J Korean Med Sci 1999; 14: 455-9
ISSN 1011-8934

Colonic Adenocarcinoma Metastatic to the Thyroid Gland
: A Case Report with Immunohistochemical Investigation

Clinically evident metastases of carcinomas to the thyroid gland are rare, particularly from a colorectal primary tumor. We present a case of colonic adenocarcinoma metastatic to the thyroid gland with histopathologic and immunohistochemical findings. A 68-year-old woman with a history of Dukes' stage B colon carcinoma presented a mass in the thyroid gland. The tumor was confirmed to be metastatic adenocarcinoma from the colon. The immunohistochemical findings demonstrated positive staining for cytokeratin 20, low-molecular-weight cytokeratin, villin and carcinoembryonic antigen, but stains were negative for cytokeratin 7 and thyroglobulin.

Key Words: *Adenocarcinoma; Neoplasm metastasis; Immunohistochemistry; Thyroid gland*

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Received: 24 December 1998
Accepted: 6 March 1999

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INTRODUCTION

Carcinoma metastatic to the thyroid gland is rare, with an overall incidence of 1.25% to 24.2% reported in autopsy studies (1-5) and the most frequent sites of primary carcinomas metastasizing to the thyroid gland are breast and lung (1-3). On the other hand, clinically metastasis to the thyroid gland is even rarer with the most common evident metastatic tumor being renal cell carcinoma in clinical studies (6-12). Gastrointestinal malignancies, particularly colorectal cancers that metastasize to the thyroid gland are extremely rare, with a 4% incidence from autopsy data (4). Clinically, only six cases of colorectal cancer metastatic to the thyroid gland have been reported in the literature (12-17). Despite their rare occurrence, the possibility of metastatic carcinoma should be considered in the differential diagnosis for any patient with thyroid nodules and a history of cancer.

A thyroid nodule in a patient with a history of cancer presents a difficult diagnostic problem. Such a lesion could be benign, could be metastatic, and could be a new primary malignancy of the thyroid gland. In such cases, immunostaining for cytokeratins 7 (CK 7) and 20 (CK 20) is useful for differentiating primary thyroid cancers from metastatic adenocarcinomas from the colon, because thyroid carcinoma is positive for CK 7 and negative for CK 20, whereas colon cancer is negative for CK 7 and positive for CK 20 (18, 19).

We present a rare case of metastatic colonic adenocarcinoma of the thyroid gland, which demonstrates the help of immunohistochemistry in diagnosing thyroid nodule with a history of colonic adenocarcinoma.

CASE REPORT

The patient, a 68-year-old woman, was admitted because of a midline neck mass for one month. On past history, the patient had a sigmoid colon cancer two years ago. At that time, she had a moderately differentiated adenocarcinoma, which disclosed the presence of a T2N0M0 stage II, Dukes' stage B colon cancer. No involvement of regional lymph nodes was identified, but the tumor penetrated into the serosa. The patient did not receive any adjuvant treatment. On admission, a computed tomographic (CT) scan revealed a mass (5×4 cm) in the right lobe of her thyroid gland and a mildly enlarged left lobe of thyroid gland with slight heterogenous attenuation (Fig. 1). Results of fine-needle aspiration biopsy revealed a poorly differentiated carcinoma. Preoperative chest x-ray revealed a nodule in the upper lobe of right lung that had not been present previously. An equivocal

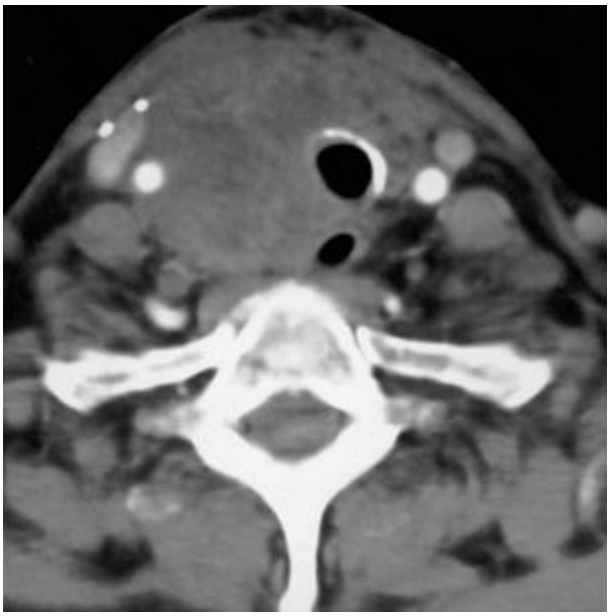

Fig. 1. Postcontrast computed tomographic scan shows a 5× 4-cm mass on the right lobe of the thyroid gland. This extends posteromedially towards the right side and is compressing the esophagus. The upper trachea is displaced to the left side.

