

CASE REPORT

Metastasis of extra-ampullary duodenal adenocarcinoma to the uterine cervix

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Abstract

Secondary metastatic tumours of the uterine cervix are rare. There have been no reports of duodenal cancer metastasizing to the uterine cervix. Here we present a rare case of an extra-ampullary duodenal adenocarcinoma that has metastasized to the uterine cervix. The patient was a 71-year-old woman who had surgery for an extra-ampullary duodenal adenocarcinoma five years previously. Follow-up examination revealed a suspicious right ovarian mass and nodules in the cervix and posterior fornix of the vagina. Biopsies suggested squamous cell carcinoma in the cervix and adenocarcinoma in the fornix. Intraoperatively, the right ovary was enlarged and peritoneal disseminations were found in the pouch of Douglas and the sigmoid colon mesentery. Histopathology of the subsequent hysterectomy and bilateral salpingo-oophorectomy specimen revealed a cervical squamous cell carcinoma categorized as pT1b1. Adenocarcinoma infiltration into the ovaries, uterine cervix and vagina, with vascular involvement was detected. Immunohistochemistry revealed the tumour in the cervix and ovaries to be positive for CK7, MUC5AC and MUC6, and immunonegative for CK20, CDX2, Pax8, ER, MUC2 and CD10, similar to the original duodenal adenocarcinoma. This case illustrates the difficulty in making a preoperative diagnosis of metastatic adenocarcinoma in the uterine cervix with a coexisting primary cervical squamous cell carcinoma. The absence of atypia in cervical glandular cells and immunohistochemical profiling of the adenocarcinoma clusters helped to reach a final diagnosis. This is the first report of an extra-ampullary duodenal adenocarcinoma metastasis to the uterine cervix.

Keywords: Extra-ampullary duodenal adenocarcinoma, metastatic tumour, uterine cervix

INTRODUCTION

Because of the size of uterine cervix, its relatively limited blood flow, distal circulation and abundant fibrous tissue content, occurrence of secondary metastatic tumours are rare.^{1,2} Adenocarcinomas of the breast, stomach, and colon are known to be the common metastases to the cervix.^{3,4} To the best of our knowledge, there have been no reports of duodenal cancer metastasizing to the uterine cervix. Here, we report a patient with extra-ampullary duodenal adenocarcinoma, which has metastasized to the uterine cervix. It was difficult to preoperatively diagnose whether the adenocarcinoma in the uterine cervix was a primary or metastatic tumour as a primary cervical squamous cell carcinoma was incidentally coexistent.

CASE REPORT

A 71-year-old woman had a history of surgery for an extra-ampullary duodenal adenocarcinoma in the second to third portion of her duodenum five years prior to this presentation. Histopathological examination revealed a well-differentiated adenocarcinoma proliferating in the duodenal mucosa, which displayed tubular and papillary configurations and invaded to the right renal capsule (Figure 1).

The patient had not experienced any recurrence, but four and half years after the operation, a follow-up examination using whole body computed tomography showed a right ovarian mass suspected to be a malignancy. Subsequent gynaecological examination detected

