A Case of Metastatic Squamous Cell Carcinomas from the Endocervix to the Stomach without Local Recurrence

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Extra-pelvic spread of squamous cell carcinoma (SCC) of the cervix to the stomach is extremely rare. We report a case of a 50-year-old woman who presented with dysphagia two years after diagnosis of SCC of the cervix. At esophagogastroduodenoscopy, there was a 1.5×1.2 cm sized ulcero-fungating mass at the cardia portion just beneath the esophagogastric junction which was biopsied for a suspected neoplastic lesion. Histologic and immunohistochemical examinations showed a SCC with characteristics identical to her original tumor from the cervix confirming gastric metastasis. Therefore, we report a case of endocervical SCC with metastatic lesions in the stomach 2 years after the initial diagnosis.

Key Words: Carcinoma, Squamous cell; Uterine cervical neoplasms; Neoplasms metastasis

INTRODUCTION

Cervical cancer is the second most common type of cancer in women worldwide, after breast cancer. Widespread use of the Papanicolaou (PAP) smear has dramatically reduced the incidence of cervical cancer, especially in developed countries. Even though patients now survive longer due to radiation therapy and more effective chemotherapy, cervical cancer is also one of the most frequent causes of death in women. In spite of these advances in the methods of treatment, approximately 30% of women with invasive cervical carcinoma die as a result of recurrent or persistent disease. Typical manifestations of recurrent cervical carcinoma involve the pelvis and lymph nodes around the pelvis or retro-peritoneum, but atypically recurrent cervical cancer may involve the solid organs of the abdomen as well as the peritoneum, mesentry, and omentum (implants); gastrointestinal tract (obstruction, fistula formation, ischemia); chest (metastases to the lung parenchyma, pleura, and pericardium); bones (destructive lesions); and other sites. Of these atypical metastasis, abdominal metastasis occurred in the peritoneal cavity and solid organs such as the liver and adrenal gland. The involvement of another abdominal solid organ such as the spleen, pancreas or gastrointestinal tract is very rare and in almost all cases, widespread metastasis involving other organ also occurs. Hence, we report a case of a 50-year-old women who underwent concurrent chemoradiation therapy (CCRT) due to cervical cancer and then suffered from multiple recurrence including stomach.

CASE REPORT

Patient was a 50-year-old woman who was diagnosed with cervical cancer at May 2008. At that time, the radiologic result showed cervical cancer, Federation of Gynecology and Obstetrics stage IIB with regional lymphadenopathy and the histological type was a SCC with focal stromal invasion. The patient underwent 6 cycles of CCRT of cisplatin-based chemotherapy and radiation therapy from May 2008 to July 2008. During the follow-up the day after performing CCRT, abdomino-pelvic CT and PET CT was conducted and there was complete response state till June 2009. After then, the patient was
lost to follow up in outpatient clinic.

The patient visited the gastroenterology outpatient department in October 2011 due to complaining dysphagia and abdominal pain for 1 month. On physical examination, she was found to have a distended abdomen with mild tenderness on the right upper quadrant and epigastric area. She did not experience vaginal bleeding, loss of weight or menstrual irregularity in the previous 6 months. On the PAP smear, there was no intra-epithelial lesion or malignancy. Abdomino-pelvic CT showed newly developed, variable sized nodules of liver and multiple lymph-node metastases (Fig. 1). Serum SCC antigen (SCC Ag) level was 126.0 ng/mL and serum CA 125 was 138.9 U/mL. For evaluation the cause of dysphagia, the patient was taken the esophagogastroduodenoscopy (EGD).