small nodule was also found in the middle of the left lung. The patient underwent left thyroidectomy and lymph node resection. Right thyroidectomy was not performed because the mass compressed esophagus and trachea, and displaced right internal jugular vein and carotid artery. The lymph nodes near the left thyroid revealed poorly differentiated metastatic adenocarcinoma, and the left thyroid showed moderately differentiated metastatic adenocarcinoma, morphologically consistent with a colonic primary tumor. During a six-week course of radiation therapy for palliation of the metastasis, a CT scan of the chest revealed multiple nodules that measured up to 1.5 cm and spread diffusely throughout both lungs. Hoarseness had developed, but the patient had no other related complaints such as dysphagia, odynophagia, otalgia, or shortness of breath. Currently, she is alive with the disease and receiving supportive care.

PATHOLOGY

Gross findings

The resected left lobe of the thyroid gland measured 3.5×2×1 cm and weighed 4.5 g. The thyroid gland was serially sectioned, and the cut surface revealed lobulated pink-tan moderately firm parenchyma. There were no discrete lesions. The lymph node measured 0.6 cm at its greatest dimension, which was replaced by firm, white-gray tumor.

Histologic findings

The entire thyroid tissue was permeated by moderately differentiated adenocarcinoma. Rather significant areas of intraluminal or "dirty" tumoral necrosis typical of colonic adenocarcinoma were noted (Fig. 2A). Tumor cells were columnar and had elongated hyperchromatic nuclei (Fig.

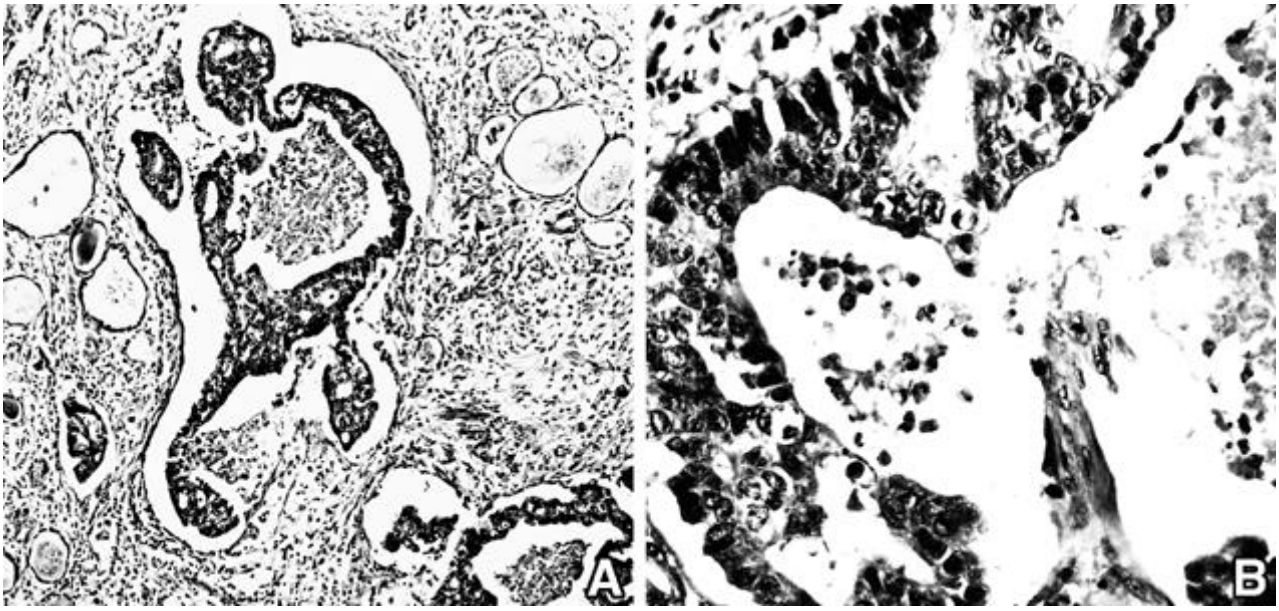

Fig. 2. Microphotography of the thyroid: A prominent intraluminal "dirty" necrosis typical of colonic adenocarcinoma are seen in the thyroid (A). The tumor cells are columnar and have elongated hyperchromatic nuclei (B). (H&E, A: ×40, B: ×400)