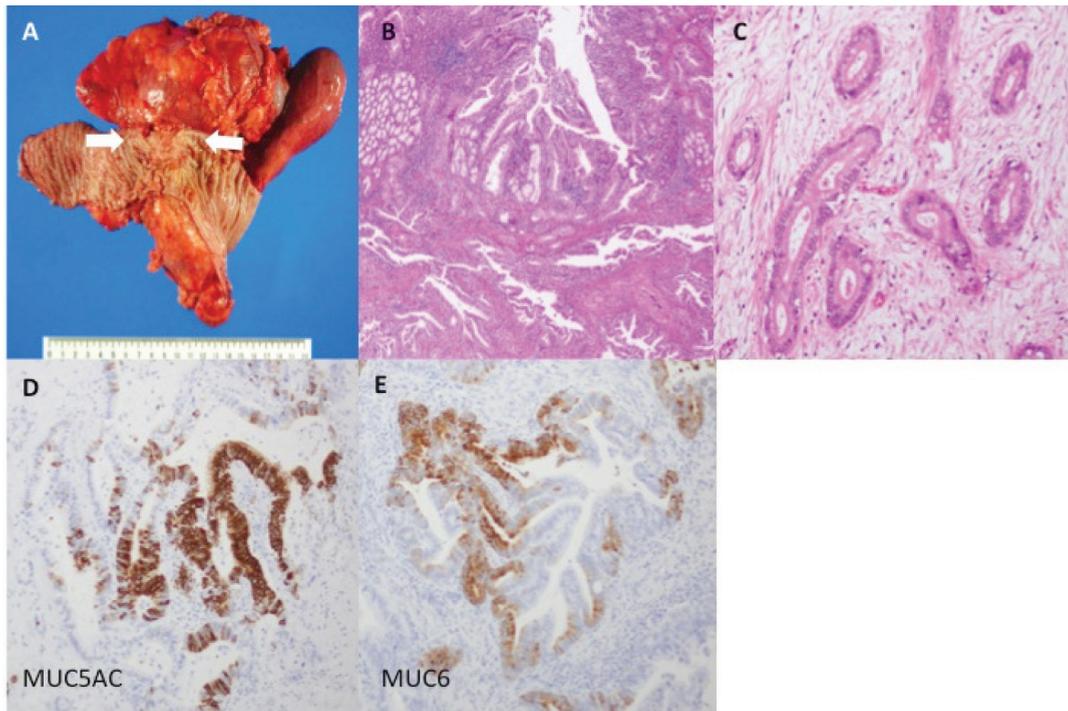


FIG. 1: Extra-ampullary duodenal adenocarcinoma: (A) Pancreaticoduodenectomy specimen (white arrows indicate ulcerated tumour). (B) Well-differentiated adenocarcinoma proliferating in the duodenal mucosa and infiltrating into submucosa and deeper layers (HE, $\times 40$). (C) Adenocarcinoma cells invading into right renal capsule (HE, $\times 400$). (D-E) Immunohistochemical images showing positive staining for MUC5AC and MUC6 ($\times 100$).

two lesional nodules. The first nodule was in the uterine cervix and the second was in the posterior fornix of the vagina. Biopsies were performed and histopathological analysis suggested squamous cell carcinoma in the uterine cervix, and adenocarcinoma in the posterior fornix of the vagina. Immunohistochemical analyses of the adenocarcinoma showed positive staining for CK7, and immunonegativity for CK20 and CDX2.

Although we did not observe any atypia in cervical glandular cells during histopathological examination of the cervical biopsy, we suspected the adenocarcinoma originated from the cervix and regarded the ovarian tumour as a metastasis from the cervical or duodenal primary tumours. As primary cervical squamous cell carcinoma often coexists with cervical adenocarcinoma and with the observation of CK7 positive and CK20 negative immunohistochemical characteristics, this led to the initial suspicion that the adenocarcinoma was a metastasis from the primary cervical carcinoma, and not from the gastrointestinal tract. The patient was treated surgically by hysterectomy and bilateral salpingo-oophorectomy.

Operative findings

On macroscopical examination, the right ovary was enlarged 7 cm in diameter. Peritoneal disseminations were found in the pouch of Douglas and the mesentery of the sigmoid colon. The peritoneal dissemination in the pouch of Douglas was dissected along with the uterus because the dissemination had infiltrated the uterine cervix and the vagina.

Pathology

The pathological findings are illustrated in Figure 2. Histopathological examination of the resection specimen revealed a cervical squamous cell carcinoma categorized as pT1b1 (Figure 2C). Adenocarcinoma infiltration into the uterine cervix and vagina, along with vascular involvement by adenocarcinoma was also observed. The adenocarcinoma infiltrated a wider area in the uterine cervix than the exposed dissemination, leading to the suspicion that the adenocarcinoma did not infiltrate from the dissemination but spread from the infiltrate to the extraserous membrane. These adenocarcinoma clusters showed irregularly shaped and branched

