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CASE REPORT

Occult Multiple Mediastinal Lymph Node Metastasis and Malignant Pleural Effusion Due to Signet Ring Cell Gastric Cancer

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Introduction

Mediastinal lymph node metastasis occasionally occurs in patients with advanced gastric cancer of the cardia with esophageal invasion, but is rarely encountered in patients with gastric cancer at other sites [1]. Here we report an extremely rare case of occult hilar and mediastinal lymph node metastasis and malignant pleural effusion after distal gastrectomy for antral signet ring cell gastric cancer.

Case

A 66-year-old-male underwent right lower lobectomy and mediastinal lymph node dissection for squamous cell lung cancer. Five years previously, he had undergone laparoscopic distal gastrectomy for antral gastric cancer (pT2N2, pStage 3A, moderately differentiated adenocarcinoma-poorly differentiated signet ring cell carcinoma). Preoperative fluorodeoxyglucose (FDG)-positron emission tomography (PET) demonstrated an uptake of FDG (maximum standardized uptake value 6.3) in the pulmonary tumor, but no other significant uptake was evident (Fig. 1). Chest computed tomography (CT) demonstrated no abnormal lymph node swelling (Fig. 2). The preoperative levels of tumor markers (carcinoembryonic antigen, CYFRA, pro-gastrin releasing peptide) were below the reference values. During lung cancer surgery, a small amount of serous pleural effusion was observed and collected. No pleural dissemination was evident, and hilar and mediastinal lymph nodes showed no macroscopic enlargement. Pathological examination showed that the lung tumor was poorly differentiated squamous cell carcinoma (Fig. 3a). The hilar and mediastinal lymph nodes were found to contain metastasis of signet ring cell cancer, and not squamous cell carcinoma (Fig. 3b), and pleural effusion cytology demonstrated adenocarcinoma cells (Fig. 3c). Signet ring cancer cells were found mainly in the lymphatic sinus of pulmonary lymph nodes. After surgery, the patient received chemotherapy for the signet ring cell gastric cancer, but multiple bone metastases were recognized in the third year after surgery and he died of gastric cancer 4 years after surgery. Mediastinal lymph node swelling was not evident by chest CT 3 years after the lung cancer surgery.

Comment

Among the various pathways of metastasis, the spread of lymphangitic tumor may reach the lungs and mediastinum via the vasculature, the paraaortic lymph nodes, and thoracic duct [1]. In the present case, malignant cells were detected in the lymph nodes located along the left gastric artery, the common hepatic artery, and the celiac artery at the previous gastric surgery. Considering the absence of hematogenous metastasis, malignant signet ring cells are thought to have reached the thoracic cavity via lymphatic flow from the paraaortic lymph nodes.

Although the incidence of gastric cancer is decreasing, the relative proportion of cases of signet ring cell gastric cancer has shown an increasing tendency [2–5]. In comparison with gastric adenocarcinoma, signet ring cell gastric cancer has a distinct presentation, tending to arise in younger patients and showing a female predominance [3–7]. It is reported that signet ring cell carcinoma shows a higher incidence of lymph node metastasis than other histological subtypes, and a tendency to be advanced at the time of discovery [2, 5, 6, 8]. Although the prognosis of early-stage signet ring cell gastric cancer is considered to be more favorable than that of other histologic subtypes, the outcome is often poor when the

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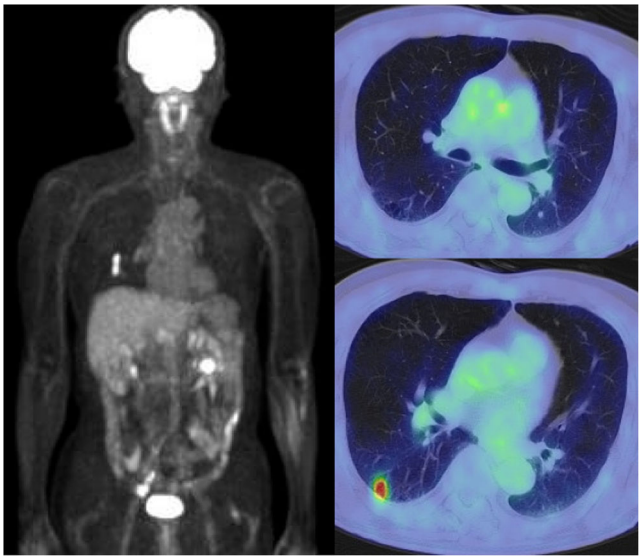

Fig. 1 Preoperative FDG-PET demonstrated an uptake of FDG in the pulmonary tumor, but no other significant uptake was evident. FDG uptake was not observed in the mediastinal and hilar lymph nodes

