

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

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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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Abstract

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

INTRODUCTION

Common metastatic sites of lung cancer are the brain, liver, adrenal glands and bone^[1]. Gastrointestinal metastasis is quite rare. On the other hand, thyroid transcription factor-1 (TTF-1) is a very useful immunohistochemical marker for determining thyroid cancer and lung cancer. We report on a case of duodenal metastasis, the primary site of which was determined correctly to be the lung by using TTF-1 immunostaining despite the total shrinkage of the primary lesion by chemotherapy.

CASE REPORT

A 69-year old man was admitted to our hospital for cough

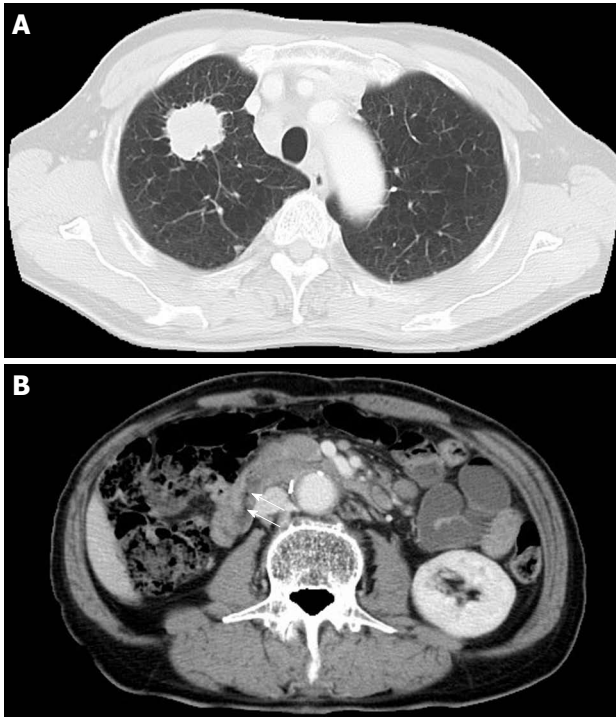


Figure 1 Chest computed tomography images of primary lung adenocarcinoma (A) and abdominal computed tomography images before gemcitabine (B). A: Chest computed tomography before chemotherapy revealed a tumor of 2.5 cm in diameter with spike-like projections; B: Walls of the duodenum become thickened at the second portion (arrows).

and hoarseness. His past history was a right nephrectomy for renal pelvic cancer in July, 2006. Pathological examination of this cancer revealed ureteral transitional cell carcinoma, G2, pT1, It-u0, ly0, v0. He was diagnosed as having right lung adenocarcinoma with lymph node metastasis (cT2N3M0, Stage IIIb) in our respiratory unit (Figure 1A). Histology was poorly differentiated adenocarcinoma. He received combined chemotherapy with carboplatin and paclitaxel associated with the focused irradiation of 60Gy. After four courses of chemotherapy, primary lesion and lymph node metastasis were totally shrunk but, in turn, the para-aortic lymph node swelling and thickening of the duodenal walls (Figure 1B) appeared in computed tomography. Tumor markers of primary lung cancer such as CEA, SLX and CYFRA were under the normal upper limit. He had no clinical symptoms, including melena and abdominal pain.

Esophagogastroduodenoscopy (EGD) was performed and three submucosal tumors were found located at the second portion of the duodenum. Endoscopic appearances varied among these 3 tumors. One showed a widely flat elevation with large central ulceration associated with a central tumorous protrusion (Figure 2A and B). Another one formed a tumorous protrusion with central ulceration (Figure 2C). The covering mucosa of the tumors looked normal with regular villi. Therefore, these lesions were thought to be non-epithelial tumors or tumors of submucosal origin. Based on these findings, malignant lymphoma or metastatic tumor to the duodenum was a possible diagnosis and primary duodenal carcinoma much less likely.

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^[2,3]. 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]. On the other hand, metastasis to the digestive tract is rare^[4]. The site of metastasis to the digestive system is as follows: small intestine only (4.6%); large intestine only (2.0%); 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 with central ulceration, so called 'bull's-eye'^[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^[1,2,8]. Recently, TTF-1 has become one of the best immunohistochemical markers to determine the lung or thyroid origin^[2,8,9]. 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^[10]. It is a transcription activator of the lung epithelial cell-specific surfactant protein B genes^[11]. TTF-1 is expressed frequently in small cell carcinoma (85%-90%) 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%^[8]. 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