On EGD image, there was 1.5×1.2 cm-sized ulcer-fungating mass at cardia portion closely under the esophagus-gastric junction (Fig. 2). Biopsy was taken from the mass at 5 times and specimens were sent to the pathologic department. On histopathological examinations, they showed the presence of highly reminiscent of malignant SCC (Fig. 3A). In this context, additional immunohistochemical analysis showed the regional cells to be strongly positive with staining to antibodies of p16 (Fig. 3B). In order to confirm the metastatic nature of these cells, the previous histological slides of the cervix biopsies (Fig. 4) were reviewed, which was confirmed their histomorphological similarity to the neoplastic cells in the current stomach sample. Based on results of these imaging studies, laboratory results and histopathologic findings, the patient was diagnosed as multiple metastases including stomach from cervical cancer without local recurrence. The patient received 6 cycles of chemotherapy with paclitaxel and cisplatin every 3 weeks from November, 2011. She received their treatment on scheduled. At the end of the chemotherapy courses, there was
Fig. 3. Stomach biopsy. (A) Photomicrograph of haematoxylin and eosin stained slide at lower power (H&E, ×100) shows the presence of cohesive sheets of malignant squamous cells (*) adjacent to normal gastric mucosa (#). (B) Photograph of staining with P16 shows diffuse cytoplasmic and nuclear staining of the lesional cells (*) with no staining in the adjacent gastric mucosa (#) (P16 stain, ×100).

Fig. 4. Cervical biopsy at first diagnosis. Photomicrograph of haematoxylin and eosin stained slide at low power (H&E, A; ×100) and high power (H&E, B; ×200) shows the presence of cohesive sheets of malignant squamous cells (*) similar to the cells seen in Fig. 3A (*).

no reduction in size of hepatic metastasis, but more than 50 percent reduction in size of the prior ulcero-fungating mass on EGD (Fig. 5). We performed biopsies to the prior mass lesion again and there was no evidence of malignancy based on the results of biopsy. Serum SCC Ag level was decreased up to 49.8 ng/mL and serum CA 125 was decreased up to 45.3 U/mL.

**DISCUSSION**

SCC of the cervix is the second most common gynecologic malignancy. In the cervix, SCC accounts for 80~85% of all cases, with 15~20% being adenocarcinomas. This common neoplasm may occur at any stage of life; however, it is most commonly diagnosed in the fifth decade, with nearly half of the cases being diagnosed before the age of 35. The decreasing age of occurrence is attributed to the accepted social norms of earlier onset of sexual activity and complemented with earlier detection by active screening programs. In North America, as a result of the implementation of active screening programs, approximately 60% of cases are identified at stage I, with 25%, 10% and 5% detected in stages II, III and IV respectively.
The earliest and most common metastases are by direct extension to the contiguous structures including the vagina, peritoneum, urinary bladder, ureters, rectum and paracervical tissue, however, distant metastatic spread with unusual patterns such as pulmonary lymphangitic carcinomatosis have also been reported. Up to 50% of stage IV patients can present with distant metastases. Common sites of such occurrences are the liver, lungs, and bone marrow. The gastrointestinal tract is involved in approximately 8% of patients with carcinoma of the cervix: these being commonly found in the rectosigmoid as a result of local extension. Gastric lesions are identified in less than 2% of patients with carcinoma of the cervix, and are usually asymptomatic. Such spread is believed to occur commonly through the lymphatics, usually the para-aortic or mesenteric nodes to the gastric serosa and less often via the blood stream or by peritoneal seedlings.

On the other hand, the most prevalent primary sites of metastasis to the stomach are the lung, breast, skin (melanoma), and esophagus. Lung and breast neoplasia were the most common primary sites of gastric metastases in several series, and these findings reflect the high incidence of these tumors among the general population. Corroborating the data from other authors, the clinical symptom most frequently requiring an EGD was upper gastrointestinal bleeding. Within the sub-group of patients with cancer of the esophagus, the symptoms justifying EGD were dysphagia and chest pain. Unfortunately, the diagnosis of metastasis in the symptomatic phase signifies a late diagnosis, at a stage which renders any treatment procedure ineffective. The macroscopic features observed by EGD vary considerably and are, therefore, not specific of metastatic disease. Oda et al. in a large series, list eight different endoscopic manifestations. The case we have described showed a predominance of ulcerofungating lesions, resembling advanced gastric carcinoma.

Single-agent cisplatin remains the current standard therapy for advanced, persistent or recurrent cervical cancer. Recently, topotecan or paclitaxel in combination with cisplatin, have yielded superior response rates and progression-free survival without diminishing patient quality of life.

In conclusion, Stomach metastasis from SCC of the cervix is an extremely uncommon 'malignant'. Yet, accurate recognition of such unusual patterns of metastases in cervical cancer by histopathology is vital for best practice therapeutic decisions in these patients.

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