〈Case Report〉

A case of pulmonary metastasis with interstitial spread of sinonasal adenoid cystic carcinoma

Takeshi MATSUNO[1)], Takae INAYOSHI[1)], Hironori MIYAKE[2)], Takashi MATSUTANI[3)]
Hirotake NISHIMURA[1)], Tatsushi SHIOMI[1)], Takuya MORIYA[1)]

1) Department of Pathology,
2) Department of Otolaryngology-Head and Neck Surgery,
3) Department of General Thoracic Surgery, Kawasaki Medical School

ABSTRACT A 64-year-old woman was diagnosed with sinonasal adenoid cystic carcinoma (cT4N0M0, cStage IVB) and received induction chemotherapy and proton beam therapy. Four years later, the first local recurrence was identified. At the same time, computed tomography (CT) showed a partial solid ground glass nodule (24 mm in size) in the right upper lobe; this lesion was suspected to be a primary lung adenocarcinoma, so a wedge resection of the right upper lobe was carried out.

Grossly, the surgical specimen revealed a gray-white solid mass. Histologically, the mass was made up of atypical cells that proliferated in tubular, cribriform, and solid structures. At the lesion's margins, tumor cells infiltrated the alveolar septa (known as interstitial spread), and the overlying pneumocytes showed hyperplastic changes and nuclear atypia.

Two cell types were identified using immunohistochemistry. One was a distribution of epithelial cells with cytokeratin (CK) 5/6, CK AE1/AE3 positivity. The other was the proliferation of cells with positive myoepithelial markers, such as p40, p63, and αSMA. The lesion's myoepithelial cells also tested partially positive for C-Myb. TTF-1 and Napsin A were positive for overlying pneumocytes but negative for tumor cells.

Based on the above findings, we diagnosed pulmonary metastasis of sinonasal adenoid cystic carcinoma. Metastatic tumors with interstitial spread and pneumocyte hyperplasia appear to be rare. The disparity between the chest CT image and the pathology findings could be attributed to this distinct growth pattern; however, more data to confirm this relationship needs to be collected.

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Corresponding author
Takeshi Matsuno
Department of pathology, Kawasaki Medical School,
577 Matsushima, Kurashiki, 701-0192, Japan

Phone : 81 86 462 1111
Fax : 81 86 464 1153
E-mail: matsunot@med.kawasaki-m.ac.jp

INTRODUCTION

Adenoid cystic carcinoma is a rare malignant tumor that primarily occurs in the salivary glands, accounting for 3%-5% of the cancers of the head and neck[1, 2]. Histologically, adenoid cystic carcinoma is a basaloid tumor consisting of epithelial and myoepithelial cells in variable morphologic configurations, including cribriform, tubular and solid patterns. The most predominant site of distant metastasis is the lung[3-6]; this must be related to the fact that blood returning from the entire body to the heart first travels through the lungs. Pulmonary metastases usually presented as single or multiple solid nodules. Thus, it is often difficult to distinguish solitary metastatic solid nodule of adenoid cystic carcinoma from primary lung adenocarcinoma. On the other hand, primary lung cancer is more suspected if single nodule presented as ground glass opacity. We present a case of solitary pulmonary metastasis of sinonasal adenoid cystic carcinoma, which was suspected for primary lung adenocarcinoma. It showed partial ground glass opacity, owing to its unusual growth pattern.

CASE PRESENTATION

A 64-year-old woman was referred to our hospital with vision loss, nose bleeds, and sinus tenderness. After a diagnosis of adenoid cystic carcinoma of the left sphenoid sinus (cT4N0M0, cStage IVB), based on clinical, radiological, and histopathological examinations (Fig. 1), she received induction chemotherapy and proton beam therapy. Four years later, PET/CT showed a local recurrence of sinonasal adenoid cystic carcinoma, and incidentally, a lung lesion was also discovered. This lesion revealed a 24 mm partial solid ground glass nodule on the chest CT (Fig. 2A). Since this lesion

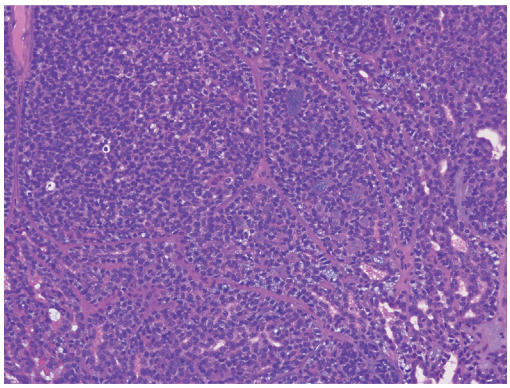

Fig. 1. Histological view of the primary adenoid cystic carcinoma of the left sphenoid sinus. Tumor cells proliferated as tubular, cribriform, and solid structures.