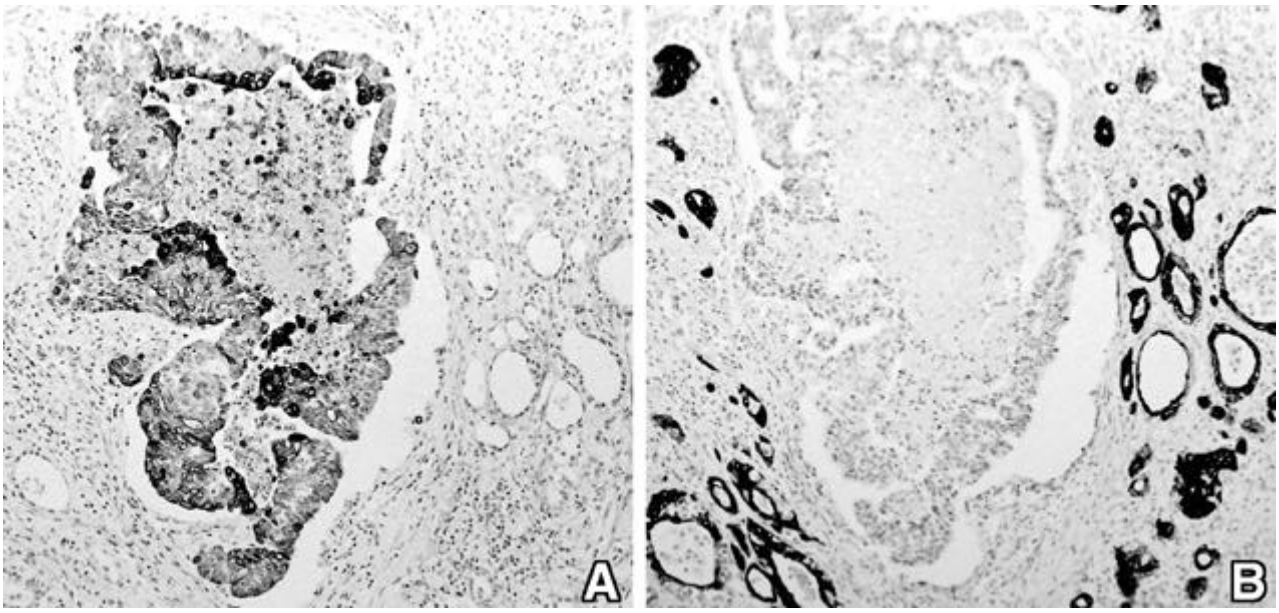

Fig. 3. Immunohistochemistry: The tumor cells are positive for cytokeratin 20, but the follicular cells of the thyroid are negative (A) whereas the intervening normal thyroid follicular cells are positive for cytokeratin 7, but the tumor cells are negative (B). (Avidin-biotin complex immunoperoxidase staining, ×100)

2B). Along the luminal surfaces, brush border materials were well observed. Findings in the uninvolved areas of the thyroid gland were unremarkable. A lymph node was largely replaced by solid sheets of poorly differentiated adenocarcinoma.

Immunohistochemical findings

Formalin-fixed, paraffin-embedded sections of the tumor were immunohistochemically examined using the standard streptoavidin-biotin system. The tumor cells were stained positively for CK 20 (Fig. 3A), low-molecular-weight cytokeratin, villin, and CEA. The tumor cells were negative for CK 7 (Fig. 3B), thyroglobulin, synaptophysin, chromogranin, and calcitonin. The surrounding thyroid follicular cells were positive for CK 7 (Fig. 3B), low-molecular-weight cytokeratin, and thyroglobulin but were negative for CK 20 (Fig. 3A), villin, CEA, synaptophysin, and chromogranin. These immunohistochemical findings were consistent with those of metastatic colonic adenocarcinoma.

DISCUSSION

Autopsy studies show that less than 1% of all primary tumors occur in the thyroid gland, whereas metastasis has an incidence of 1.25% to 24.2% (1-5). Carcinomas of the breast and lung are the most common malignancies to metastasize to the thyroid gland (1-3), but malignant melanoma, lymphoma/leukemia, renal cell carcinoma, and head and neck tumors such as cancer of the larynx are also known to do so. In clinical series, renal cell carcinoma was found to be the most common source of metastasis to the thyroid gland (6-12), whereas malignant melanoma, while commonly found in the thyroid gland at autopsy, is relatively uncommon in clinical series (1, 4, 12). Clinically evident colonic adenocarcinoma metastatic to the thyroid gland is quite rare although autopsy studies have shown a higher rate of subclinical involvement. An incidence of 4% of those dying of colorectal carcinoma in a large autopsy study had thyroid metastases (4). In comparison, the most common gastrointestinal site of primary cancer to metastasize to the thyroid gland is the esophagus with eight cases (8, 10-12). In the review of the literature (12-17), six cases of colorectal carcinoma metastatic to the thyroid gland have been reported (Table 1). All cases were female with age ranging from 37 to 69 years. The propensity of metastasis to the right side of the thyroid gland was noted in these cases. Even though clinically evident metastases of malignancy to the thyroid gland are unusual, they occur more frequently than does a separate primary malignancy in patients who have a history of malignancy (4).

