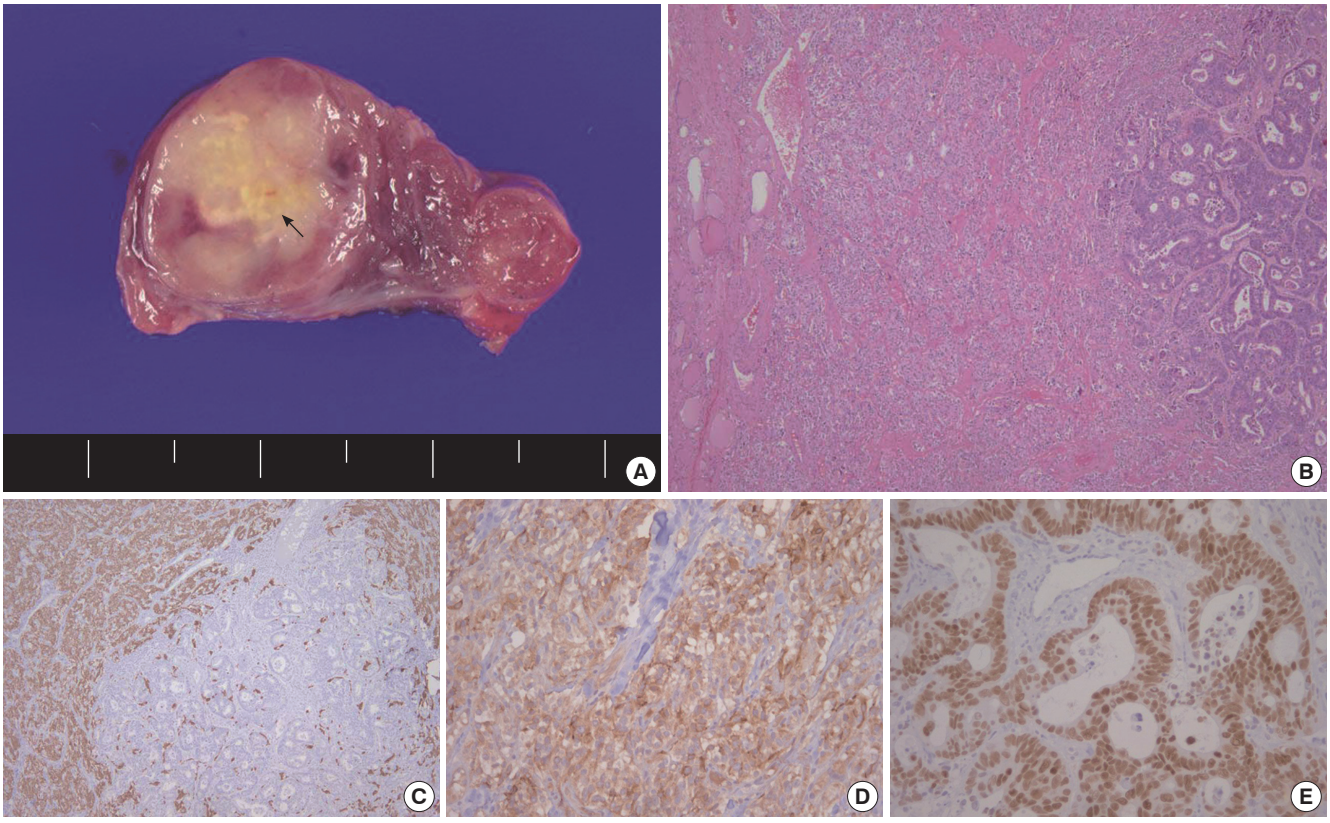

Fig. 2. Histopathologic and immunohistochemical staining findings of thyroid lesion. (**A**) Gross findings reveal a well circumscribed round gray-tan nodular mass with an ill defined white solid portion and central irregular yellow necrosis (arrow). (**B**) Microscopic findings show a medullary carcinoma which is composed of nests or sheets of round or spindle tumor cells and acellular eosinophilic stroma (center), and colonic adenocarcinoma with glandular differentiation (right) in the normal thyroid parenchyme (left), (H&E stain, ×40). (**C**) Immunohistochemical staining for chromogranin A reveals positive staining in medullary carcinoma (brown) and negative staining in colonic adenocarcinoma (×40). (**D**) Immunohistochemical staining for calcitonin shows diffuse strong cytoplasmic positivity (brown) in the tumor cell of medullary component (×100). (**E**) Immunohistochemical staining for CDX2 shows a strong positive nuclear staining (brown) in colonic adenocarcinoma (×200).

The cut sections revealed a well-circumscribed, round gray-tan nodular mass, measuring 1.5 × 1.2 cm. There is an ill defined white solid mass with central irregular yellow necrosis, measuring 0.8 × 0.7 cm in the gray-tan nodular mass (Fig. 2A). Histological examination revealed metastatic colonic adenocarcinoma in MTC (Fig. 2). An immunohistochemical stain of CEA and caudal type homeobox protein CDX-2 showed a strong, diffuse positivity in colonic adenocarcinoma. In contrast, the medullary thyroid cancer cells were positive for chromogranin-A and calcitonin and negative for the colonic adenocarcinoma marker. Results of immunohistochemical stain of tumor cells are described in Table 1. There was no regional lymph node metastasis.