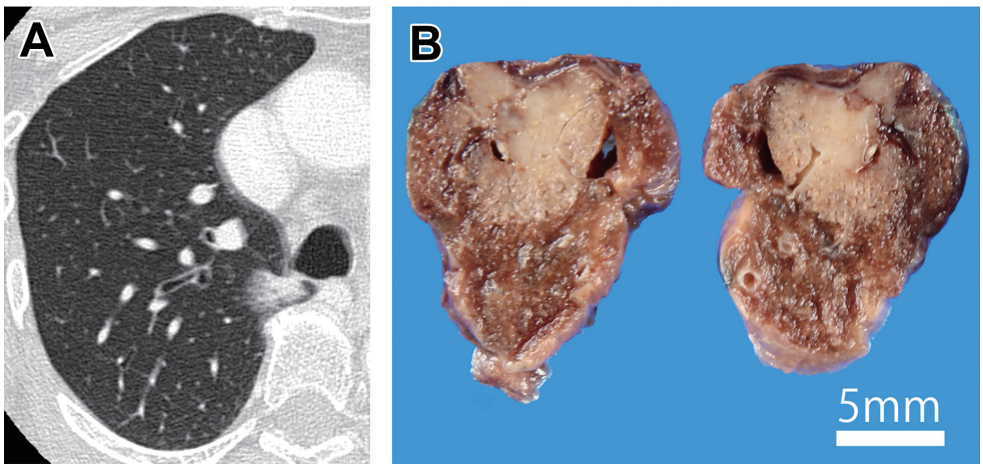

Fig. 2. Chest CT image of the lung lesions, as well as a gross image of the lesion in the surgical material. Chest CT revealed a 24 mm partial solid ground glass nodule (A). In the surgical specimen, a gray-white solid mass was found (B).

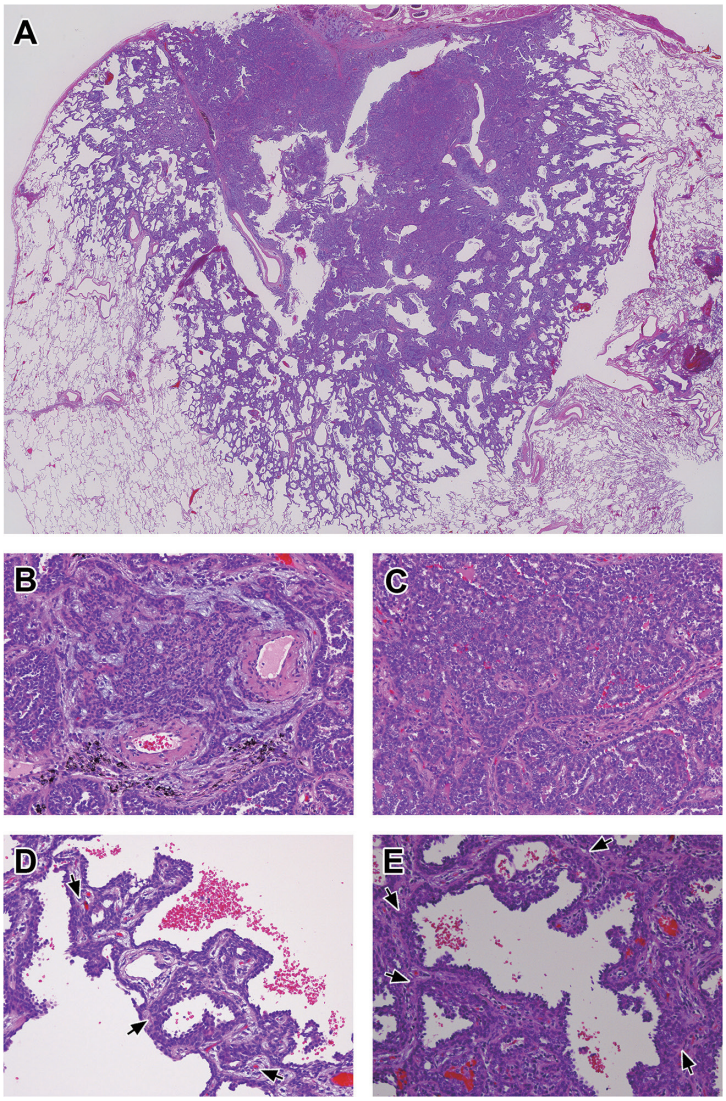

Fig. 3. Histological image of pulmonary metastasis from sinonasal adenoid cystic carcinoma. At the lesion's margin, the tumor grew into the alveolar septa and spread like a finger to the surrounding tissue (a process known as interstitial spread) (A). Similar to the primary lesion, the tumor cells proliferated in tubular, cribriform, and solid structures (B, C). Tumor cells also grew into the alveolar septa (arrow), and atypical overlying pneumocytes demonstrated hyperplasia (D, E).

was thought to be a primary lung adenocarcinoma, the right upper lobe was removed using a wedge technique.

