A Case of Metastatic Lymph Node of Invasive Cervical Cancer Diagnosed by Endoscopic Ultrasonography-Guided Fine Needle Aspiration Biopsy

Cervical cancer is the seventh most common cancer in Korean women according to national cancer statistics in 2009. Human papillomavirus (HPV) infection is reported as the most important risk factor in development of cervical neoplasms such as cervical cancer or cervical intraepithelial neoplasm. Because cervical cancer is one of the most common preventable cancers by vaccination of HPV and health screening, its incidence and mortality has been declining in developed countries, specifically in the United States, but it is still one of the most common cancers in women worldwide, especially in developing countries.

Prognoses of cervical cancer are based on the stage, size, histologic grade of a primary tumor and metastasis of lymph node. Most of metastasis begins in the surround lymph node, and common distant metastatic sites of cervical cancer are lung, gastrointestinal tract, bone, and liver. Distant metastases can be rarely developed in skin and central nervous system. CT and MRI are useful in staging advanced disease and in monitoring patients for recurrence of the disease. Recently, 18F-fluoro-2-deoxyglucose (FDG) PET is widely utilized and effective for detecting early recurrence of cervical cancer. It can be also a useful follow-up modality.

In general, pattern of lymph node metastasis is spread through regional lymph nodes to distant lymph nodes. Thus, EUS or EUS-guided fine needle biopsy (EUS-FNAB) are less used for detecting lymph node metastasis as a form of sub-
epithelial tumor of stomach in invasive cervical cancer. Herein, we report that a case of a 62-year-old female, who had a hypermetabolic lymph node in serial $^{18}$F-FDG PET, was definitely diagnosed as metastatic lymph node through EUS-FNAB of the lesion.

**CASE REPORT**

A 62-year-old female was referred to the department of gastroenterology for evaluation of a mass around cardia of stomach with high uptake of $^{18}$F-FDG in PET-CT. Four years ago, the patient underwent a total abdominal hysterectomy including bilateral salphingo-oophorectomy against invasive cervical cancer. According to pathologic report, the tumor was invasive squamous cell carcinoma, and nonkeratinizing type. The postoperative final stage was International Federation of Gynecology and Obstetrics (FIGO) stage IIA1, and TNM stage T2a1N0M0. Other postoperative modalities of treatment, such as radiation therapy or chemotherapy, were not applied. The patient had received treatment by anti-hypertensive drug against essential hypertension. After gynecology operation, $^{18}$F-FDG PET was conducted annually for evaluation of recurrence and metastasis. After four years, the $^{18}$F-FDG PET scan showed high uptake of $^{18}$F-FDG at ascending colon, and a mass-like lesion near the gastrohepatic area (Fig. 1). A subsequent enhanced abdominal CT revealed segmental wall thickening of hepatic flexure, pericolic fat infiltration, multiple lymphadenopathies along the gastric antrum, and a 2.5 cm-sized non-enhanced mass in the gastroesophageal junction.

The patient complained of no clinical symptoms and sign. Also, there was no abnormal finding in her physical examination. The initial vital sign was stable. Other chemical panels except tumor markers were unremarkable. Tumor makers were elevated to CA19-9: 46.48 U/mL (reference range < 37 U/mL), CEA: 32.49 ng/mL (reference range < 5.0 ng/mL), and CA-125: 122.3 U/mL (reference range < 35 U/mL), respectively. First, on the suspicious lesions at large bowel, colonoscopy was conducted. The colonoscopic findings showed several diverticuli without inflammation at ascending colon, and about 0.3 cm-sized single polyp at sigmoid colon. The pathologic result of polyp at sigmoid colon was revealed as tubular adenoma.

On a lesion in the gastrohepatic area, esophagogastroduo-

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**Fig. 1.** $^{18}$F-FDG PET (Jan. 2010) revealed hypermetabolic lesion at ascending colon, and a subepithelial tumor near the gastrohepatic area.

**Fig. 2.** Radial and linear endoscopic ultrasound images showed a hypoechoic, demarcated, and round-shaped mass.
denoscopy was conducted initially. Endoscopic findings showed about 3 cm-sized bulging mucosa such as a subepithelial tumor at cardia of stomach. Thereafter, EUS was taken, and EUS findings revealed a 3.1 × 2.0 cm-sized hypoechoic, demarcated, and round-shaped mass at cardia (Fig. 2). The extramural lesion was assumed to an enlarged lymph node or simple cyst. EUS-FNAB was performed for diagnosis of the subepithelial lesion. Turbid, yellowish discharge was aspirated by EUS-FNAB. The aspirated fluid seemed to be like pus forming an abscess (Fig. 3). The histopathologic result of aspirated specimen was confirmed as metastatic squamous cell carcinoma originated from the previous invasive cervical cancer (Fig. 4).

