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Case Report

Primary pure signet-ring cell carcinoma of the extrapulmonary left main bronchus: a case report with an immunohistochemical study

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Abstract: Although several case reports and series of primary signet-ring cell adenocarcinoma (SRCA) of the lung have been reported, primary SRCA of the extrapulmonary main bronchus has not been reported. A 61-year-old man was found to have a tumor of the mediastinum of the left pulmonary hilus on routine chest X-ray examination. A transbronchial endoscopy revealed an elevated tumor in the extrapulmonary left bronchus near the tracheal bifurcation. Biopsy was taken from the bronchial lesion. It revealed pure typical SRCA. Histochemically, Alcian-blue/PAS stain showed intracytoplasmic mucins. Immunohistochemically, the tumor cells were positive for cytokeratin (CK) AE1/3, CK CAM5.2, CK7, CK18, CEA, EMA, CA19-9, Ki-67 (labeling=20%), p53, and MUC1. They were negative for CK34BE12, CK5/6, CK8, CK14, CK19, CK20, p63, vimentin, TTF-1, CDX-2, MUC2, MUC5AC and MUC6. The pathological diagnosis of primary SRCA of the left main bronchus was made. The patient died of carcinomatosis 18 months after the first presentation. In conclusion, the author reported the first case of primary SRCA of the extrapulmonary left main bronchus near the tracheal bifurcation with an extensive immunohistochemical study.

Keywords: Bronchus, signet ring cell adenocarcinoma, histopathology, immunohistochemistry

Introduction

Extragastric signet-ring cell adenocarcinoma (SRCA) is rare. Although severe case reports and series of primary SRCA of the lung have been reported [1-5], primary SRCA of the extrapulmonary main bronchus has not been reported, to the best of the author's knowledge. Herein reported is the first case of primary SRCA of the extrapulmonary left main bronchus near the tracheal bifurcation.

Case report

A 61-year-old man was found to have a tumor of the mediastinum of the left pulmonary hilus on routine chest X-ray examination. Blood laboratory test showed no significant changes, but serum CEA was increased (342 ng/ml). Imaging modalities including CT also demonstrated the mediastinal tumor. It involved the left bronchus and aorta. A transbronchial endoscopy revealed an elevated tumor in the extrapulmonary left bronchus near the tracheal bifurcation (**Figure 1**). Six biopsies were taken from the bronchial lesions. Four of the six biopsies revealed pure typical SRCA (**Figure 2**). No other elements of adenocarcinoma were seen. The other two biopsies showed normal bronchial mucosa. Histochemically, Alcian-blue/PAS stain showed intracytoplasmic mucins (acidic and neutral mucins). An immunohistochemical study was performed with the use of Dako Envision method, as previously described [6-11]. Immunohistochemically, the tumor cells were positive for cytokeratin (CK) AE1/3 (**Figure 3A**), CK CAM5.2, CK7 (**Figure 3B**), CK18 (**Figure 3C**), CEA (**Figure 3D**), EMA, CA19-9 (**Figure 3E**), Ki-67 (labeling=20%), p53 (**Figure 3F**), and MUC1 (**Figure 3G**). They were negative for CK34BE12, CK5/6, CK8, CK14, CK19, CK20, p63, vimentin, TTF-1, CDX-2, MUC2, MUC5AC and MUC6. The pathological diagnosis of primary SRCA of the left main bronchus was made.

Upper and lower gastrointestinal endoscopy revealed no tumors. Head CT demonstrated a few brain metastases. No tumors were found

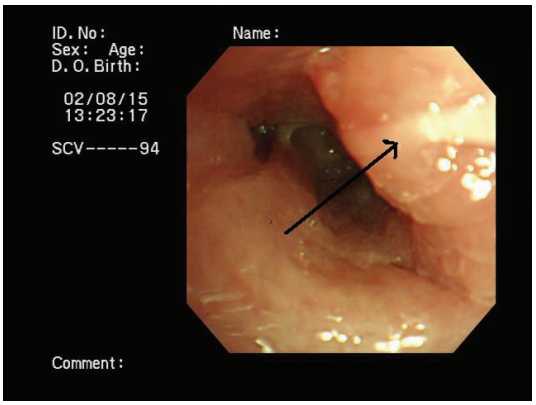

Figure 1. Bronchial endoscopy. It shows an elevated lesion (arrow) in the extrapulmonary left main bronchi near tracheal bifurcation.