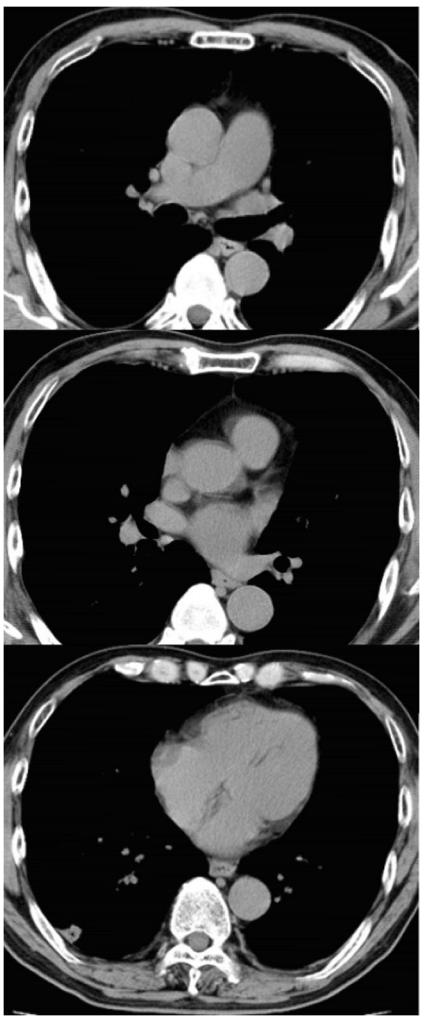

Fig. 2 Chest CT demonstrated no abnormal mediastinal and hilar lymph node swelling. Chest CT also demonstrated no pleural effusion

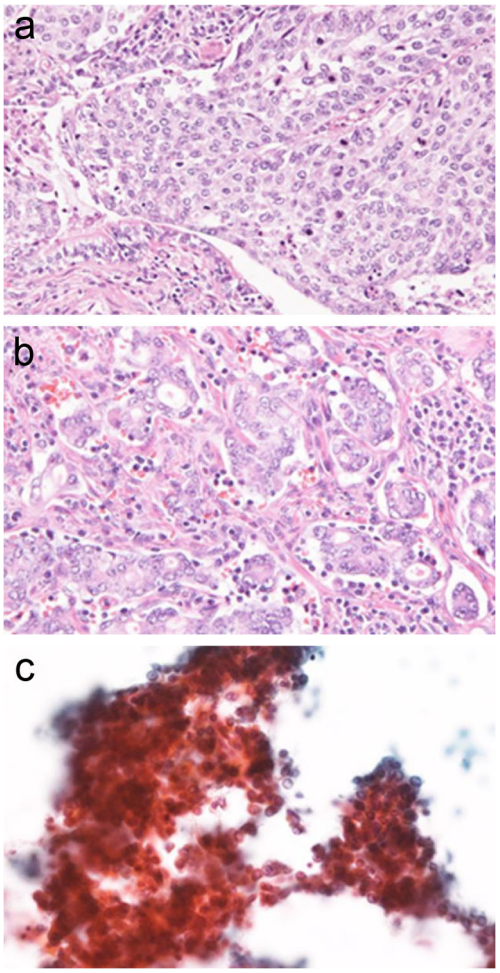

Fig. 3 Pathological examination showed that the lung tumor was poorly differentiated squamous cell carcinoma (**a**). The hilar and mediastinal lymph nodes were found to contain metastasis of signet ring cell cancer, and not squamous cell carcinoma (**b**). Pleural effusion cytology demonstrated adenocarcinoma cells (**c**)

cancer is advanced [3, 4, 7]. Thus, the survival outcome of signet ring gastric cancer appears to worsen progressively with stage advancement.

In the present case, tumor cells were found mainly in the lymphatic sinus of the mediastinal lymph nodes. Among cases of gastric cancer associated with chylothorax, it has been reported that 64% (9/14) were signet ring cell carcinomas [9]. Chylothorax is caused by obstruction of lymphatic flow, and signet ring cell carcinoma may be more likely to invade the lymphatic sinus of lymph nodes, causing stagnation of lymphatic flow. In the present case, because pleural dissemination was not observed, the pleural effusion may have been due to increasing lymphatic pressure resulting from metastasis into the lymphatic sinus, although the levels of triglyceride and cholesterol in the pleural effusion were not measured.

It has been reported that FDG-PET is a useful diagnostic modality for advanced metastatic or recurrent gastric cancer [1]. In this case, however, FDG-PET did not reveal any lymph

node metastasis. As it has been reported the PET is not effective for detection of signet ring cell carcinoma [1], careful examination for the presence of lymph node metastasis should be conducted, even if FDG uptake is not observed by PET.

Conclusion

We have experienced a case of signet ring cell gastric cancer associated with occult hilar/mediastinal lymph node metastasis and malignant pleural effusion. Preoperative thoracoabdominal CT and FDG-PET revealed no evidence of lymphatic spread or gastric cancer recurrence. This case was considered interesting as it represented an unusual form of gastric cancer progression.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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