

# Gastric adenocarcinoma diagnosed by endometrial curettage in cancer of unknown primary site

D.S. Lee<sup>1</sup>, D.W. Eom<sup>2</sup>, Y. Ahn<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, <sup>2</sup>Department of Pathology, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung (Korea)

## Summary

The authors report a case of gastric adenocarcinoma diagnosed by endometrial random biopsy in a cancer of unknown primary site patient. Even if there are no vaginal bleeding episodes, endometrial hyperplastic lesions can be a diagnostic clue to find the extrapelvic metastasis to endometrium.

*Key words:* Signet-ring cell carcinoma; Extra-pelvic metastasis to uterus; Endometrial curettage; Cancer of unknown primary site.

## Introduction

Extrapelvic metastasis to uterus is extremely rare and the presence of signet ring cells (SRC) in the uterine endometrium strongly raises the possibility of a metastasis from the breast, gastrointestinal tract, or elsewhere. Herein, the authors report a endometrial adenocarcinoma with SRC feature which originated from stomach in a 38-year-old woman, which involved the use of a endometrial biopsy to obtain adequate samples for pathological analysis; the use of endometrial biopsy in patients with no vaginal bleeding is unlike those used in previous cases.

## Case Report

A 38-year-old woman complained of dyspnea for a week and was referred to the present institution for pleural effusion. She was a multigravida without medical or surgical history of note. The authors performed physical examinations, laboratory tests, and imaging studies and they found miliary lung nodules, bilateral pleural effusion, and disseminated bone metastases in CT and positron emission tomography (PET) scans. Multifocal hypermetabolic lesions in uterine endometrium (SUV=2.4) were also observed (Figure 1). There was no gastric lesion seen on the original chest CT. At first, the authors suspected primary lung cancer but CT-guided lung biopsy revealed poorly-differentiated adenocarcinoma from unknown origin.

The patient was referred to an experienced gynecologic oncologist for evaluation. She denied prior vaginal bleeding episodes and no cervical lesions were detectable on Pap smear and colposcopy. With gynecology ultrasonography, both ovaries appeared normal; however, irregular multiple endometrial le-

sions were noticed and curettage was performed to distinguish malignancy from benign hyperplasia. Endometrial specimen turned out to be moderately-differentiated adenocarcinoma with signet ring cell feature, which is often seen in breast or gastrointestinal malignancies. Estrogen receptor and progesterone receptor were all negative on immunohistochemical staining (Figure 2). Based on these findings, the authors looked into gastrointestinal tract and found gastric mucosal lesion in lower body of greater curvature in gastroduodenoscopy. Histopathologic findings of gastric specimens were identical to endometrial ones on slide review (Figure 3).

Despite two cycles of palliative chemotherapy (FOLFOX, 5-fluorouracil/leucovorin plus oxaliplatin) for advanced gastric cancer, treatment-refractory lymphangitic lung metastases progressed and led the patient to respiratory failure (only four weeks since treatment).

## Discussion

First case of extrapelvic metastasis to uterus was described in 1878 [1]. Only 13 metastasis to uterine corpus from gastric origin are available in English literature to date. Because of relative ease of detection, cancer metastasis to uterine cervix seems to be more common than to corpus uteri. So endometrial metastasis of SRC is extremely rare [2, 3] and in corporeal metastasis, myometrium was involved in most of the cases and concurrent endometrial presentation were found in one-third of the cases [1, 4-8].

SRC carcinoma is an epithelial carcinoma mainly arising from the breast, stomach, colon, testis, prostate, blad-

