

A Case of Thyroid Metastasis Originating from Early Gastric Cancer

We report a rare case of thyroid metastasis from early gastric cancer with lymph node metastasis in a 63-yr old woman. She was diagnosed with metastatic adenocarcinoma one and a half years after distal subtotal gastrectomy, by fine needle aspiration (FNA) using thyroid sonography. Thyroid metastasis from gastric cancer is extremely rare, and this case is particular in that it is the first report of thyroid metastasis from early gastric cancer.

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INTRODUCTION

Early gastric cancer (EGC) is defined as gastric cancer invading the gastric mucosa or submucosa, regardless of lymph node metastasis. The prognosis for patients with early gastric cancer after surgical resection is excellent. The 5-yr and even 10-yr survival is more than 90%, as confirmed in both Eastern and Western studies (1-5). Nevertheless, some patients experience recurrence after curative surgery. It has been shown that lymph node status is the most important risk factor for recurrence (6).

Hematogenous metastasis is the most common route of recurrence from EGC and then lymph node metastasis and peritoneal metastasis, in that order (7, 8). However, thyroid metastasis has rarely been reported in the literature. Although there have been two reports of thyroid metastasis from gastric adenocarcinoma (9, 10), to our knowledge, there is no report regarding thyroid metastasis from EGC. We report a case of thyroid metastasis from EGC with a review of the literature about this rare entity.

CASE REPORT

A 63-yr-old woman received distal subtotal gastrectomy and D2 lymph node dissection under diagnosis of stomach cancer in June of 2005. Histopathologic examination of the stomach resulted in the diagnosis of poorly differentiated ade-

nocarcinoma confined to the submucosa with 12 lymph node metastasis, classified as T1N2M0-stage II according to the TNM system (Fig. 1, 2). After the surgery, we performed 6 cycles of adjuvant chemotherapy with 5-FU (1,000 mg/m² continuous infusion on day 1-5) plus cisplatin (60 mg/m² on d 1) intravenous continuous infusion from July of 2005 to January of 2006 in four week intervals.

The patient's condition showed good progress until August of 2006, when a periodic follow-up showed suspicious para-aortic lymph node metastasis (Fig. 3) and the patient complained of diffuse neck swelling on early September of 2006. There were no other clinical symptoms such as dyspnea or neck pain. Upon physical examination, small and hard nodules were palpated on both lobes, no tenderness was noted. Thyroid sonogram findings showed diffuse nodular enlargement in both lobes of thyroid gland (Fig. 4). Initial impression of thyroid sonogram suggested goiter, but we cannot excluded malignant nodules. So we performed thyroid fine needle aspiration (FNA). It disclosed diffuse infiltration of malignant tumor cells with a few residual thyroid follicles. The morphology of tumor cells were malignant signet ring cells same as the gastric neoplastic cells. Immunohistochemistry was done to rule out the possibility of metachronous primary thyroid cancer. Tumor cells were positive for carcinoembryonic antigen and negative for thyroglobulin, consistent with metastatic gastric carcinoma (Fig. 5). The follow-up tumor marker tests showed a slight increase of CA19-9, from 21.03 U/mL to 41.39 U/mL (normal range: 0-37.0 U/mL).

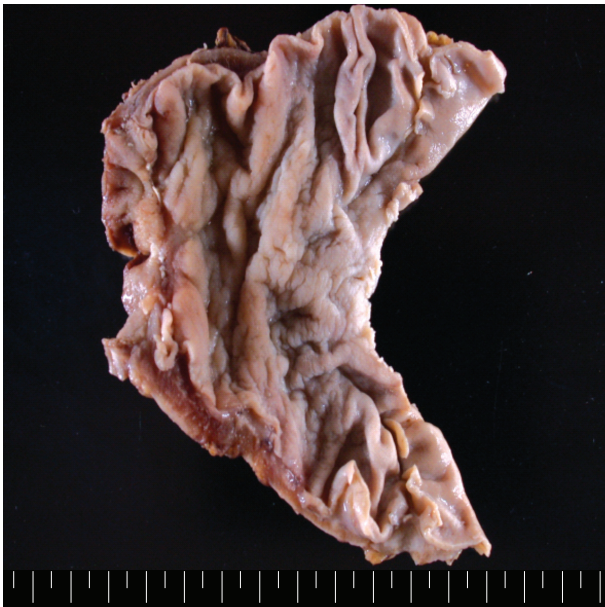


Fig. 1. Macroscopic finding of the resected stomach. An irregular ulceroinfiltrative lesion is noted at the pylorus on the lesser curvature side, measuring 2.0 cm in diameter.