Metastatic tumor involving the thyroid gland may pose a diagnostic problem. The characteristic clinical pattern associated with metastatic tumors does not differ from that of primary thyroid cancer. Hence, it is important to consider the possibility of metastatic disease to the thyroid gland in a patient who presents with a thy-

Table 1. Summary of reported cases of colonic adenocarcinoma metastatic to the thyroid gland

Author	Age/Sex	Stage of colon cancer	Side of thyroid gland	Other metastatic sites	Interval (month)	Follow-up (month)
Rosen IB (12)	46/F	NA	NA	NA	NA	NA
Mesko TW (13)	59/F	Dukes' B	Right lobe	Vertebrae, kidney	21	NA
Lester JW (14)	55/F	NA	Both lobes	Liver, lung	30	NA
Cristallini EG (15)	64/F	NA	Right lobe	Liver	48	12, AWD
Nachtigal D (16)	69/F	Dukes' A	Right lobe	Lung	96	8, DOD
Kim S (17)	37/F	NA	Left lobe	Lymph node, skin	84	2, AWD
Present case	68/F	Dukes' B	Both lobes	Lung	28	6, AWD

NA, not available; AWD, alive with disease; DOD, dead of disease

roid mass to avoid misdiagnosis, particularly common to this presentation.

Anticytokeratin antibodies provide an important diagnostic tool for establishing the epithelial origin of poorly differentiated tumors (20). The recent identification of several CK subtypes that have a limited range of tissue distribution can help to locate the origin of tumor. Among these CK subtypes, the polypeptide CK 20 of the acidic small type I cytokeratin group has been identified (21) and is remarkable for its great sequence divergence from all other known CKs in this subfamily because it can be particularly be associated with a small subset of epithelia and their corresponding tumors. CK 20 has been demonstrated specifically for adenocarcinomas of the colon, mucinous ovarian tumors, transitional cell carcinomas and Merkel cell carcinoma (21, 22). This spectrum of activity is somewhat complementary to that seen with antibodies to CK 7, a neutral-basic type II cytokeratin found in adenocarcinomas of the breast, lung, and other glandular tumor types (18, 19). In our case, the tumor cells were stained positively for CK 20 and negatively for CK 7, which is compatible to the findings of the patient's primary tumor of the colon. The remaining normal thyroid follicular cells were stained negatively for CK 20 but positively for CK 7. Thus, in this case, immunostaining for CK 20 and CK 7 helped us to differentiate a new primary cancer of the thyroid gland from metastatic colon cancer. Tumor cells were also stained positively for villin and CEA, and they were stained negatively for thyroglobulin, calcitonin, chromogranin, and synaptophysin, all of which further supported the diagnosis for metastatic colonic adenocarcinoma over a newly developed primary carcinoma of the thyroid gland. In the present case, the patient was initially diagnosed as a primary thyroid cancer by fine- needle aspiration. Immunostaining for CK 20 and CK 7 could be applied on the fine-needle aspiration material.

The interval between the diagnosis of primary tumor and metastatic thyroid mass varies with the behavior of the primary tumor but has been reported to be as long as 26 years for renal cell carcinoma (10). A lengthy time interval has also been seen in breast and gynecological cancers and melanoma (8, 9). Among six reported cases of colonic adenocarcinoma metastatic to the thyroid gland (12-17), the time from diagnosis of the primary tumor to diagnosis of metastasis to the thyroid gland ranged from 30 months to eight years. In the present case, metastasis to the thyroid gland was noted 28 months after the diagnosis of colonic adenocarcinoma.

Therapy for metastasis to the thyroid gland is often considered to be palliative surgical resection of affected thyroid tissue. The extent of the surgical procedure varies from partial lobectomy to total thyroidectomy and lymph node dissection. Usually, the affected lobe and isthmus are removed. The extent of the surgical procedure does not seem to influence the prognosis (8).

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