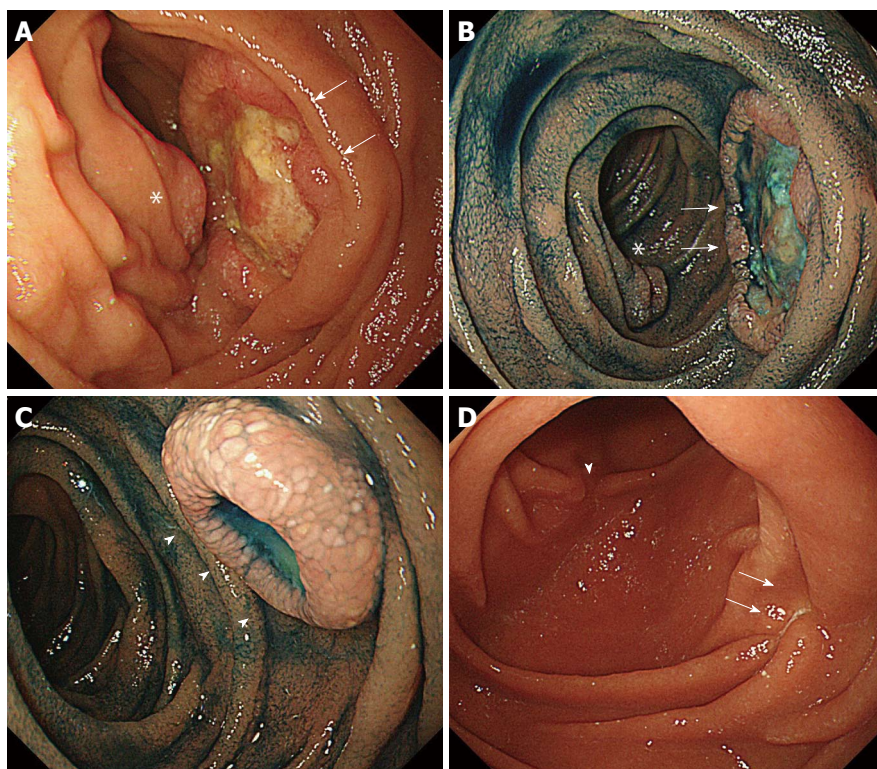


Figure 2 Esophagogastroduodenoscopy images of duodenal tumors. A: There are two tumors at the second portion of the duodenum. Largest one (arrow) shows broadly elevated ulceration with central protrusion. Another tumor is located at the opposite side of the largest one (asterisk); B: After indigo carmine dye, ulcer base reveals a non-structural mucosal pattern with white coats. The edge of the tumor appears to be covered by normal-looking mucosa. Another tumor is located at the opposite side of the largest one (asterisk); C: Smallest one (arrowhead) is located at the most anal side. All three tumors have common features of a so-called submucosal tumor; D: After three courses of gemcitabine, three tumors at the second portion of the duodenum disappeared and are only discernible as scars in esophagogastroduodenoscopy (EGD). The scar that is derived from largest one (arrows) and another derived from the tumor located at the opposite side of the largest one (arrowheads) are discernible. The scar that is derived from the smallest is hard to see in this view of EGD.

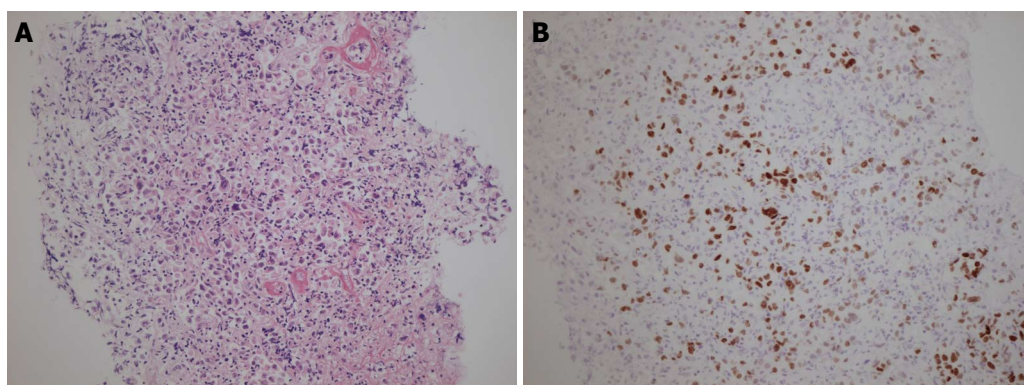


Figure 3 Histological findings of biopsied specimen. A: High degree of cellular atypia, elevated nucleus/cytoplasm ratio and anisonucleosis at hematoxylin and eosin stain all reveal the presence of poorly differentiated adenocarcinoma in a biopsied specimen, × 100. B: Tumor cells were positive for thyroid transcription factor-1. Avidin-biotin-peroxidase stain, × 100.

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 immunohistochemical marker to determine the lung origin.

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