After thyroidectomy, the patient continued palliative chemotherapy for the colon cancer and supportive care. One year lat-

Table 1. Results of immunohistochemical stain

Immunohistochemical stain	MTC	Colonic adenocarcinoma
Chromogranin A	Positive	Negative
Synaptophysin	Positive	Negative
Calcitonin	Positive	Negative
TTF-1	Positive	Negative
CEA	Positive	Positive
CK20	Negative	Positive
CDX-2	Negative	Positive

MTC, medullary thyroid carcinoma; TTF-1, Thyroid Transcription Factor-1; CEA, carcinoembryonic antigen; CDX2, caudal type homeobox 2.

er, he died from dyspnea due to the aggravation of pulmonary metastases.

DISCUSSION

While the coincident occurrence of multiple primary malignant tumors in the same host is not unusual, tumor-to-tumor metastasis is a rare phenomenon. Berent (12) first documented this phenomenon in 1902. Campbell et al. (13), proposed criteria for the diagnosis of tumor-to-tumor metastasis; 1) the presence of more than one primary malignant tumor must be proved, 2) the recipient tumor must be a true neoplasm, and 3) the donor malignant tumor must be a true metastasis, with established growth and invasion in the tumor. Direct contiguous growth of one tumor into another adjacent tumor (collision tumor), embolism of tumor cells, and metastasis to leukemic nodes are not defined as metastases. Our case satisfies the Campbell's criteria.

Previous studies reported the prevalence of metastases to the thyroid gland varied greatly (14-17). However, the previous studies included preexisting or coexisting thyroid conditions, such as benign thyroid diseases (goiter and adenoma), and primary thyroid neoplasms. Cases involving metastasis to primary thyroid carcinoma only, have a prevalence rate estimated to be less than 1%, and only 14 cases have been reported in the literature (Table 2). Rosai (3) reported the first documented case of metastatic breast carcinoma to a papillary thyroid carcinoma (PTC) in 1992. The most commonly reported non-thyroid malignancies to metastasize to the thyroid gland are renal cell carcinoma and lung cancer (18). Colorectal carcinoma was an uncommon donor, accounting for only two of the cases (2, 4).

Willis (19) proposed a hypothesis for why the thyroid gland receives few metastatic deposits despite its rich blood supply. According to the Willis hypothesis, fast arterial flow through the thyroid and the high oxygen saturation and iodine content of the thyroid gland prevent of metastatic tumor survival in the thyroid (19). Due to the rarity and complexity of tumor metastasis, the mechanisms of metastasis to thyroid neoplasm are unclear. Some views suggested that the thyroid tumor makes an environment in which metastatic tumor cells can easily grow by altering the normal thyroid structure as stated above (20).

Table 2. Tumor-to-tumor metastases to a primary thyroid malignancy

Case	Donor tumor	Recipient tumor	Reference
1	Lung, small cell carcinoma	FVPTC	[1]
2	Kidney, clear cell carcinoma	FVPTC	[1]
3	Pancreas, neuroendocrine carcinoma	FVPTC	[1]
4	Rectal, adenocarcinoma	PTC	[2]
5	Breast, carcinoma	PTC	[3]
6	Colon, adenocarcinoma	Hurthle cell carcinoma	[4]
7	Lung, adenocarcinoma	FVPTC	[5]
8	Lung, adenocarcinoma	FVPTC	[6]
9	Kidney, clear cell carcinoma	PTC	[7]
10	Kidney, clear cell carcinoma	Oncocytic carcinoma	[8]
11	Kidney, clear cell carcinoma	FVPTC	[9]
12	Breast, lobular carcinoma	FVPTC	[9]
13	Skin, malignant melanoma	FTC	[10]
14	Lung, small cell carcinoma	PTC	[11]
15	Colon, adenocarcinoma	MTC	Current case

FVPTC, follicular variant of papillary thyroid carcinoma; PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma; MTC, medullary thyroid carcinoma.

MTC originates from the parafollicular C cells, which produce the hormone calcitonin. MTC is a relatively rare type of primary thyroid carcinoma, accounting for only about 5% of all thyroid carcinomas. The majority of previously reported recipient primary thyroid carcinomas were PTC, including FVPTC (12 among 14 cases) (1-3, 5-7, 9, 11). The other two cases were oncocytic/hurthle cell carcinomas (4, 8). As far as we know, cases of metastatic tumor to MTC have not been reported previously.

FNAB diagnosis of both primary thyroid malignancy and non-thyroid malignancies metastasizing to the thyroid gland at the same time is difficult and often incorrect (18). In most cases, FNAB can diagnose primary thyroid carcinoma but not the metastases to the thyroid. In the present case, FNAB allowed us to diagnose MTC, but we did not find the colorectal cancer with the technique. After surgical resection of the thyroid gland and several specific stains, we were able to diagnose the tumor-to-tumor metastasis (MTC and colorectal cancer). Although tumor-to-tumor metastasis to the primary thyroid carcinoma is very rare, metastasis to the thyroid gland should be considered, when a patient with history of other malignancies presents with a new thyroid finding.