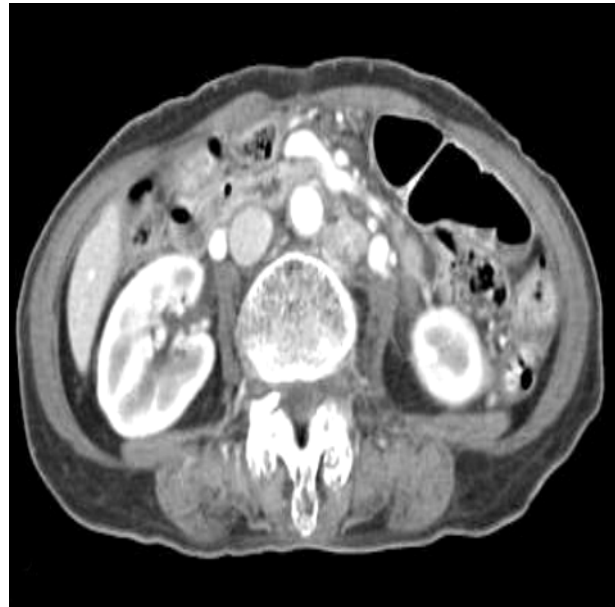


Fig. 3. Abdominal computed tomography findings one and half years after gastrectomy. There are newly developed multiple paraaortic lymph node enlargement.

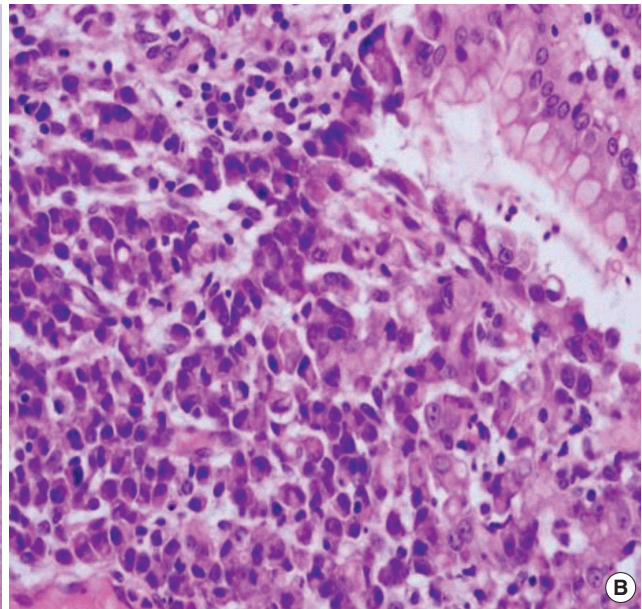
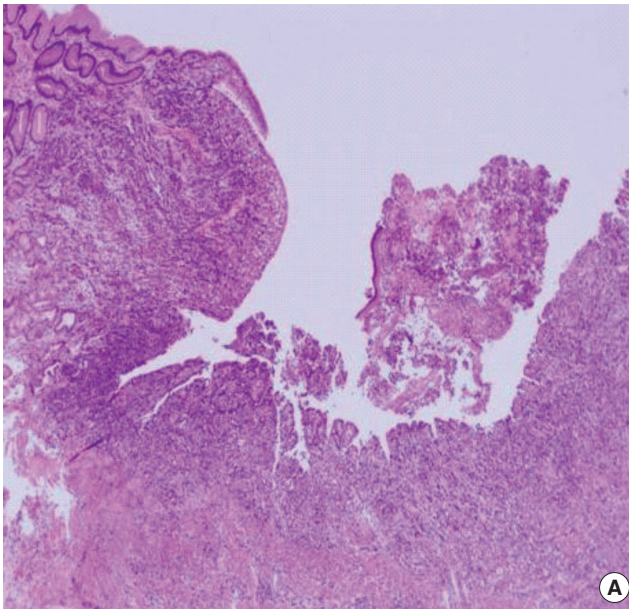


Fig. 2. Microscopic findings of the resected stomach. (A) Diffuse proliferation of tumor cells are noted without gland formation (H&E, $\times 40$). (B) Each tumor cell is signet ring in shape and their nuclei are displaced eccentrically by intracytoplasmic mucin vacuoles (H&E, $\times 400$).