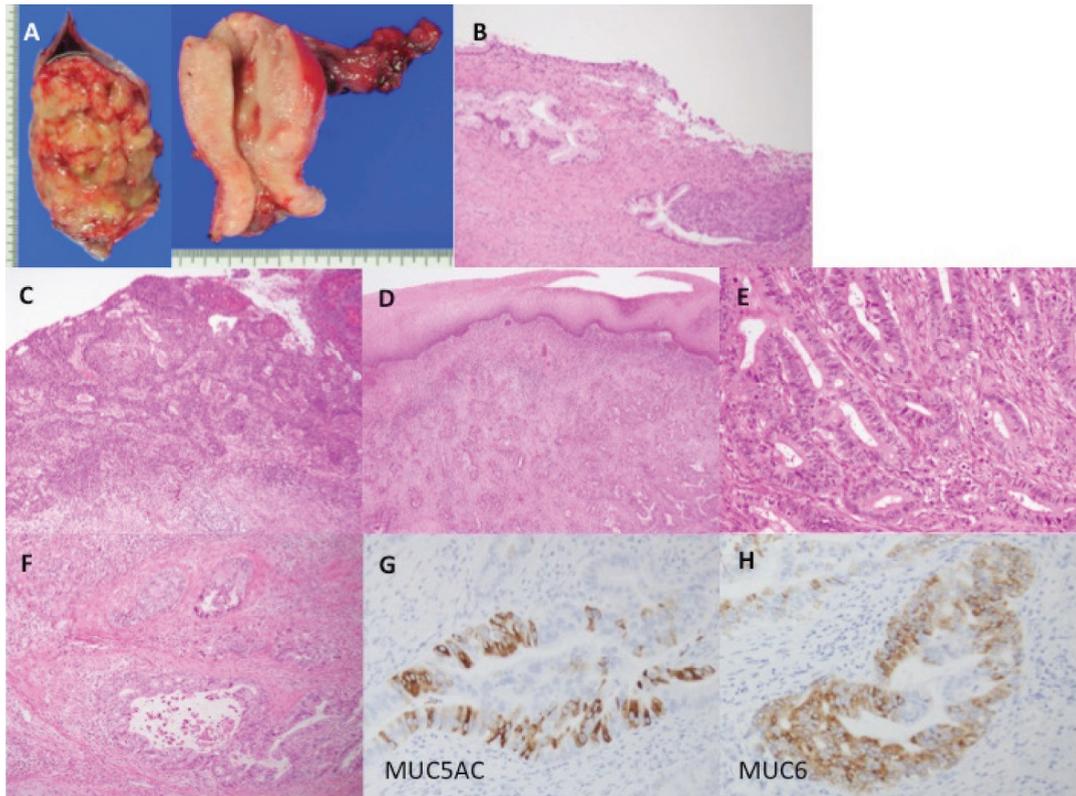


FIG. 2: Metastases to the uterine cervix and the ovary: (A) Right ovary and uterus specimens. Note that deformity of the uterine cervix is not observed. (B) No glandular lesions are observed at the squamocolumnar junction (HE, $\times 100$). (C) Invasive squamous cell carcinoma in the uterine cervix (HE, $\times 40$). (D) Adenocarcinoma in the uterine cervix mainly proliferating under non-tumorous squamous epithelium (HE, $\times 100$). (E) Adenocarcinoma in the uterine cervix closely resembles the primary extra-ampullary duodenal adenocarcinoma (shown in Figure 1C), in a high-power field ($\times 400$). (F) Vascular involvement ($\times 100$). (G-H) Immunohistochemical images show positive staining for MUC5AC and MUC6 ($\times 400$).

tubular glands that were lined by neoplastic cells with rounded nuclei and open chromatin.

Bilateral ovarian lesions were found to be adenocarcinoma with similar histopathology. Morphological features of these adenocarcinoma clusters showed a close resemblance to the primary extra-ampullary duodenal adenocarcinoma (Figure 1C, Figure 2E). Immunohistochemical stains for CK7, CK20, CDX2, Pax8, and ER exhibited similar staining patterns in these adenocarcinomas (Table 1).

Therefore, a diagnosis was made of recurrent duodenal adenocarcinoma that had metastasized to the uterine cervix and both ovaries based on the clinical course and similarities in cellular morphology and immunohistochemical phenotype of these adenocarcinomas. The patient will undergo chemotherapy for metastatic duodenal adenocarcinoma.

DISCUSSION

This is the first report describing a uterine

TABLE 1: Immunohistochemical profile of the tumours

Tumour site	CK7	CK20	CDX2	Pax8	ER	MUC5AC	MUC6	MUC2	CD10
Duodenum	+	-	-	-	-	+	+	-	-
Cervix	+	-	-	-	-	+	+	-	-
Ovary	+	-	+/-	+/-	-	+	+	-	-

metastasis from a duodenal cancer. Although the liver has been reported to be the most common metastatic site for duodenal cancer, the mechanism of distant metastasis remains unclear because of its rarity.^{5,6} In this patient, based on the clinical course of disease progression and comparison of histopathological findings, adenocarcinomas in the uterine cervix and ovaries were diagnosed as metastases from the previously treated extra-ampullary duodenal adenocarcinoma. These metastases might have been formed by peritoneal dissemination and haematogenous spread.

Recently, extra-ampullary duodenal adenocarcinoma has been reported to be classified into four subtypes: intestinal, gastric, pancreaticobiliary, and indeterminate types. It was suggested that compared with the intestinal type, gastric type adenocarcinomas appeared to be associated with poorer prognosis.⁷ The present case was considered to be a gastric type with the exhibition of typical cytological features, positive staining for gastric markers MUC5AC and MUC6, and negative staining for the intestinal markers MUC2 and CD10 (Table 1). The unusual metastasis to the uterine cervix observed in the present case might be associated with aggressive behavior of “poor prognostic” gastric type extra-ampullary duodenal adenocarcinoma.

It is important for clinicians and pathologists to pay attention to the possibility of metastatic adenocarcinoma to the cervix even if primary cervical squamous cell carcinoma is detected concurrently, especially when the patient has had a history of other malignancies. The malignancies most likely to metastasize to the uterine cervix or corpus originate from the breast, the stomach, and the colon.^{3,4} As previously reported, it is difficult to distinguish colon cancer metastasis to the uterine cervix from primary cervical adenocarcinoma.^{3,8} However, several factors to aid in differential diagnosis have been suggested. Absence of atypia in cervical glandular cells, and intact squamo-columnar junctions are important histological findings that suggest metastatic adenocarcinoma. In addition, a tumour mass located in the cervical stroma with lack of deformity of the cervix also supports a diagnosis of metastatic adenocarcinoma. Furthermore, comparison of the morphological features and immunohistochemical phenotype of tumours can aid in solving this sometimes difficult differential diagnosis. In the present case, cervical squamous cell carcinoma was also observed, however careful observation of the features described

above lead to the correct final diagnosis.

In conclusion, primary extra-ampullary duodenal adenocarcinoma can metastasize to uterine cervix. Further reports are needed to confirm the significance of this unusual metastasis and any association between cervical metastasis and specific subtypes of extra-ampullary duodenal adenocarcinoma. An important clinical issue reported in this case is that the possibility of metastatic adenocarcinoma should be considered, even in the presence of coincidental primary cervical squamous cell carcinoma.

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