In this case, although the patient already had pulmonary metastasis of colonic adenocarcinoma, he underwent surgical treatment. The prognosis of the patient was determined by the coexisting advanced colon cancer.

In conclusion, metastasis to the primary thyroid carcinoma is extremely rare. The present patient is the first example of colonic adenocarcinoma metastasizing to medullary carcinoma of the thyroid.

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REFERENCES

1. Baloch ZW, LiVolsi VA. *Tumor-to-tumor metastasis to follicular variant of papillary carcinoma of thyroid. Arch Pathol Lab Med 1999; 123: 703-6.*
2. Cherk MH, Moore M, Serpell J, Swain S, Topliss DJ. *Metastatic colorectal cancer to a primary thyroid cancer. World J Surg Oncol 2008; 6: 122.*
3. Rosai J, Carcangiu ML, DeLellis RA. *Atlas of Tumor Pathology: tumors of the thyroid gland. 3rd series, Fascicle 5. Washington, DC: Armed Forces Institute of Pathology, 1992.*
4. Witt RL. *Colonic adenocarcinoma metastatic to thyroid Hürthle cell carcinoma presenting with airway obstruction. Del Med J 2003; 75: 285-8.*
5. Hashimoto K, Yamamoto H, Nakano T, Oyama M, Shiratsuchi H, Nakashima T, Tamiya S, Komune S, Oda Y. *Tumor-to-tumor metastasis: lung adenocarcinoma metastasizing to a follicular variant of papillary thyroid carcinoma. Pathol Int 2011; 61: 435-41.*
6. Mori K, Kitazawa R, Kondo T, Kitazawa S. *Lung adenocarcinoma with micropapillary component presenting with metastatic scrotum tumor and cancer-to-cancer metastasis: a case report. Cases J 2008; 1: 162.*
7. Bohn OL, De las Casas LE, Leon ME. *Tumor-to-tumor metastasis: renal cell carcinoma metastatic to papillary carcinoma of thyroid-report of a case and review of the literature. Head Neck Pathol 2009; 3: 327-30.*
8. Ryska A, Cáp J. *Tumor-to-tumor metastasis of renal cell carcinoma into oncocytic carcinoma of the thyroid. Report of a case and review of the literature. Pathol Res Pract 2003; 199: 101-6.*
9. Yu J, Nikiforova MN, Hodak SP, Yim JH, Cai G, Walls A, Nikiforov YE, Seethala RR. *Tumor-to-tumor metastases to follicular variant of papillary thyroid carcinoma: histologic, immunohistochemical, and molecular studies of two unusual cases. Endocr Pathol 2009; 20: 235-42.*
10. Terzi A, Altundag K, Saglam A, Gurlek A, Aksoy S, Baltali E, Uner AH. *Isolated metastasis of malignant melanoma into follicular carcinoma of the thyroid gland. J Endocrinol Invest 2004; 27: 967-8.*
11. Matsukuma S, Kono T, Takeo H, Hamakawa Y, Sato K. *Tumor-to-tumor metastasis from lung cancer: a clinicopathological postmortem study. Virchows Arch 2013; 463: 525-34.*
12. Berent W. *Seltene metastsenbildung. Zentralbl Allg Pathol Int 1902; 13: 406-10.*
13. Campbell LV Jr, Gilbert E, Chamberlain CR Jr, Watne AL. *Metastases of cancer to cancer. Cancer 1968; 22: 635-43.*
14. Moghaddam PA, Cornejo KM, Khan A. *Metastatic carcinoma to the thyroid gland: a single institution 20-year experience and review of the literature. Endocr Pathol 2013; 24: 116-24.*
15. Papi G, Fadda G, Corsello SM, Corrado S, Rossi ED, Radighieri E, Miraglia A, Carani C, Pontecorvi A. *Metastases to the thyroid gland: prevalence, clinicopathological aspects and prognosis: a 10-year experience. Clin Endocrinol (Oxf) 2007; 66: 565-71.*
16. Calzolari F, Sartori PV, Talarico C, Parmeggiani D, Beretta E, Pezzullo L, Bovo G, Sperlongano P, Monacelli M, Lucchini R, et al. *Surgical treatment of intrathyroid metastases: preliminary results of a multicentric study. Anticancer Res 2008; 28: 2885-8.*
17. Cichoń S, Anielski R, Konturek A, Barczyński M, Cichoń W. *Metastases to the thyroid gland: seventeen cases operated on in a single clinical center. Langenbecks Arch Surg 2006; 391: 581-7.*
18. Chung AY, Tran TB, Brumund KT, Weisman RA, Bouvet M. *Metastases to the thyroid: a review of the literature from the last decade. Thyroid 2012; 22: 258-68.*
19. Willis RA. *Metastatic tumours in the thyreoid gland. Am J Pathol 1931; 7: 187-208.3.*
20. Stevens TM, Richards AT, Bewtra C, Sharma P. *Tumors metastatic to thyroid neoplasms: a case report and review of the literature. Patholog Res Int 2011; 2011: 238693.*