Examinations such as simple chest radiography, bone scan, and other hematologic signs showed no particular findings. Thyroid function test also showed normal results. We did palliative chemotherapy with TS-1 (administered orally, 80 mg/m², days 1 to 21) plus cisplatin (60 mg/m², day 8). Although the tumor was under control at first, after 2 cycles the disease worsened, spread to the thyroid and abdomen, and the patient died of peritoneal carcinomatosis on February of 2007.

DISCUSSION

The recurrence rate of node-positive EGC was about 15% and overall 5-yr survival rate was 84% (11). Although gastric carcinoma is the most frequent type of malignancy in Korea, thyroid metastasis is extremely rare. There was previously reported case in Korea where metastasis to the breast and thyroid was seen at time of diagnosis (12), but this is a

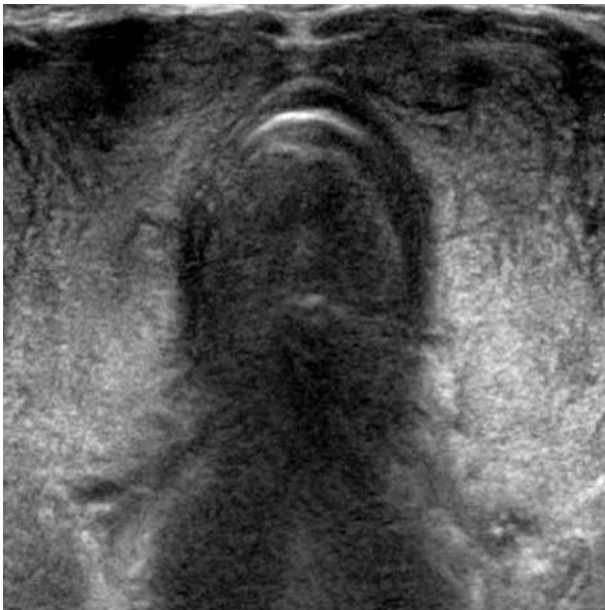


Fig. 4. Thyroid sonogram shows diffuse nodular enlargement of both lobes.

first case of recurrence in the thyroid confirmed at the follow-up period after radical excision.

The thyroid gland is generally considered to be a very infrequent site of metastatic disease in clinical setting. However, according to autopsy series, the frequency of thyroid metastasis varies between 1.2% and 24% (13, 14).

In clinical practice, the most frequently diagnosed primary tumor sites are the kidney, breast, and lung (15-18). Occasionally, metastatic lesions from gastrointestinal neoplasm such as colo-rectal and esophageal cancer are seen, but metastasis from gastric cancer has been reported only 2 cases in the English literature.

The similarity between this case and the previously reported cases is that the primary cancer was poorly differentiated, lymph node metastasis was present, and follow-up tests showed an increase of AFP. In this case, the primary cancer showed extensive lymph node metastasis, even though the infiltration of the tumor was limited to the submucosa, allowing us to assume that the route of metastasis to the thyroid may be by the lymphatic system. Also, there were reports that AFP-producing gastric cancers showed poor prognosis, and such biologic behavior may be a possible cause of the strange metas-

