

# Metastatic Gastric Adenocarcinoma of the Uterine Cervix – A Case Report and Review of the Literature

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## Case report

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# Abstract

**Background:** Poorly differentiated diffuse-type gastric adenocarcinoma typically presents at an advanced stage, however, metastasis to the uterine cervix is extremely rare. To our knowledge, less than forty cases have been described worldwide.

**Case presentation:** We report a case of a 47-year-old woman who presented to us with symptomatic uterine fibroids and subsequently underwent a successful total laparoscopic hysterectomy and bilateral salpingo-oophorectomy. The diagnosis of metastatic cancer involving the cervix was established incidentally on histopathology, which showed atypical signet ring cells in the lymphovascular spaces of the cervix. Further investigations for a primary malignancy revealed a poorly differentiated diffuse-type gastric adenocarcinoma.

**Conclusion:** Gastric cancer involving the uterine cervix is rare and associated with a poor prognosis. When presented with isolated cervical metastases, the gastrointestinal tract should be considered as a possible primary source. Due to the limited publications on this clinical entity, we expect to raise awareness and study of this unique manifestation of gastric cancer by presenting our case.

## Background:

Gastric cancer typically presents at an advanced stage and up to 85% of tumors may be accompanied by lymph node metastasis at diagnosis.[1] In general, non-gynaecological malignancies rarely metastasize to the uterine cervix. Currently, less than 1% of all cervical cancers originate from an extra-genital primary and when implicated, approximately 11.1% arise from metastatic gastric cancer. [2] Like the Krukenberg tumour of the ovary, lymphatic dissemination is regarded as the route of metastasis from primary gastric cancer to the uterine cervix.[3]

The presentation of both primary cervical cancer and metastatic cancer involving the cervix are the same. Patients present with postcoital or intermenstrual bleeding, and a foul-smelling vaginal discharge.[4] Advanced disease manifests as pelvic or lower back pain and with bowel or urinary symptoms.

Gastric cancer with metastasis to the uterine cervix carries a poor prognosis and due to the paucity of publications on this clinical entity, there are no established treatment protocols. Hysterectomy does not improve outcomes and chemotherapy utilizing platinum-based compounds and fluoropyrimidine appear to maximize quality of life.[5]

Herein we report a case of a 47-year-old woman who underwent a successful total laparoscopic hysterectomy and bilateral salpingo-oophorectomy for symptomatic uterine fibroids. Histopathology revealed an incidental finding of signet ring cells in the cervix. Immunohistochemistry suggested an adenocarcinoma of unknown primary. Further investigation with CT chest/abdomen/pelvis and upper gastrointestinal (GI) endoscopy led to the diagnosis of poorly differentiated diffuse-type gastric adenocarcinoma.

## Case Description:

A 47-year-old, woman presented to us with a history of menometrorrhagia and dysmenorrhea for eight months. She denied experiencing postcoital bleeding, urinary symptoms and symptoms of anaemia. Her past gynaecologic, obstetric and surgical history was unremarkable. She had a normal cervical smear three years prior. Her past medical history included gastritis which was self-treated with over-the-counter medications. She was a non-smoker and had no family history of cancer.

At the time of referral, her general physical examination was normal. Pelvic examination revealed a mobile uterus of 10 weeks size. There were no masses or adnexal tenderness. On speculum examination, the cervix was grossly normal and 2cm long. Pelvic ultrasonography revealed a 6.7cm x 4.5cm subserosal uterine fibroid. There was mild left hydronephrosis with hydroureter and moderate pelvic free fluid noted. Biochemical blood investigations including a renal function test were all within normal limits. Her haemoglobin was 10.5g/dL.

