

A Rare Case of Bronchial Epithelial-Myoepithelial Carcinoma with Solid Lobular Growth in a 53-Year-Old Woman

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Epithelial-myoepithelial carcinoma (EMC) of lung is a minor subset of salivary type carcinoma of lung of known low grade malignancy. Histologically, two-cell components forming duct-like structure with inner epithelial cell layer and outer myoepithelial cell layer are characteristics of EMC. In salivary gland, dedifferentiation of conventional low grade malignancy has been reported and is thought to be related with poor prognosis. However, precise histomorphology and prognostic factors of pulmonary EMC have not been clarified due to its rarity. Herein, we reported a rare case of EMC presented as endobronchial mass in a 53-year old woman, which showed predominant solid lobular growth pattern and lymph node metastases.

Keywords: Bronchial Neoplasms; Carcinoma; Lung

Introduction

Primary epithelial-myoepithelial carcinoma (EMC) is rare subset of salivary gland-type tumor in tracheobronchial tree, and only about 50 cases have been reported in English literature^{1,2}. In salivary glands, most EMC are considered as low grade malignancy, although local recurrence is occurred. In spite of its rarity, typical two-cell component of EMC—inner

epithelial and outer myoepithelial cells—is diagnostic histologic feature. However, other than biphasic pattern, histological spectrum and prognosis are not well established in EMC of tracheobronchial tree. To date, only five patients have been reported to have recurrence or metastasis¹⁻⁵, and only one patient has been reported to have lymph node metastasis at presentation⁴. Herein, we present an EMC of tracheobronchial tree with unusual solid lobular growth pattern and lymph node metastases in a 53-year-old woman.

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Case Report

A 53-year-old woman presented with blood tinged sputum. She was a never-smoker and had a history of diabetes on medication. Chest computed tomography scan revealed endobronchial obstructive lesion in right bronchus intermedius (Figure 1A). Bronchoscopic examination showed lobulated mass in endobronchial lesion (Figure 1B), and bronchoscopic biopsy for mass was performed. Preoperative positron emission tomography—computed tomography revealed multiple fluorodeoxyglucose uptake in right bronchus intermedius and lymph nodes in right paratracheal area (Figure 1C). On biopsy specimen, subepithelial infiltrating nests of atypical cells were