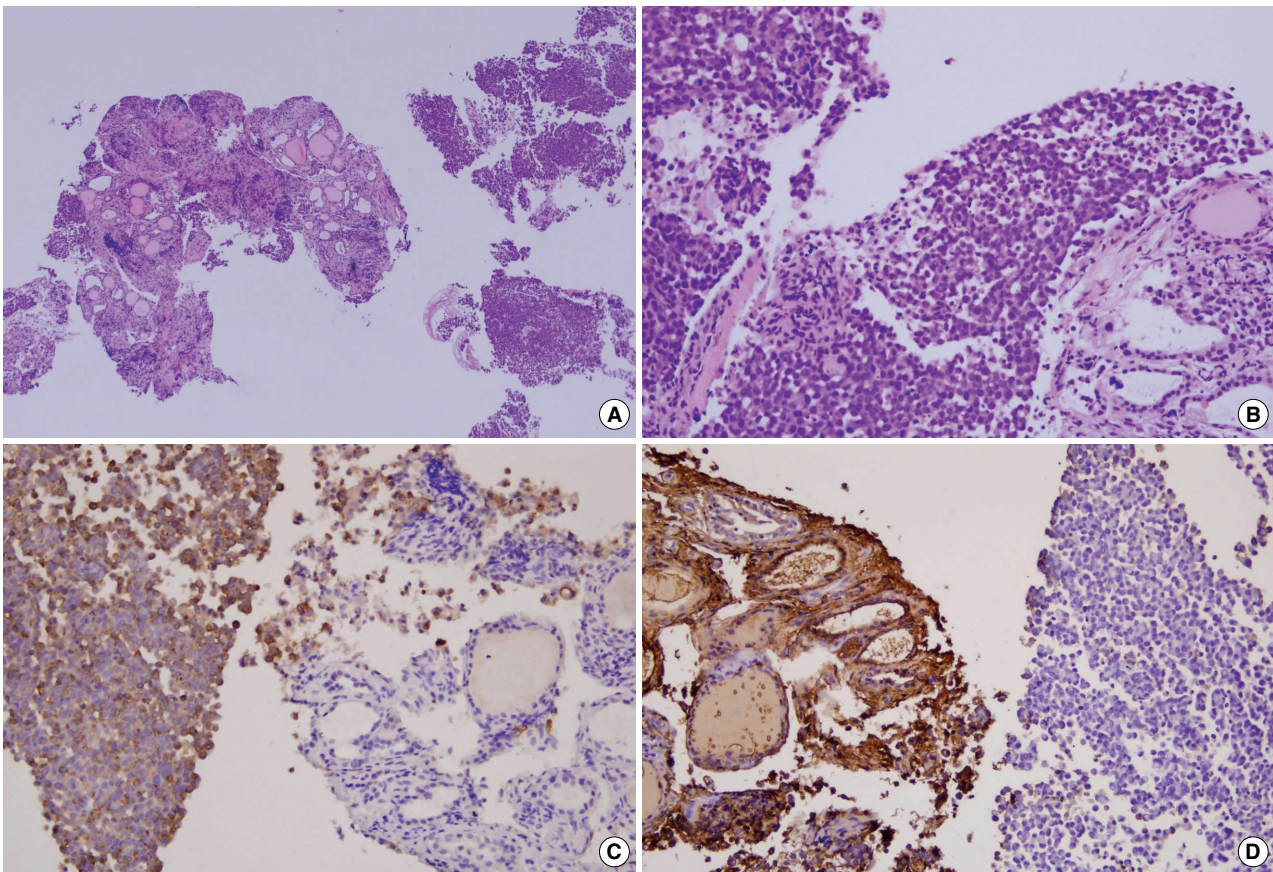


Fig. 5. Microscopic findings of needle biopsy specimen of the thyroid metastasis. (A) Normal thyroid follicles are destroyed by dispersed tumor cells (H&E, $\times 40$). (B) Atypical signet ring cells identical to the gastric cancer are noted (H&E, $\times 400$). Immunohistochemistry demonstrates positive staining for carcinoembryonic antigen (C) and negative for thyroglobulin (D) (C&D: avidin biotin complex method, $\times 400$).

tasis seen in the present case, as is also in the previous cases (19, 20).

There is no clear consensus regarding the role of surgery for metastatic thyroid cancers. Some authors support thyroidectomy for slowly growing tumors, whereas others argue that thyroidectomy has no survival benefit for rapidly growing tumors (16-18, 21). Thyroidectomy was done on the previously reported 2 cases, because the tumor was limited to the thyroid and there were no evidence of metastasis to the other sites. But the results showed an abrupt aggravation of the cancer. In our case, surgical resection was not considered an option, due to the presence of para-aortic lymph node metastasis, and the tumor showed a comparably stable response to chemotherapy for 2 cycles. But after the initial response the tumor showed sudden exacerbation and the patient expired 5 months after the diagnosis of metastasis.

Thyroid metastasis in gastric cancer is extremely rare, but shows extensive lymph node metastasis, undifferentiated feature of tumor, and a poor prognosis. Although this case report was of early gastric cancer, the tumor showed poor clinical prognosis. Since it is the first case of thyroid metastasis from EGC, we report this with the related references.