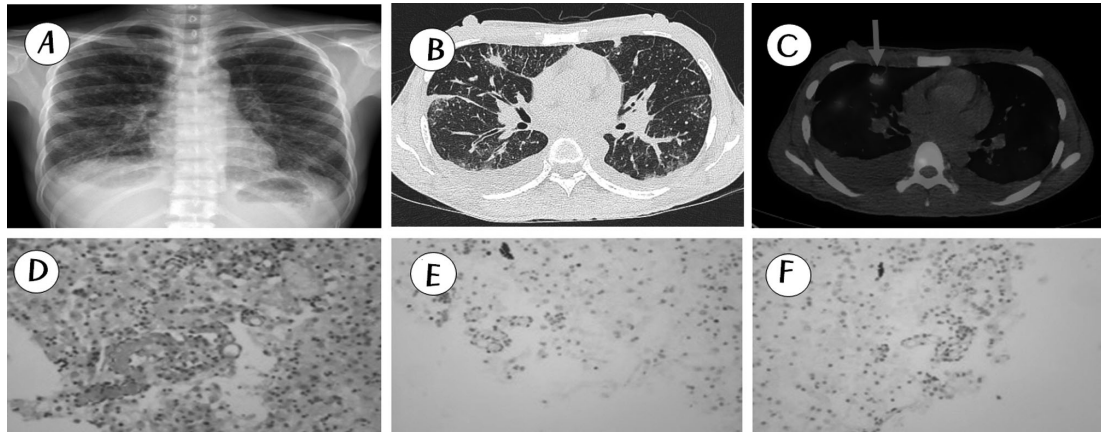


Figure 1. — (A)(B) Chest X-ray and chest metastasis with miliary pattern. (C) PET-CT: 15 mm-sized lung nodule. (D) Histological analysis: adenocarcinoma with signet ring cell features (H&E  $\times 200$ ). (E) Immunohistochemically negative for ALK. (F) Immunohistochemically negative for TTF-1.

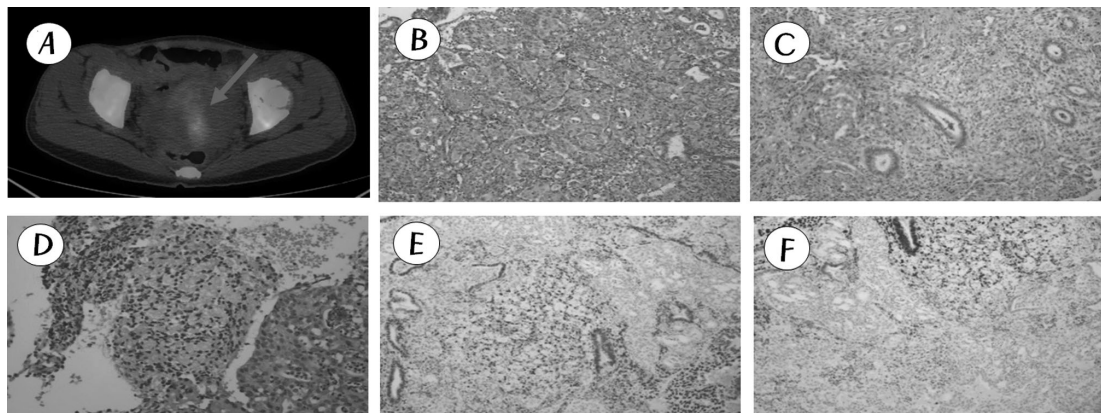


Figure 2. — (A) PET-CT: focal tiny unusual hypermetabolic lesion in the uterine endometrial cavity. (B) Histological analysis: adenocarcinoma with signet ring cell features (H&E  $\times 100$ ). (C) H&E  $\times 200$ . (D) Desmoplastic reaction between benign-looking endometrial glands. (E) Immunohistochemically negative for ER. (F) Immunohistochemically negative for PR.