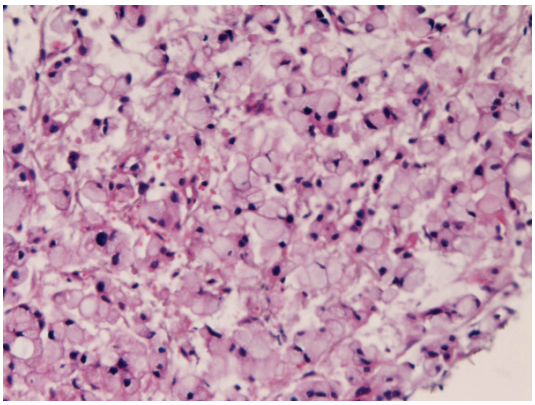

Figure 2. Biopsy features. The biopsy shows typical pure signet ring cell adenocarcinoma. HE, x200.

except for the mediastinum and brain. Therefore, the mediastinal tumor was thought primary. Since brain metastasis was present and the resection of the tumor was impossible because the tumor involved the aorta, the patient underwent chemo-radiation therapy. However, his condition showed downhill course, and died of carcinomatosis 18 months after the first presentation.

Discussion

The present case was the first case report of the pure SRCA of the extrapulmonary main bronchus near the tracheal bifurcation. In the lung, several case reports and case series of primary SRCA have been reported [1-5]. Most of the cases of gastric and lung SRCA, signet-ring carcinoma cells are present in addition to other histological subtypes such as mucinous carcinoma and tubular carcinoma [4], and pure SRCA in the extragastric locations is extremely rare. The present case is pure SRCA. In making the diagnosis of extragastric SCRA, it is very important to exclude metastatic SRCA from the stomach and breast. In the present case, the stomach and breast were free from tumors. Thus, the present case is primary SRCA arising from the extrapulmonary left main bronchus neat the tracheal bifurcation. In the lung SRCA, the clinicopathology was unclear, because of the rarity of lung SCRA. According to the largest series (n=39) [4], lung carcinoma with signet-ring cell components accounted for 1.5% (39/2640) of all lung malignancies. The mean age was 54.6 years (range 32-76 years). The male to female ratio was 1.16:1.00, and 5-year survival was 28% [4].

Three immunohistochemical studies are available in lung SRCA [1-3, 5]. Hayashi et al [1], who reported 5 cases of lung SRCA, showed that 80% (4/5) was immunoreactive for lactoferrin, 100% (4/4) showed k-RAS mutations, 100% (5/5) was positive for MUC1, and 100% (5/5) was negative for MUC2. Merchant et al [2], who investigated 17 cases of lung SRCA, showed that 82.4% (14/17) showed TTF-1 positivity, CK7+/CK20- pattern was seen in 94% (16/17). Villin expression was seen in 29.4% [2]. Castro et al [3], who examined 15 cases of lung SCRA, showed immunoreactivity of TTF-1 (100%, 6/6), CEA (100%, 9/9), and CK7 (50%, 3/6). CK20, estrogen receptor, progesterone receptor, and GCDFP-15 were negative [3].

In the present bronchial SRCA, the cytokeratin profile was as follows: CK AE1/3+, CK CAM5.2+, CK7+, CK18+, CK34BE12-, CK5/6-, CK8-, CK14-, CK19-, and CK20-. Thus, it is thought that the SRCA cells of the main bronchus shows low-molecular weight cytokeratin. The CK7+/CK20- pattern is consistent with lung SRCA cases of Merchant et al [2]. In the current case, immunoreactive CEA was positive, being compatible with lung SRCA cases of Castro et al [3]. In the current case, serum CEA was increased, suggesting that the SRCA cells produce a large amount of CEA. CA19-9 and EMA were positive in the present study, indicating that these molecules are present in bronchial SRCA. In the present case, Ki-67 labeling is relatively high (20%), indicating active proliferation. In the present study, p53 was positive, suggesting p53 mutations. In the present study, MUC1 was positive, while MUC2, MUC5AC and MUC6 were negative. MUC1 positivity and MUC2 negativity