REFERENCES

1. Maehara Y, Orita H, Okuyama T, Moriguchi S, Tsujitani S, Korenaga D, Sugimachi K. *Predictors of lymph-node metastasis in early gastric cancer*. *Br J Surg* 1992; 79: 245-7.
2. Habu H, Takeshita K, Sunagawa M, Endo M. *Lymph node metastases in early gastric cancer*. *Int Surg* 1986; 71: 244-7.
3. Guadagni S, Reed PI, Johnston BJ, De Bernardinis G, Catarci M, Valenti M, di Orio F, Carboni M. *Early gastric cancer: follow up after gastrectomy in 159 patients*. *Br J Surg* 1993; 80: 325-8.
4. Folli S, Dente M, Dell'Amore D, Gaudio M, Nanni O, Saragoni L, Vio A. *Early gastric cancer: prognostic factor in 223 patients*. *Br J Surg* 1995; 82: 952-6.
5. Kitamura K, Yamaguchi T, Taniguchi M, Hagiwara A, Sawai K, Takahashi T. *Analysis of lymph node metastasis in early gastric cancer: rationale of limited surgery*. *J Surg Oncol* 1997; 64: 42-7.
6. Sano T, Sasako M, Kinoshita T, Maruyama K. *Recurrence of early gastric cancer: follow-up of 1475 patients and review of Japanese literature*. *Cancer* 1993; 72: 3174-8.
7. Ahn JS, Bang HY, Lee JI, Noh WC, Hwang DY, Choi DW, Paik NS, Moon NM, Choi TI. *Recurrence of early gastric cancer*. *J Korean Surg Soc* 2001; 61: 491-7.
8. Jung SJ, Kim BS, Oh ST, Yook JH, Choi WY, Lee CH. *Characteristics of recurred early gastric cancer after gastric resection*. *J Korean Surg Soc* 2003; 65: 13-7.
9. Yoshida A, Imamura A, Tanaka H, Hirano M, Kamma H, Ueno E, Ushio H, Aiyoshi Y, Soeda S. *A case of metastasis from gastric cancer to the thyroid gland*. *Jpn J Surg* 1989; 19: 480-4.
10. Ok E, Sozuer E. *Thyroid metastasis from gastric carcinoma: report of a case*. *Surg Today* 2000; 30: 1005-7.
11. Cheong JH, Hyung WJ, Shen JG, Song C, Kim J, Choi SH, Noh SH. *The N ratio predicts recurrence and poor prognosis in patients with node-positive early gastric cancer*. *Ann Surg Oncol* 2006; 13: 377-85.
12. Yoon SH, Kim SM, Yoo SJ, Yu WY, Han JH, Jeong DK, Kang SJ, Kim HY, Lee CJ, Kim DS, Lee HK. *A case of endoscopically diagnosed gastric cancer with metastasis to thyroid and breast*. *Korean J Gastrointest Endosc* 1993; 13: 701-5.
13. Nakhjavani MK, Gharib H, Goellner JR, van Heerden JA. *Metastasis to the thyroid gland. A report of 43 cases*. *Cancer* 1997; 79: 574-8.
14. Lam KY, Lo CY. *Metastatic tumors of the thyroid gland: a study of 79 cases in Chinese patients*. *Arch Pathol Lab Med* 1998; 122: 37-41.
15. Pillay SP, Angorn IB, Baker LW. *Tumour metastasis to the thyroid gland*. *S Afr Med J* 1977; 51: 509-12.
16. Ericsson M, Biorklund A, Cederquist E, Ingemansson S, Akerman M. *Surgical treatment of metastatic disease in the thyroid gland*. *J Surg Oncol* 1981; 17: 15-23.
17. Czech JM, Lichter TR, Carney JA, van Heerden JA. *Neoplasms metastatic to the thyroid gland*. *Surg Gynecol Obstet* 1982; 155: 503-5.
18. McCabe DP, Farrar WB, Petkov TM, Finkelmeier W, O'Dwyer P, James A. *Clinical and pathologic correlations in disease metastatic to the thyroid gland*. *Am J Surg* 1985; 150: 519-23.
19. Kodama T, Kameya T, Hirota T, Shimosato Y, Ohkura H, Mukojima T, Kitaoka H. *Production of alpha-fetoprotein, normal serum proteins, and human chorionic gonadotropin in stomach cancer: histologic and immunohistochemical analyses of 35 cases*. *Cancer* 1981; 48: 1647-55.
20. Ishikura H, Kirimoto K, Shamoto M, Miyamoto Y, Yamagiwa H, Itoh T, Aizawa M. *Hepatoid adenocarcinomas of the stomach. An analysis of seven cases*. *Cancer* 1986; 58: 119-26.
21. Murakami S, Yashuda S, Nakamura T, Mishima Y, Iida H, Okano H, Nakano M. *A case of renal cell carcinoma with metastasis to the thyroid gland and concomitant early gastric cancer*. *Surg Today* 1993; 23: 153-8.