Isolated sigmoid colon metastasis from lung micropapillary adenocarcinoma: a case report

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Abstract: Lung cancer is a common malignant neoplasm that is prone to distant metastasis. Gastrointestinal metastasis from lung cancer is rather rare no matter what stage. Herein, we presented a case of pulmonary adenocarcinoma six months after thoracoscopic Lobectomy isolated metastasis to sigmoid colon. Then the patient underwent radical resection of metastatic tumors of sigmoid colon. The pathologic morphology and immunohistochemistry of lung adenocarcinoma is highly consistent with the sigmoid colon tumor and their gene profiles are likely similar except for an AXIN1 mutation in primary tumor and not in the metastatic lesion.

Keywords: Micropapillary, lung cancer, sigmoid metastasis, genetic profiles

Introduction

Lung cancer is the leading cause of cancer related deaths worldwide. One half of the disease with prior diagnoses have distant metastasis. The most common metastasis sites include the lungs, liver, bone, brain, and adrenal glands [1]. Gastrointestinal (GI) metastasis from lung cancer is considered rare, although there is about 4.7%-14% prevalence at autopsy [2, 3]. Due to a lack of pathology and molecular detection, lung cancer with GI metastasis is reported to have a poor prognosis with a mean survival of only 4-8 weeks [4].

Herein, we describe a case of lung adenocarcinoma characterized by partial micropapillary component, parabronchial lymph node metastasis, and lymphovascular infiltration six months after lobectomy, presenting as isolated metastasis sigmoid colon lesion. The morphology and immunohistochemistry of the primary are highly consistent with the metastasis sigmoid colon tumor. The two tumors shared similar gene profiles of EGFR exon 19 deletion mutations, the frameshift mutation of ARID1A 8 exon, and the missense mutation of SMAD4 9 exon expect for AXIN1 mutation only in the primary tumor.

Case presentation

In December 2017, a 47 year old non-smoking, otherwise healthy female was admitted to our hospital due to a nodule on the left upper lung, found in her physical checkup. Chest contrast enhanced computed tomography (CT) revealed an irregularly mixed-ground-glass nodule with the whole lesion sized 3.5 × 3.1 cm and the solid portion sized 2.1 × 1.3 cm in diameter was observed on apicoposterior segment of the left upper lung. The lump presented with lobulated, vacuolar, and pleural traction signs. Slight to moderately enhancement of the solid portion and no mediastinal lymphadenopathy was also revealed (Figure 1A, 1B). Cranial contrast enhanced magnetic resonance, abdominal ultrasonography, and emission computed tomography of bone scan indicated no neoplasm dependent signs.

She was treated with thoracoscopic left upper lobectomy and mediastinal lymph node dissection. Postoperative pathology indicated invasive adenocarcinoma with 2.4 × 1.6 × 1.6 cm in diameter which was mainly composed of papillary type (Figure 1E), and the minor compositions of micropapillary type (Figure 1F) and aci-
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Lymphovascular invasion was positive, perineural invasion was negative, and the tumor was close to pleura. Lymphatic metastasis was found in 1 of the 2 parabronchial lymph nodes and none of the dissected group 7, 10, 11 lymph nodes. Immunohistochemistry showed that the carcinoma cells were positive for CK7, Napsin A, SP-A and TTF1 (strong positive), Carcinoembryonic antigen (CEA) (focally positive), and negative for CK20, CDX2. TNM was defined as T1cN1M0 and she was diagnosed with primary adenocarcinoma of the lung stage IIB (according to the eighth edition of TNM classification of pulmonary carcinoma). According to guidelines, the patient received 3 cycles of 500 mg/m² pemetrexed on day 1 and carboplatin AUC 5 on day 1 every 3 weeks. Subsequently, chemotherapy was aborted because of liver dysfunction and intolerance.

