

## Case Report

## Late, isolated metastasis from poorly differentiated gastric cancer to the uterine cervix



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## Introduction

Late recurrence of gastric cancer after curative resection is rare. Distant metastasis to the uterine cervix is also quite rare, especially from extrapelvic organs (Abrams et al., 1950; Lemoine and Hall, 1986). Despite its rarity, it is important to consider the possibility of metastasis from gastric cancer to the uterine cervix if a female patient experiences genital bleeding or presents with a cervical tumor. Here, we present a case of gastric cancer metastasis to the uterine cervix 10 years after distal gastrectomy.

## Case description

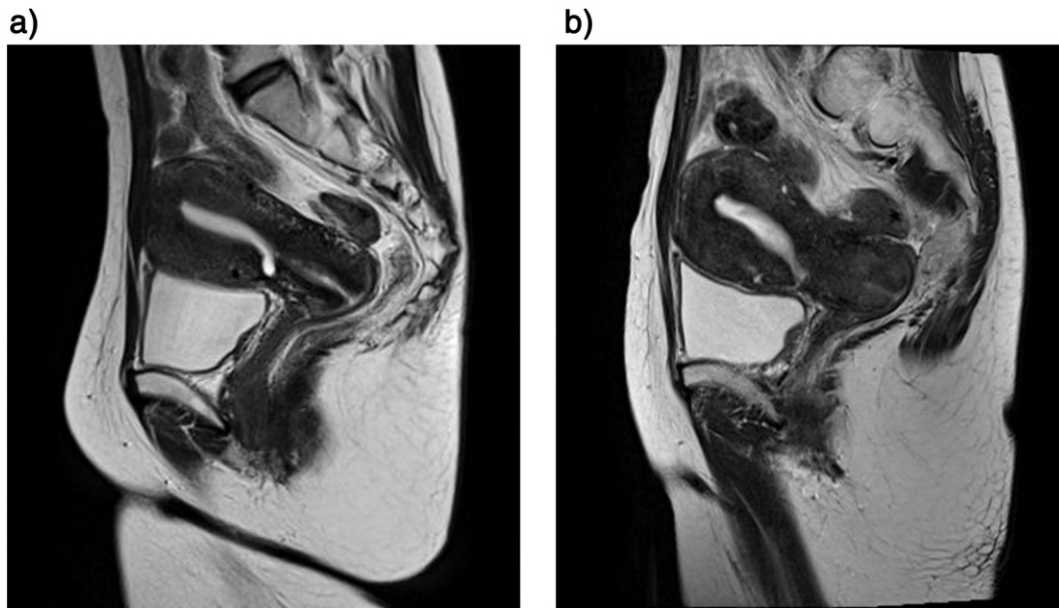
A 46-year-old woman, gravida 2 para 2, presented to our hospital with a complaint of irregular genital bleeding and a 27.1 × 20.7 mm uterine cervix tumor, which was detected on pelvic magnetic resonance imaging (MRI). One year prior to the present event, her cervical and endometrial cytology had been negative, and a pelvic MRI examination had shown normal findings (Fig. 1a). Ten years prior, the patient had undergone adjuvant chemotherapy following distal gastrectomy for pathologically diagnosed stage IIIB poorly differentiated gastric adenocarcinoma. The exact pathological stage of disease was pT3N2M0 according to the 5th edition Union for International Cancer Control (UICC) classification, and pT4aN2M0 according to the 7th edition UICC classification.

The patient's father had a history of prostate cancer. She showed no signs of recurrence during the 10 years following distal gastrectomy. The occurrence of her last menstrual period was unclear because of irregular vaginal bleeding. At the first clinical examination, genital bleeding was present and the patient bled easily from her uterine cervix. A transvaginal sonography revealed a 22 × 20 mm high echoic lesion at the dorsal side of the cervix. Biochemical blood examination results were all within normal limits, but the level of squamous cell carcinoma-related antigen was slightly elevated at 2.4 ng/mL. The result of a high-risk human papillomavirus (HPV)-DNA hybrid capture test was negative. Neither an upper gastrointestinal nor a colon fiberoscopy showed any evidence of abnormalities.

A Papanicolaou (Pap) smear of the uterine cervix revealed atypical glandular cells, and a biopsy specimen taken from the uterine cervix indicated poorly differentiated adenocarcinoma, which made us suspect recurrence of the previous gastric cancer. Pelvic MRI showed a high-intensity 27.1 × 20.7 mm irregular mass on T2-weighted images of the cervix (Fig. 1b). Fluorine-18-fluorodeoxyglucose (<sup>18</sup>F-FDG) positron emission computed tomography did not show increased FDG uptake in the uterine cervix or other organs. Accordingly, the patient was diagnosed as having gastric cancer metastasis to the uterine cervix. Modified radical hysterectomy with bilateral salpingo-oophorectomy was performed with a curative intent and for diagnostic confirmation. Intraoperative examination did not reveal any ascitic fluid, palpable lymph nodes, or peritoneal seeding. The pathological diagnosis was metastatic adenocarcinoma in the uterine cervix, originating from the known gastric cancer. Subsequently, a postoperative Pap smear revealed atypical glandular cells because of residual tumor in the vaginal stump. First, the regimen with S-1 (tegafur, gimeracil and oteracil potassium) and cisplatin, which is one of the standard regimens for a recurrent gastric cancer in Japan, was presented to the patient however she didn't accept it because of the side effect. Therefore, chemotherapy with S-1 was originally planned to be administered daily for the first week of every 3-week cycle. However, the administration schedule was reduced due to side effects. The patient eventually received adjuvant chemotherapy with 100 mg/day S-1 administered daily during the first week of every 6-week cycle for 1 year. Pap smear results became negative for an intraepithelial lesion after chemotherapy. Follow-up computed tomography scans have not indicated any recurring tumor to date. At the time of this report, the patient remains alive and is believed to have achieved complete response 24 months after surgery.