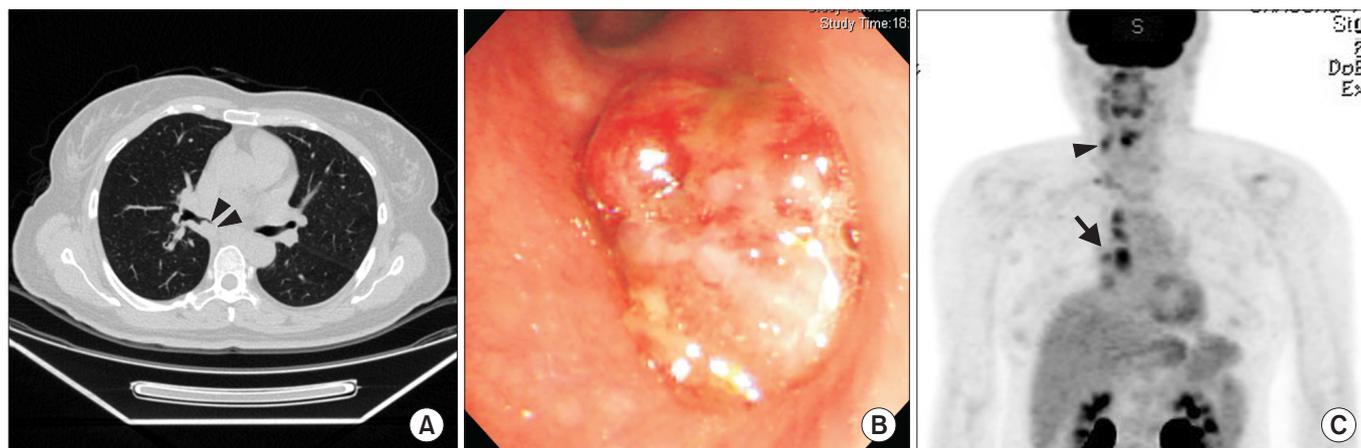


Figure 1. (A) Chest computed tomography reveals endobronchial mass in right bronchus intermedius (arrowheads). (B) Bronchoscopy shows lobulated endobronchial mass. (C) Multifocal fluorodeoxyglucose uptake in right bronchus intermedius (arrow) and right paratracheal area (arrowhead) on preoperative positron emission tomography–computed tomography.

identified, and differential diagnoses were neuroendocrine carcinoma such as carcinoid and poorly differentiated non-small cell carcinoma (Figure 2A). Subsequent biobectomy of right middle lobe and right lower lobe with mediastinal lymph node dissection was performed.

On cut section, a 2.2-cm-sized endobronchial polypoid mass was identified (Figure 2B). The yellow-tan, solid mass was relatively well-defined, but focal interruption of bronchial cartilage was found. Microscopically, central area of the mass was composed of variable sized solid lobules of tumor cells. Tumor cells were evenly distributed in solid lobules, and central necrosis was found in the lobules. Nuclei of tumor cells showed moderate atypia and cytoplasm was eosinophilic and partly granular (Figure 2C). At the periphery, transition from small infiltrating duct-like structures to solid lobules were identified (Figure 2D). These duct-like structures resembled bronchial submucosal glands but showed nuclear atypia and infiltrative growth into peribronchial soft tissue, which were typical features of EMC. Due to the solid lobular area, differential diagnoses included collision tumor with EMC component such as metastatic lobular breast cancer, carcinoid, lymphoma, and pulmonary adenocarcinoma with solid pattern. To make final diagnosis, immunohistochemical stainings for thyroid transcription factor 1 (TTF-1; 1:100, 8G7G3/1, Dako, Carpinteria, CA, USA), p63 (1:200, 4A4, Biocare Medical, Concord, CA, USA), cytokeratin (CK; 1:500, AE1/AE3, Dako), chromogranin A (1:400, DAK-A3, Dako), CD56 (1:200, CD564, Novocastra, Newcastle upon Tyne, UK), smooth muscle actin (SMA; 1:1,000, 1A4, Dako), and Ki-67 (1:300, MIB1, Dako) were performed. Tumor cells were positive for CK (AE1/AE3) and SMA, whereas negative for remaining TTF-1, p63, chromogranin A, and CD56. In solid area, CK (AE1/AE3) was positive in inner center of the lobules and SMA was positive in the outer layer of the lobules. Peripheral duct-like structures

also showed CK (AE1/AE3) positive cells in inner layer, and SMA positive cells in outer layer (Figure 2E, F). S-100 protein highlighted myoepithelial component of the peripheral duct-like structure, whereas only focal area of positivity was found in the solid lobules (Figure 2G). Ki-67 revealed high proliferative index in outer area of solid lobules, up to 40%. However, the center of solid lobules and adjacent duct-like structure showed less than 1% of proliferative index (Figure 2H). Finally, diagnosis of poorly differentiated EMC was rendered. Since there were metastases in right hilar and subcarinal lymph nodes, patient underwent adjuvant chemotherapy.

Discussion

Clinically, endobronchial mass may cause hemoptysis and pulmonary parenchymal obstruction. Primary endobronchial lesions are benign in most cases. However, malignancy is more common when endobronchial lesion presents as mass lesion⁶. Benign endobronchial mass lesions include infection, foreign bodies, vascular malformation and broncholith etc. Malignant endobronchial mass lesions include squamous carcinoma, primary lung adenocarcinoma, small cell carcinoma, bronchial carcinoid and salivary gland type tumors such as mucoepidermoid carcinoma, adenoid cystic carcinoma and EMC.