Chest and abdomen CT surveillance were performed 3 months after chemotherapy, indicated an isolated lesion of sigmoid. Colonoscopy revealed sigmoid colon focal ulcerative lesion with a diameter of approximate 1 cm (Figure 1D). Pathologic findings of biopsy showed a poorly differentiated adenocarcinoma with prominent composition of papillary type. Immunohistochemical staining was consistent with intestinal metastasis of lung cancer. Positron emission tomography computed tomography (PET-CT) examination revealed an abnormal fluorodeoxy glucose (FDG) metabolism nodule in the sigmoid wall with the maximum standardized uptake value (SUV) value of 8.9 (Figure 1C). The patient underwent radical resection of sigmoid tumors in May 2018. Postoperative lesion sampling was macroscopically characterized as a 0.7 × 0.7 cm local mucosa rough area no higher than the mucosal surface in sigmoid with no myometrium involvement, gray-yellow cut section, and medium texture. Microscopic pathological findings suggested poorly differentiated invasive adenocarcinoma cancer from mucosal layer to muscular layer whose pathological subtypes are similar to those of previous lung cancer (Figure 1G, 1H). Positive for lymphovascular invasion, negative for perineural invasion and four of nine peri-intestinal lymph nodes infiltrated by cancer cells were also observed. Immunohistochemistry showed that the carcinoma cells were positive for CK7, napsin A, SP-A and TTF1 (strong positive), carcinoembryonic antigen (CEA) (focally positive), and negative for CK20 and CDX2. Thus, the patient was diagnosed with sigmoid colon metastasis of lung adenocarcinoma.

Capture-based ultra-deep targeted NGS (Burning Rock, Guangzhou, China) was synchronously performed on lung primary tumor and sigmoid metastasis tumor tissue biopsy using a
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Panel consisting of 520 cancer-related genes, spanning 1.6 MB of human genome. Our data revealed the presence of EGFR exon 19 del in both specimens and the abundance of this mutation was 27.40% and 13.11%, respectively. The frameshift mutation (p.Met883) of AT-rich interactive domain 1A (ARID1A) 8 exon and the missense mutation (p.Asp351Val) of SMAD family member 4 (SMAD4) 9 exon were also found in both specimens, with the abundance of 6.75%, 9.45% and 17.46%, 7.18%, respectively. However, the AXIN1 missense mutation (p.Gln224His) was only detected in lung primary tumor. The tumor mutation burden (TMB) was 2.4/Mb in lung primary tumor and 1.6/Mb in sigmoid metastasis tumor.

Gastrointestinal metastasis from lung cancer is considered to be rare, although there is about 4.7%-14% prevalence at autopsy [2, 3]. Yoshimoto et al. identified 56 (11.9%) cases in 470 patients with gastrointestinal metastasis confirmed by autopsied [5]. Kim et al. reported the incidence of the intestinal metastasis from lung cancer is as low as 0.2-1.7% [6].

Immunohistochemistry is an effective method to differentiate primary or metastatic pulmonary adenocarcinoma. The immunohistochemical markers of TTF-1, CK-20, CK-7, and CDX-2 are vital to identify origin from lung or intestinal tumors [7]. In our case, the morphology and immunohistochemistry of lung tumor is highly consistent with the sigmoid colon tumor. All the immunohistochemical markers supported their origin from lung. Moreover, both of the tumors sharing similar gene profile proved the homology of the two neoplasms from lung.

Discussion

We present a rare case of isolated sigmoid metastasis from adenocarcinoma of the lung diagnosed six months after lobectomy. As far as we know, this is the first reported case comparing the primary adenocarcinoma with the isolated sigmoid metastasis tumors in the pathologic morphology, immunohistochemistry and genetic profile in detail.
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ERBB2 and AKT signaling pathways can ultimately promote lung cancer growth and metastasis in mouse model [12]. Mutations of AXIN gene have been detected in a few types of malignant tumors and these sporadic mutations hardly explain the reduced expression of AXIN which directly correlates with disease progression and poor prognosis [13]. As narrated above, the frame shift mutation of ARID1A 8 exon, the missense mutation of SMAD4 9 exon, and the AXIN1 missense mutation may also play a role in tumor metastasis.

In conclusion, lung carcinoma presenting with gastrointestinal metastasis is rather rare even at advanced stages. In our case, the morphology and immunohistochemistry of the primary were highly consistent with the metastatic tumor. The gene profiles are likely similar between the two except for AXIN1 mutation in the primary tumor which is not in the metastatic lesion. Components of micropapillary type, lymphovascular invasion, parabronchial lymph node metastasis, EGFR 19 del, ARID1A, SMAD4, and AXIN1 mutation may play a key role in tumor metastasis.

Disclosure of conflict of interest

None.

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