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**Fig. 1.** Pelvic magnetic resonance images. (a) No abnormalities are evident 1 year before the patient was referred to our hospital. (b) A mass in the uterine cervix is observed at the time of admission.

### Pathological findings

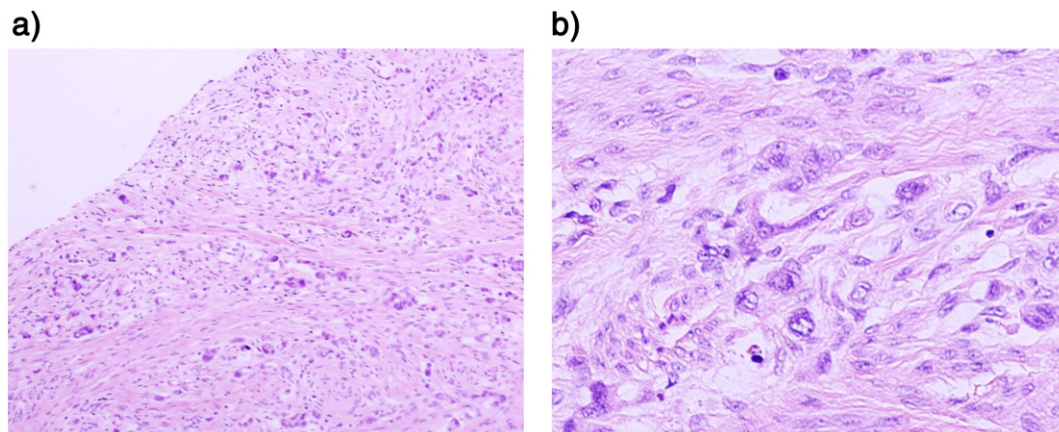
A mass with a focus on the dorsal side of the uterine cervix was observed. The tumor cells produced mucus and formed clusters, the findings are consistent with a poorly differentiated adenocarcinoma (the same type of adenocarcinoma as the patient's previous gastric cancer). The tumor cells mainly developed in the uterine cervical stroma, rather than in the epithelia of the uterine cervix (Fig. 2). An immunohistochemical analysis of the specimen was performed. Cancer cells stained positive for cytokeratin (CK) 7, CK20, carcinoembryonic antigen (CEA), mucin (MUC) 2, CDX2, p16 and p53, but negative for MUC1, MUC5 and MUC6. There was no evidence of cancer cells in the ovaries or the fallopian tubes. Tumor cells were not observed on peritoneal washing cytology analysis. Therefore, the patient was diagnosed with metastasis from the previous gastric cancer to the uterine cervix, involving the uterine corpus, vagina and uterosacral ligament.

### Discussion

Metastasis from extrapelvic organs to the uterine cervix is rare. Abrams et al. reported that metastatic involvement of the uterine cervix

occurred in only 3 of 1000 cases of metastatic cancer (Abrams et al., 1950). It has also been reported that, of all metastases to the uterine cervix except for the result of direct extension of a primary tumor, 36.4% originated from ovarian cancer, 30.3% from colorectal cancer, 15.2% from gastric cancer, 12.1% from breast cancer, 3.0% from renal cell cancer, and 3.0% from transitional cell cancer of the renal pelvis (Lemoine and Hall, 1986). The reason why incidence of metastasis to the uterine cervix is low remains unclear. However, Lemoine et al. suggested that this low incidence might result from an abundance of fibrous matrix and a low degree of vascularity (Lemoine and Hall, 1986). To our knowledge, only one case has been previously reported on the diagnosis of an isolated metastasis of gastric cancer to the uterine cervix by surgical specimens (Yokoyama et al., 2000). To identify relevant case reports, we searched PubMed for cases of metastatic gastric cancer to the uterine cervix, and reviewed 39 such cases from 7 references listed in Table 1 (Lemoine and Hall, 1986; Yokoyama et al., 2000; Perez-Montiel et al., 2012; Imachi et al., 1993; Matsuura et al., 1997; Zhang et al., 1983; Kashimura et al., 1983). In the following paragraphs, we present a summary of these cases.

Among patients with cervical metastases, the median age at the time of metastasis diagnosis was 44 years (range, 23–75 years), and only 9



**Fig. 2.** Microscopic findings of metastatic adenocarcinoma at the uterine cervix. (a) Hematoxylin and eosin staining, 100 $\times$ . (b) Hematoxylin and eosin staining, 400 $\times$ .

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