**TTF-1 is useful for primary site determination in duodenal metastasis**

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We report here on a case of duodenal metastasis from primary lung adenocarcinoma. A 69-year old man was diagnosed with primary lung adenocarcinoma. Four courses of combined chemotherapy with carboplatin and paclitaxel associated with irradiation of 60 Gy shrunk the lung tumor. However, soon after, the para-aortic lymph node became swollen. Esophagogastroduodenoscopy revealed three duodenal tumors. Differential diagnosis between malignant lymphoma and metastatic duodenal cancer was endoscopically difficult. The histology of biopsied specimens was poorly differentiated adenocarcinoma. Immunohistochemical analysis revealed a positive reaction for thyroid transcription factor-1 (TTF-1). Thus, we concluded that these were metastatic duodenal tumors from lung adenocarcinoma. Two courses of gemcitabine led to a complete remission in this duodenal metastasis and para-aortic lymph node swelling with only scarring remaining in computed tomography. He is now on the continuous generalized chemotherapy. In conclusion, duodenal metastasis from primary lung adenocarcinoma is rare and hard to diagnose. In such an instance, TTF-1 immunostaining is crucial to obtain the correct diagnosis.

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**Key words:** Lung adenocarcinoma; Duodenal metastasis; Thyroid transcription factor-1

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The histopathological diagnosis of the biopsied specimens was poorly differentiated adenocarcinoma (Figure 3A). We thought metastasis from lung adenocarcinoma was less suspicious because the first-line therapy was very effective and the duodenal metastasis in lung adenocarcinoma was rare. To further characterize the nature of the tumor, we carried out immunostaining of TTF-1 and it was positive (Figure 3B). TTF-1 positivity is highly restricted to primary lung carcinoma and thyroid tumor[7,8]. Since CT revealed no thyroid tumor, we finally diagnosed this tumor as duodenal metastasis from primary lung adenocarcinoma. He received second-line generalized chemotherapy using gemcitabine. After 3 courses of gemcitabine, the para-aortic lymph node swelling and the thickening of the duodenal wall both disappeared in CT. The duodenal tumors disappeared and only scars remained in EGD (Figure 2D).

He is now receiving the additional courses of chemotherapy with gemcitabine.

DISCUSSION

Primary lung cancer often metastasizes to the brain, liver, adrenal glands and bone[1,2]. On the other hand, metastasis to the digestive tract is rare[2]. The site of metastasis to the digestive system is as follows: small intestine only (4.6%); large intestine only (2.9%); stomach only (1.6%); stomach and small intestine (0.6%); small and large intestine (0.6%); and stomach and large intestine (0.3%) [4]. Duodenal metastasis is very rare, even in autopsy[5].

Small bowel metastasis from primary lung cancer exhibits symptoms such as abdominal pain, vomiting, melena, weight loss, gastrointestinal perforation and obstruction, but most cases are asymptomatic[6].

Morphological features of duodenal metastasis are divided into four types: compression, protrusion, ulcer and stenosis[7]. Appearance of a metastatic lesion from extra-abdominal primary cancer is all protrusion type. All cases of duodenal metastasis from lung carcinoma were protrusion type[7]. This type of metastatic lesion is probably hematogenous. The gross appearance of our case was protrusion type, widely elevated, having a central ulcer and resembling a submucosal tumor. Among all duodenal metastasis, the second portion (descending portion) is most frequent (58.7%)[7].

It is important to differentiate between primary and metastatic duodenal adenocarcinoma to make an appropriate choice of therapy, although it is difficult on occasion. Recently, TTF-1 has become one of the best immunohistochemical markers to determine the lung or thyroid origin[2,3]. TTF-1 is tissue-specific for the thyroid gland and lung[2,3]. It is expressed in the type II alveolar cells and bronchial cells[8]. It is a transcription activator of the lung epithelial cell-specific surfactant protein B genes[9]. TTF-1 is expressed frequently in small cell carcinoma (85%-95%) and in adenocarcinoma (75%-80%) [9]. Sensitivity of TTF-1 for primary lung adenocarcinoma is 57.5 to 76% and the specificity is almost 100%[10]. Thus, TTF-1 is a very good marker to determine the lung origin in duodenal metastasis, as shown in our case.

The prognosis of lung cancer patients with metastasis...
to the digestive tract is poor\(^{12}\). Indication for emergency surgery is bleeding, perforation and obstruction\(^{12}\). There is a possible risk of gastrointestinal perforation due to chemotherapy\(^{13}\). In our case, duodenal tumors and lymph nodes shrank by systemic chemotherapy using gemcitabine without any serious adverse reaction.

In conclusion, duodenal metastasis from primary lung adenocarcinoma is rare and therefore difficult to diagnose. On such an occasion, TTF-1 can be a very useful immuno-histochemical marker to determine the lung origin.

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