EMC is a rare malignant tumor in the salivary glands, accounts for about 1% of salivary gland tumors, and EMC of pulmonary system is much rarer, and only handful of case reports are exist^{1,2}. Most of EMC have been considered to have low malignant potential, but precise prognosis of EMC patients is not established due to its rarity. So far, only five patients with EMC have been reported to demonstrate recurrence or metastasis¹⁻⁵, which is summarized in Table 1. Among five pa-

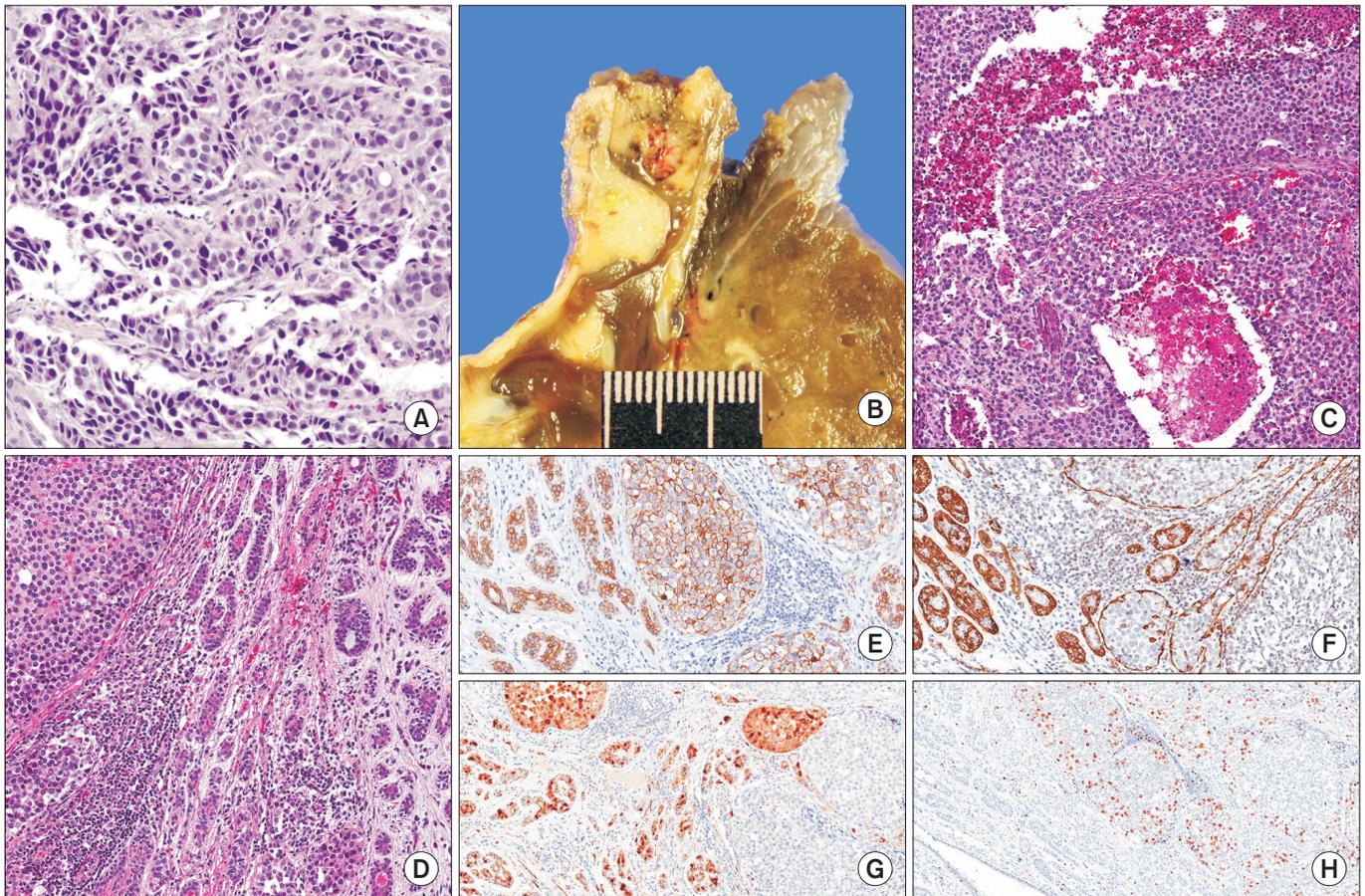


Figure 2. (A) Infiltrating atypical nests are identified on histologic examination of biopsy specimen (H&E stain, $\times 200$). (B) Grossly, endobronchial yellow-tan solid mass focally interrupts the bronchial cartilage. (C) Tumor cells of solid lobular area demonstrate moderate cytologic atypia and discohesive pattern with accompanied multifocal central necrosis (H&E stain, $\times 100$). (D) Toward the periphery of mass transition from duct-like two-cell layered area to the solid lobules is present (H&E stain, $\times 100$). (E) Cytokeratin (CK) (AE1/AE3) is strong positive in tumor cells of inner layer of duct-like area. Outer layer of duct-like structure and solid area show variable intensity of CK (AE1/AE3) positivity (CK [AE1/AE3], $\times 100$). (F) Smooth muscle actin (SMA) highlights the outer myoepithelial layer of duct-like area, which is only focally expressed in solid lobular area (SMA, $\times 100$). (G) S-100 protein is positive in the outer myoepithelial layer of duct-forming area and variably expressed in solid lobular area (S-100 protein, $\times 100$). (H) Ki-67 proliferative index is notably higher in periphery of solid lobular area, as compared to the center of solid lobules and adjacent duct-like structure (Ki-67, $\times 100$).

Table 1. Reported cases of epithelial-myoepithelial carcinoma with recurrence or metastasis

No. of patients/ Total	Sex/Age (yr)	Recurrence or metastasis	Site	Survival	Reference
1/5	F/52	Recurrence	Chest wall	Alive	Song et al. ¹
1/7	Not mentioned	Recurrence	Bone	Alive	Zhu et al. ²
1/1	M/74	Recurrence	Both lung nodules	Alive	Muslimani et al. ³
1/5	F/56	Metastasis	Peribronchial lymph node	Alive	Nguyen et al. ⁴