Three weeks later, the patient underwent a cystoscopy with left ureteric stenting for left hydroureter and a total laparoscopic hysterectomy with bilateral salpingo-oophorectomy for symptomatic uterine fibroids. Intraoperatively, there was no obstruction within the left ureter and the hydroureter had resolved at the time of the procedure. Grossly, the uterus, cervix and adnexae appeared unremarkable. Histopathology showed a benign leiomyoma, unremarkable adnexae and no evidence of malignancy. The cervix was widely sampled and there were no evidence of in-situ or invasive neoplasia. However, several sections revealed aggregates of atypical cells within the lymphovascular spaces of the cervix (Figure 1A). These cells showed moderate, syncytial cytoplasm and round to ovoid nuclei with indistinct nucleoli. Immunohistochemistry was recommended and further study of these atypical cervical cells revealed positive stains for CK7 (Figure 1B) and CDX2 (Figure 1C). Negative stains included CK20, CK5/6, CD45, desmin, GATA3 and PAX8. The overall features were highly suspicious for metastatic adenocarcinoma.

A computed tomography (CT) scan of the chest, abdomen and pelvis was requested. CT scan revealed mild thickening of the gastric fundus, and no lymphadenopathy or other features suggestive of malignancy. An upper gastrointestinal (GI) endoscopy was arranged and an atypical gastric fundus with thickened irregular folds (Figure 2) was discovered, giving the impression of a diffuse gastric lesion. The gastric cardia, antrum and pylorus appeared normal and there was no evidence of a gastric gastrointestinal stromal tumour (GIST). Several endoscopic biopsies were taken of the gastric fundus.

Gastric fundal biopsies revealed multiple fragments of gastric mucosa infiltrated by dissociated single cells which had high nuclear to cytoplasmic ratios and prominent nucleoli. Immunohistochemistry of gastric samples also stained positive for CK7 and CDX2. Considering the pattern of infiltration, it was best regarded as poorly differentiated diffuse-type gastric carcinoma which metastasized to the uterine cervix. The patient's case was subsequently discussed at a multidisciplinary team meeting (MDT) where a decision for chemotherapy was made.

The patient was referred to the Medical Oncology team for further management. She eventually decided to stop treatment due to side effects from chemotherapy and progression of disease. The patient succumbed to her disease a few months later.

## Discussion:

Gastric cancer is the fifth most common cancer among women and the fourth leading cause of cancer-related death worldwide.[6] The most prevalent subtype of gastric cancer is adenocarcinoma, which is subdivided into the intestinal-type and diffuse-type according to the Lauren classification.[1] Additional subtypes include signet ring cell carcinoma, adeno-squamous carcinoma and squamous cell carcinoma, among others.[7] Metastatic gastric cancer commonly involves the liver (48%), peritoneum (32%), lung (15%) and bone (12%).[8] Metastatic gastric cancer presenting in the uterine cervix is a rare occurrence.

In general, metastasis to the female genital tract from extrapelvic malignancies is highly unusual. Regardless of the location of the primary cancer, metastasis commonly affects the ovaries and vagina.[9] The cervix is less affected compared to the uterine corpus.[9, 10] Moreover, less than 1% of all cervical malignancies originate from non-gynaecological metastatic primaries. These metastatic primary cancers originate from the breast (42.9%), colon (17.5%), stomach (11.1%), pancreas (11.1%), gallbladder (4.8%), cutaneous melanoma (3.2%) urinary bladder (3.2%) and thyroid (1.6%).[2] In 1999, an examination of 40 cases of primary extragenital malignancies with metastasis to the cervix found that the most common source of primary malignancy was that of breast cancer and gastric cancer.[11]

Non-gynaecological cancers may metastasize to the cervix according to three mechanisms: haematogenous spread, retrograde lymphatic spread and transperitoneal seeding.[10, 11] Wallach and Edberg proposed several reasons for the rare presentation of metastatic cancer in the cervix. These include – the small size of the target area, limited blood and lymphatic supply of the cervix and unfavourable conditions for growth of a tumour in the fibromuscular stroma.[11] Similar to the Krukenberg tumour of the ovary, it is postulated that lymphatic dissemination is responsible for metastasis from a gastric primary cancer to the cervix.[11]