Systemic chemotherapy as a therapeutic strategy for the metastatic lesion was performed. Paclitaxel and carboplatin were administered intravenously after definite diagnosis and total six cycles of systemic chemotherapy were conducted. The patient completely cured by means of the systemic chemotherapy. Without recurrence of disease, the patient has been examined at the outpatient clinic regularly. The last 18F-FDG PET (Dec. 2011) also showed a complete remission of the metastatic lesion.

**DISCUSSION**

Cervical cancer is the most common malignant gynecological cancer, and lymphatic metastasis is one of the most important metastasis routes of this cancer. Lymphatic spread goes along external and internal iliac nodal chains and the presacral route to the paraaortic nodes. Distant metastasis without locoregional lymph node metastasis is rare. Probability of metastatic nodes in patients with stage IIB or less is 18.6%, and those of patients with higher stage is 44.3%. Despite of carefully planned and executed treatments, about 30% of cervical cancer is known to eventually recur after treatment. In our case, the patient was in FIGO stage II A1 on initial cervical cancer diagnosis. After five years of initial diagnosis and surgical treatment, lymph node metastasis around cardia of stomach was detected without locoregional lymph node metastasis. In general, CT, MRI, and 18F-FDG PET have been utilized as modalities for detecting metastatic lymph nodes. The accuracy of CT is between 65% and 80% for detection of metastatic involvement, and biopsy of suspicious nodes is necessary for confirmation. 18F-FDG PET is a useful imaging modality for detection of recurrent cervical cancer, and its overall sensitivity is 86% and its specificity is 87%.

The metastasis of cervical cancer has been rarely evaluated by EUS or EUS-FNAB, because there is seldom a case that metastatic lymph node is developed as a form of subepithelial tumor of stomach. This case is very significant in the aspect that EUS-FNAB might be a useful technique for assessing distant metastatic lymph nodes in invasive cervical cancer. EUS is one of the most accurate diagnostic tools for gastrointestinal malignancies and other malignancies with lymph node metastasis. Endosonographic features of malignant lymph nodes were reported as enlarged nodal size, hypoechoic echo-
nicity, and sharply-demarcated borders. Catalano et al. reported that four specific criteria thought to be most important in determining metastatic disease. These criteria were (1) hypoechoic structure, (2) sharply demarcated border, (3) round contour, and (4) larger than 10 mm in size. In our case, these four criteria were all met as a result of examining the endosonographic views. When all four criteria were met, this could predict a malignant lymph node with 100% accuracy. A recent study has demonstrated an accuracy of 80% when all criteria are met. Other criteria that define benign or malignant lymphadenopathy would be helpful in case of multiple lymph nodes. Sawhney et al. put forth opinion that intact vasculature through a lymph node should present benign nature. Some study also reported that presence of intranodal vasculature was universally associated with a benign diagnosis. In this case, the vasculature of lymph node was not assessed.

However, EUS findings related to malignant lymph node might cause a misdiagnosis in spite of its high accuracy functionally. Consequently, definitive diagnosis requires pathologic examination. For this reason, EUS-FNAB has been introduced as an alternative technique. EUS-FNAB is mostly utilized to evaluate pancreatic lesions and lymphadenopathy, but some reports have specifically investigated the use of EUS-FNAB for examination of intramural and extramural structures of the gastrointestinal tract. Vander Noot et al. reported that the sensitivity and specificity of EUS-FNAB became 96% and 81%, respectively, and the diagnostic accuracy was improved up to 92%, when obscure diagnosis due to specimens with suspicious but indefinite cytolologic results were classified as malignancy. If specimen adequacy and additional data for ancillary studies, such as flow cytometric and immuno-cytochemical analyses, can be obtained, the results of EUS-FNAB will be improved.

Saftoiu et al. reported a case in which a cystic tumor mass was differentiated from an abscess by EUS-FNAB. In their case, EUS finding revealed a hypoechoic, inhomogenous, and well-delineated mass. According to such criteria as mentioned above, a malignant lymph node was applicable, but the patient had a high fever and leukocytosis. To compensate for incomplete diagnosis, EUS-FNAB was conducted. Pus was extracted after EUS-FNAB and they finally diagnosed the retroperitoneal abscess after cytology and specimen culture. In our case, the aspirated specimen was similar to pus seemingly. However, the clinical condition of patient was not infectious, and serum WBC count was also normal. If the specimen was regarded as simple pus forming abscess, it might be discarded or misinterpreted as a benign lesion. Therefore, in case of a clinical clue, EUS-FNAB should be actively recommended for a definitive diagnosis and any morphologic specimen obtained by EUS-FNAB should be immediately sent to a pathologic laboratory, and be analyzed.

In conclusion, most of patterns in metastasis of malignancy are generally consistent, but some lymph node metastasis may be infrequently detected at unexpected sites. Further assessments including EUS or EUS-FNAB for a rare case of gastric subepithelial lesion with likelihood of malignancy will be needed. In addition, all the acquired specimens, irrespective of nature of specimens, should be assessed in a laboratory without any adjustments.

REFERENCES

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