Grossly, a gray-white solid mass was seen in the surgical specimen (Fig. 2B). Histologically, the mass consisted of atypical cells proliferating in tubular, cribriform, and solid structures (Fig. 3A-C). At the lesion's margins, the tumor cells infiltrated the alveolar septa (a process known as interstitial spread) (Fig. 3A, D, E). In such areas, pneumocytes with cytological atypia proliferated alongside the alveolar walls (Fig. 3D, E). These proliferating

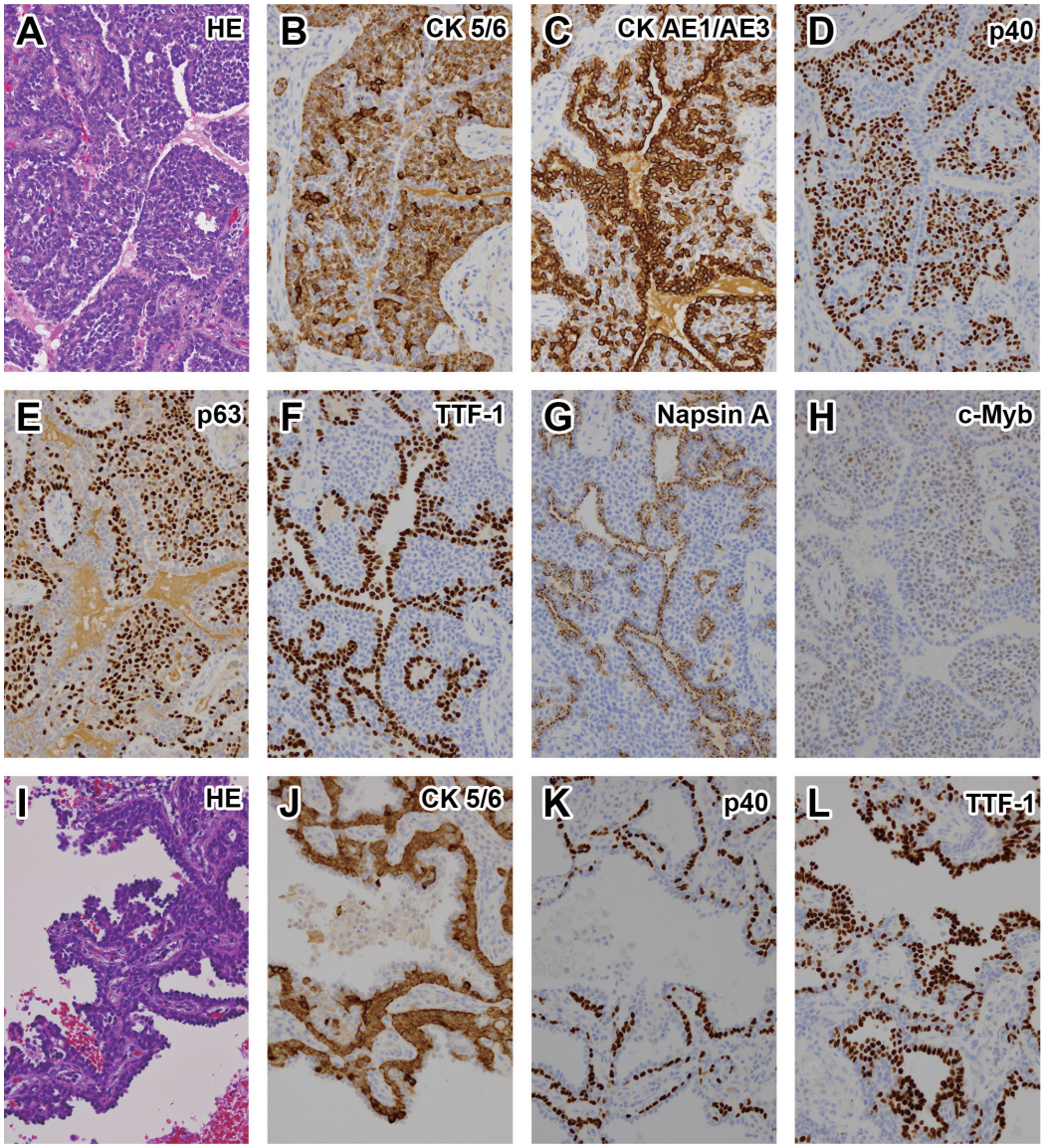

Fig. 4. Morphological and immunostaining images of pulmonary metastasis at the center (A: HE, B: CK 5/6, C: CK AE1/AE3, D: p40, E: p63, F: TTF-1, G: Napsin A, H: c-Myb) and those that grew into the alveolar septa (I: HE, J: CK5/6, K: p40, L: TTF-1). One of the tumor cells was positive for epithelial cell markers (CK 5/6, CK AE1/AE3) (B, C, J), while the other was positive for myoepithelial markers (p40, p63) (D, E, K). This biphasic differentiation of cells is one of the distinguishing features of adenoid cystic carcinoma. C-Myb was also partially positive in myoepithelial cells (F). TTF-1 and Napsin A were found in the overlying pneumocytes, confirming pneumocyte hyperplasia (F, G, L).

pneumocytes resembled the lepidic growth of adenocarcinoma; however, we classified them as benign reactive/hyperplastic changes because they were limited to the site of tumor cell invasion.

Immunohistochemistry revealed the differentiation of tumor cells. One was positive for cytokeratin (CK) 5/6 and CK AE1/AE3 (Fig. 4B, C, J), indicating epithelial cell differentiation, whereas the other was positive for p40 and p63, indicating myoepithelial cell differentiation (Fig. 4D, E, K).

C-Myb was also slightly positive in myoepithelial cells (Fig. 4H). TTF-1 and Napsin A were positive for pneumocytes, including those proliferated with atypia, but not for tumor cells (Fig. 4G, H, L). Based on the above findings, we diagnosed pulmonary metastasis of sinonasal adenoid cystic carcinoma.

DISCUSSION

Adenoid cystic carcinoma of salivary gland is a rare head and neck cancer. Local recurrence and/or distant metastases affect 40%-60% of patients with this carcinoma[4, 7], and the lung is the most common site of distant metastasis[3-6]. On chest CT, pulmonary metastases of adenoid cystic carcinoma are typically seen as single or multiple solid nodules[3]. Therefore, the ground glass nodule frequently indicated lepidic growth adenocarcinoma or intestinal pneumonia[3]. In the present case, the metastatic lesion revealed a solitary partial solid ground glass nodule, which is an unusual and uncommon imaging finding for pulmonary metastasis. Based on the disease's natural history and the high risk of developing lung metastases, proliferating lung lesions should be distinguished from pulmonary metastases, even if they appear atypical on imaging.