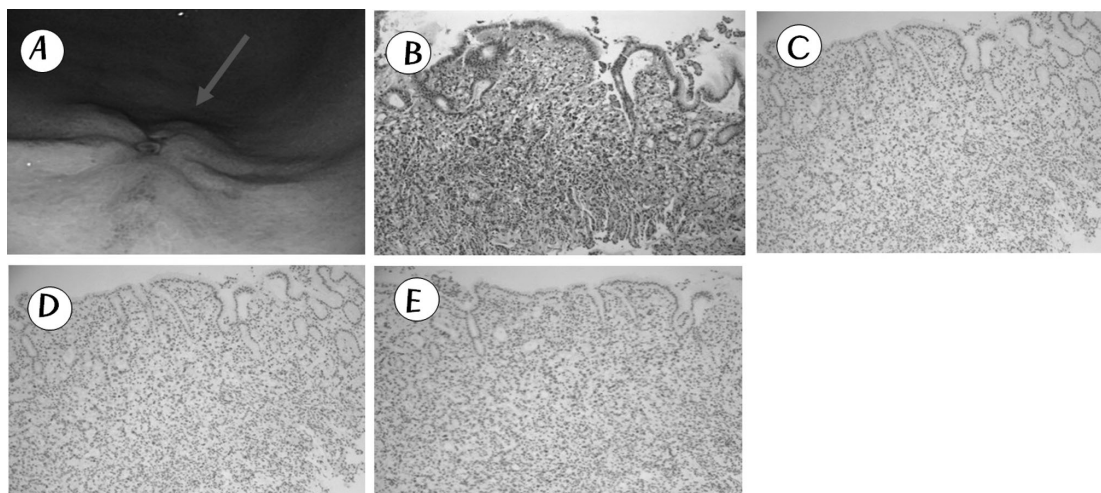


Figure 3. — (A) Endoscopic findings reveal dent and central uplift of the mucosa in the greater curvature of the stomach. (B) Immunohistochemical staining, ER negative. (C) Stomach with immunohistochemical staining, PR negative.

der, gallbladder, ovary, and so forth [5, 7, 9, 10]. Immunohistochemical and molecular studies are often helpful in differential diagnosis. Gross cystic disease fluid protein-15 (GCDFP-15) is used to find primary breast cancer and CEA, CDX-2, and CK 20 are utilized to find colon origin [3].

Pathogenesis of spread from gastric cancer to uterus is not yet fully understood. Some authors believe that most of uterine metastases are from local lymphatic drain from ovarian malignancy [10]. However another group suggested that it is primarily due to lymphatic and hematogenous disseminations [8]. The latter hypothesis is better supported by the fact that most cases are accompanied by widespread tumor dissemination at diagnosis and the present case showed both lymphangitic lung metastases and hematologic bone dissemination. This is why endometrial metastasis from SRC origin carries a dismal prognosis.

Usually, metastasis to the uterus is accompanied by vaginal bleeding. Experts recommended that uterine metastasis must be considered if breast or gastrointestinal cancer patients complain of vaginal bleeding [10]. The present patient had no menorrhea or spot bleeding symptoms but the authors found stomach cancer through endometrial curettage in an effort to find primary origin. Clinicians should always be aware that irregular endometrial hyperplasia on vaginal ultrasonography can be a diagnostic clue in cancer of unknown primary site patients.

## References

- [1] Legg J.W.: "Melanotic sarcoma of the eyeball: secondary growth in the organs of the chest and belly, particularly in the liver". *Trans. Pathol. Soc. Lond.*, 1878, 29, 225.
- [2] Imachi M., Tsukamoto N., Amagase H., Shigematsu T., Amada S., Nakano H.: "Metastatic adenocarcinoma to the uterine cervix from gastric cancer. A clinicopathologic analysis of 16 cases". *Cancer*, 1993, 71, 3472.
- [3] Suarez-Penaranda J.M., Abdulkader I., Baron-Duarte F.J., Gonzalez Patino E., Novo-Dominguez A., Varela-Duran J.: "Signet-ring cell carcinoma presenting in the uterine cervix: report of a primary and 2 metastatic cases". *Int. J. Gynecol. Pathol.*, 2007, 26, 254.
- [4] Kumar N.B., Hart W.R.: "Metastases to the uterine corpus from extragenital cancers. A clinicopathologic study of 63 cases". *Cancer*, 1982, 50, 2163.
- [5] Kumar A., Schneider V.: "Metastases to the uterus from extrapelvic primary tumors". *Int. J. Gynecol. Pathol.*, 1983, 2, 134.
- [6] Khoury S., Odeh M., Ophir E., Cohen H., Oettinger M.: "Uterine metastasis from gastric cancer". *Acta Obstet. Gynecol. Scand.*, 1997, 76, 803.
- [7] Pasini A., Mandelli P., Belloni C.: "Endometrial metastases from gastric adenocarcinoma: a case report". *Tumori*, 1995, 81, 383.
- [8] Tsoi D., Buck M., Hammond I., White J.: "Gastric adenocarcinoma presenting as uterine metastasis—a case report". *Gynecol. Oncol.*, 2005, 97, 932.
- [9] Mazur M.T., Hsueh S., Gersell D.J.: "Metastases to the female genital tract. Analysis of 325 cases". *Cancer*, 1984, 53, 1978.
- [10] Stemmermann G.N.: "Extrapelvic carcinoma metastatic to the uterus". *Am.J. Obstet. Gynecol.*, 1961, 82, 1261.

Corresponding Author:

Y. AHN, M.D.

Department of Internal Medicine  
Gangneung Asan Hospital  
38 Bangdong-gil, Sacheon-myeon  
Gangneung-si, 210-711 (Korea)  
e-mail: lephenixmed@gmail.com