In the case presented, histopathology showed aggregates of metastatic cells in the lymphovascular spaces of the cervix which correlates with current literature regarding

mechanisms of metastasis to the cervix. The lymphatic vessels of the cervix drain in a circumferential pattern.[3, 10] Metastasis by this route may only occur if tumour emboli obstruct distant lymphatic channels.[12] Of significance, conditions are unfavorable for metastatic growth in the postmenopausal cervix due to the high density of fibrous tissue and decreased blood supply.[3, 12] Therefore, patients suffering from metastatic cancer to the cervix are typically young and premenopausal.[11, 13]

The presentation of primary cervical cancer and metastatic cancer of the cervix is the same.[13] Patients commonly report abnormal vaginal bleeding, post-coital bleeding, intermenstrual bleeding and malodorous vaginal discharge.[14] Advanced disease manifests with bowel or urinary symptoms and

with pelvic or lower back pain.[15] In the case of metastasis to the cervix, symptoms of a primary cancer may or may not be present. Early cervical disease is usually asymptomatic and detected on routine screening by an abnormal cervical smear.[16] Rarely, abnormal glandular cells are seen on cervical smears which may be suggestive of ectopic tumour cells.[10, 11, 17]

Likewise, the pelvic examination findings in patients with metastasis to the cervix often resembles that of primary cervical cancer.(14) Such findings include a friable bleeding cervical lesion or mass with possible invasion into the upper vagina. The cervix may be enlarged and stony hard.[11, 14] Imachi reported that in 50% of patients, the cervix was found to be normal on pelvic examination.[10] This highlights the fact that cytologic and histological assessments of the cervix are necessary for the diagnosis of metastatic adenocarcinoma to the cervix.

In the work-up for a primary cancer, immunohistochemistry (IHC) provides guidance on the identification of carcinomas of unknown primary site, tumour classification, behaviour, and prognosis.[18] An initial immunohistochemistry profile performed on suspicious tissue samples cover a broad spectrum of cytokeratins such CK7 and CK20 followed by organ specific markers like PAX8, CDX-2 and GATA3.(19) Both intestinal and diffuse-type gastric adenocarcinoma show variable expression for CK7 and CK20.[18, 20] Specifically, CDX-2 is identified in over 70% of diffuse-type gastric adenocarcinoma.[20] Findings in our patient correlate with current literature as both cervical and gastric immunohistochemistry showed positivity for CK7 and CDX-2

The prognosis in patients with gastric metastasis to the cervix is poor and a hysterectomy does not improve the outcome.[21] The management involves chemotherapy to maximize quality of life and prolong survival.[21] Although there are no established treatment protocols for patients diagnosed with gastric cancer metastasis to the cervix, platinum-based compounds combined with fluoropyrimidine may be used.[5, 9] According to Yamamoto *et al.* the median survival from time of discovery of cervical metastasis is four months.[22]

In conclusion, this case highlights a rare manifestation of metastatic gastric adenocarcinoma in a 47-year-old woman. The histopathological findings of atypical cells in the lymphovascular spaces of the cervix following surgery for a benign indication, led to the discovery of a primary gastric cancer. For the unsuspecting gynaecologist, isolated cervical metastasis should be considered as part of the differential diagnosis when atypical cells are identified in the cervix. Furthermore, immunohistochemistry has a vital role in identifying the primary tumour site. Until treatment protocols are established, chemotherapy using fluoropyrimidine and platinum-based compounds may maximize quality of life in these patients.