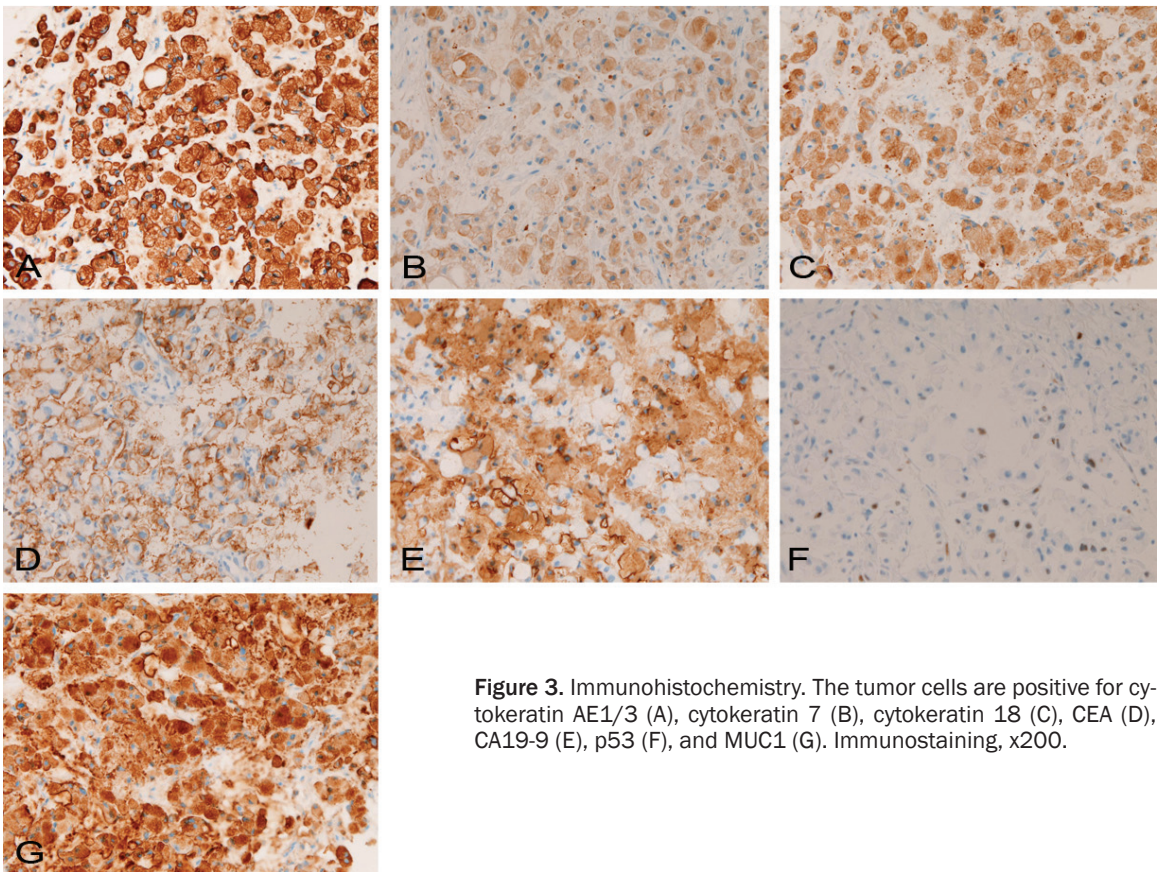

Figure 3. Immunohistochemistry. The tumor cells are positive for cytokeratin AE1/3 (A), cytokeratin 7 (B), cytokeratin 18 (C), CEA (D), CA19-9 (E), p53 (F), and MUC1 (G). Immunostaining, x200.

were reported in lung SRCA [1], being compatible with bronchial SRCA in the present case. In addition, the present case was negative for MUC5AC and MUC6, suggesting that MUC1 gene is operative while genes of MUC2, MUC5AC and MUC6 were not expressed. In the present study, there were no immunoreactivity of p63, vimentin, TTF-1, and CDX-2. p63 negativity may show the present case was not related to squamous cells or myoepithelial cells. Vimentin, a mesenchymal marker, was negative, as expected. TTF-1 negativity merits consideration. As previously mentioned, Merchant et al [2] described that TTF-1 was positive in 82.4% (14/17) in lung SCRA, and Castro et al [3] 100% (6/6). In general, pulmonary SRCA expresses TTF-1, while non-pulmonary SRCA does not [2]. The primary site of the present case of SRCA was left main bronchus, thus TTF-1 is expected to be positive. In any way, there may be cases of bronchial SRCA without TTF-1 expression. In the present case, CDX2 was negative, suggesting that the present case was not associated intestinal phenotypes.

In conclusion, the first case of SCRA of the left main bronchus was described with an immunohistochemical study.

Conflict of interest statement

The author has no conflict of interest.

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