1/1	M/81	Metastasis	Skull	Alive	Nishihara et al. ⁵
1/1	F/53	Metastasis	Hilar and subcarinal lymph node	Alive	Present case

tients, lymph node metastasis was found in only one patient who received pneumonectomy due to EMC at left main bronchus⁴. Although six patients, including present case, had me-

tastasis or recurrence, no patients have died of disease, which supports the low malignant potential of EMC and importance of complete resection of tumor.

Interestingly, proliferation of epithelial and myoeithelial component in present case made the solid architecture, mimicked other neoplasms rather than typical EMC and caused diagnostic difficulty. Furthermore, myoeithelial component of solid lobules showed relatively higher proliferative index and central necrosis, which would be responsible for the aggressive behavior in our patients, such as lymph node metastasis. In previous study, myoeithelial component has been considered to play an important role in the malignant potential of EMC¹. Song et al.¹ and Pelosi et al.⁷ suggested the malignant and proliferative role of myoeithelial cells, as p27/Kip-1 protein was aberrantly expressed in myoeithelial cells of dysplasia and well differentiated carcinoma. p27/Kip-1 protein is a cyclin-dependent kinase inhibitor, and thought to play a role in unrestricted proliferation of the myoeithelial component⁷. Although proportion of myoeithelial component has not been clearly described in previous studies with recurrence or metastasis of EMC, predominant myoeithelial component would be expected in patients with recurrence or metastasis of EMC.

In summary, we described a rare case of EMC in tracheobronchial tree that demonstrated unusual solid lobular pattern with predominant myoeithelial component and lymph node metastasis. Although implication of the solid lobular pattern in pulmonary EMC needs to be further elucidated, the possibility of aggressive EMC should be included in differential diagnoses when patient presents with endobronchial mass and unusual solid lobular area is encountered in pathologic examination.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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