## Abbreviations

CT  
Computed tomography  
GI  
Gastrointestinal

GIST  
Gastrointestinal Stromal Tumour  
MDT  
Multi-disciplinary team meeting

## Declarations

**Ethics approval and consent to participate:** Not applicable.

**Consent:**

Written informed consent was obtained from the patient's relative for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

**Availability of data and materials:** Not applicable.

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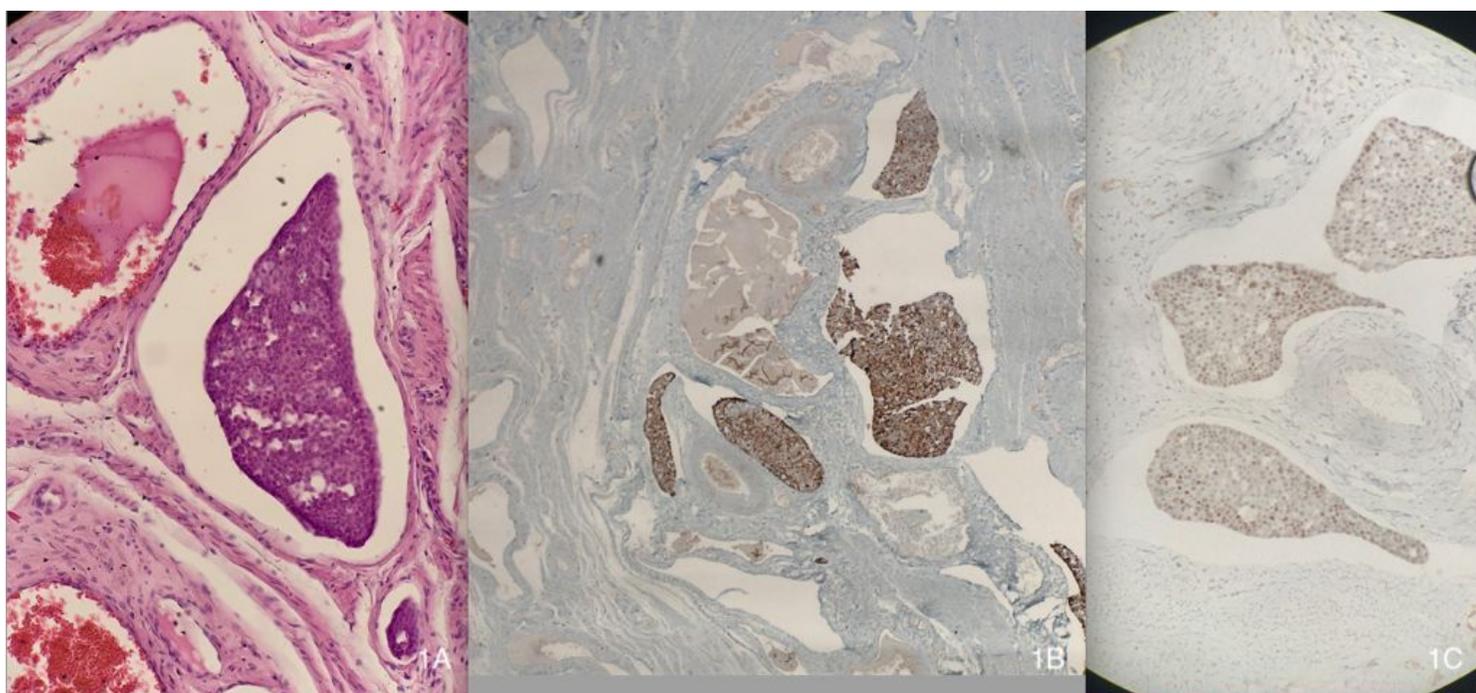
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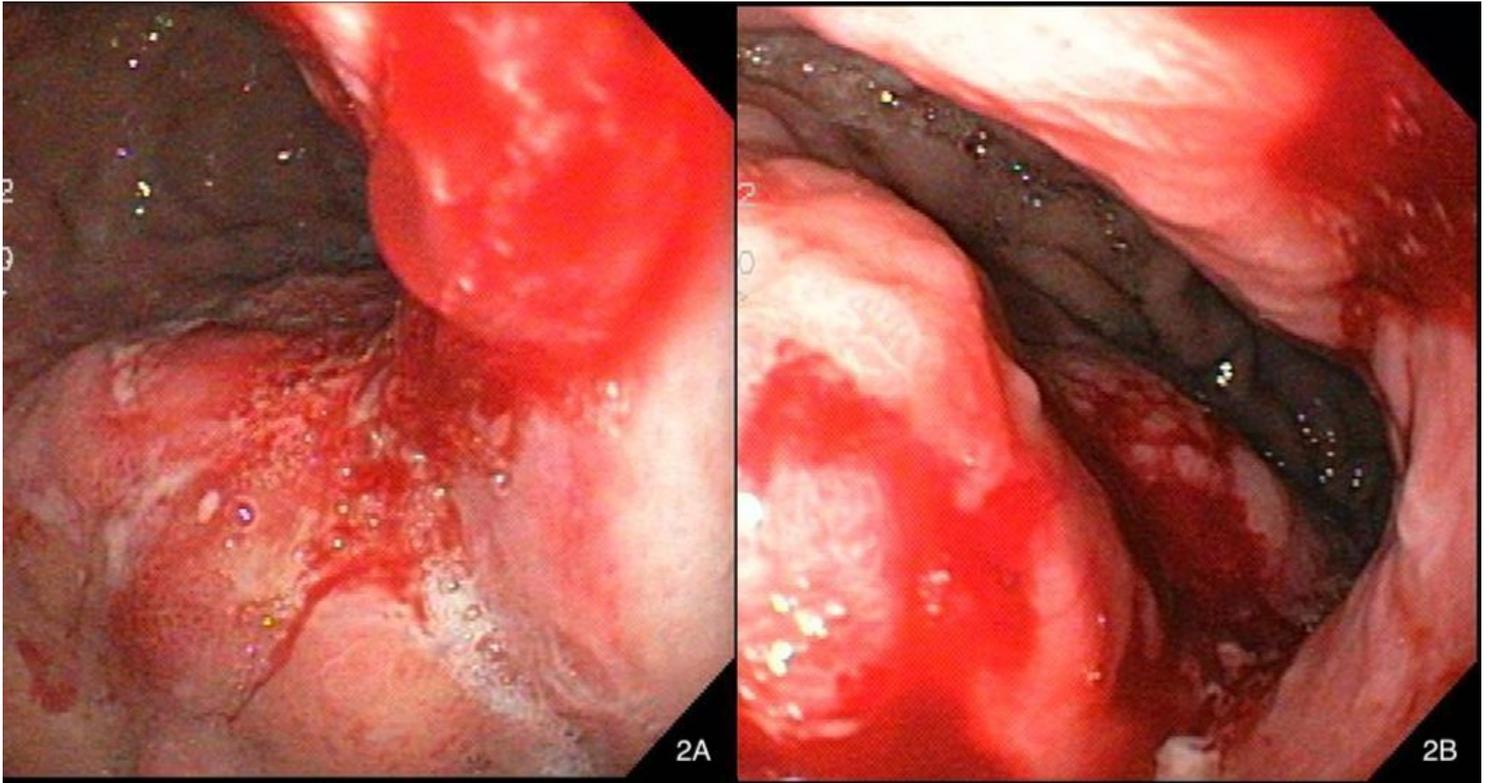
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## Figures



**Figure 1**

(1A) Hematoxylin and eosin stain of the uterine cervix showing aggregates of metastatic tumour cells within the lymphovascular spaces of the cervix. Cells display syncytial cytoplasm and round to ovoid indistinct nucleoli. (1B) Immunohistochemistry showing positive for CK7. (1C) Immunohistochemistry showing positive CDX2 staining



**Figure 2**

(2A) Endoscopic view of the stomach showing an atypical fundus with thickened, irregular folds and a diffuse gastric lesion. (2B) Endoscopic view of the gastric body/lesser curvature demonstrating a friable diffuse gastric lesion with contact bleeding.