Pulmonary metastases show various growth patterns histologically. Interstitial spread, vascular infiltration, satellite nodules, and lymphangitic spread were classified as aggressive histological growth characteristics, indicating aggressive local growth into the surrounding lung tissue[8-10]. Interstitial spread is a rare growth pattern in which tumor cells grow into the alveolar septa and spread like fingers into the surrounding tissue[8-10]. Also, interstitial spread is most common in lymphoma, but it can also occur in sarcoma, squamous cell carcinoma, melanoma, and other carcinomas[8-11]. Pulmonary metastasis of adenoid cystic carcinoma with interstitial spread appeared to be rare, although we could not find any evidence in the literature.

Pneumocyte hyperplasia is a common reaction in the injured lung[12, 13]; this is most noticeable in diffuse alveolar damage, but it can also be seen in organizing pneumonia, non-specific interstitial pneumonia, and a variety of other settings, such as acute bronchopneumonia, the lung surrounding granulomas, pulmonary Langerhans's cell histiocytosis lesions, tumors, and abscesses[12]. Even when metastatic tumor cells invade the alveolar septa, the surrounding pneumocytes exhibit hyperplastic and/or reactive changes[11]. Thus, the presence of the lung injury that caused this unusual histology, as well as the clinical history, are critical in determining the benign nature of this lesion.

In this case, the metastatic tumor spread interstitially, and the overlying pneumocyte showed hyperplasia. These histological patterns appeared to be rare for pulmonary metastasis. As a hypothesis, the discrepancy stated above between the chest CT image and the pathology findings could be related to the tumor's unique growth pattern. More data needs to be collected to confirm this relationship.

CONCLUSION

In this report, we provide a case of pulmonary metastasis of adenoid cystic carcinoma with interstitial spread. Histologically, the tumor showed interstitial spread and overlying pneumocyte hyperplasia. This rare and distinct growth pattern may be linked to the ground glass nodule image, which is unusual for metastasis.

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