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CASE REPORT

Solitary peribronchiolar metaplasia showing a sub-solid nodule on computed tomography

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Abstract
Recent advances in radiographic imaging and thoracic surgery have facilitated surgery for small lung tumors by eliminating the need for pathological diagnosis. To date, we have experienced two cases of small lung tumors that were surgically resected without pathological diagnosis as malignant. Computed tomography (CT) revealed sub-solid nodules in the peripheral lung. After tumor resection, both tumors were pathologically diagnosed as peribronchiolar metaplasia. To the best of our knowledge, solitary peribronchiolar metaplasia showing a sub-solid nodule on CT imaging has not previously been reported.

Keywords Computed tomography · Sub-solid nodule · Surgery · Peribronchiolar metaplasia

Introduction

In lung cancer screening, recent advances in radiographic imaging by computed tomography (CT) have allowed detection of small lung lesions less than 5 mm in diameter [1, 2]. CT can be used to clearly identify early lung adenocarcinoma lesions by ground-glass nodules [1]. Furthermore, advances in thoracic surgery, such as video-assisted thoracic surgery, have allowed for easy resection of lung lesions without open thoracic surgery [3]. Therefore, surgery for small pulmonary lesions can be easily performed without an initial pathological diagnosis. This facilitates the process because it is often difficult to obtain tumor tissue biopsies by transbronchial lung biopsy or percutaneous computed tomography (CT)-guided needle biopsy. If a small lung lesion is regarded as malignant from the CT image, surgical resection can be performed for diagnostic and/or treatment purposes.

In this report, we present two cases of peribronchiolar metaplasia, which were clinically diagnosed as early lung adenocarcinoma and resected without preoperative pathological diagnosis.

Case report

Case 1

A 78-year-old Japanese woman had small abnormal shadows in the right upper and lower lobe detected by CT, but they were too small for diagnosis. She had no history of smoking. Laboratory findings showed no abnormalities in tumor markers. Her chest lesions were followed periodically. Four years later, the nodule in the right lower lobe gradually increased in size to 1.1 × 1.0 cm. CT showed the lesion as an irregular speculated sub-solid nodule containing small air chambers (Fig. 1a). The size of consolidation was 0.5 cm. ^{18}F-FDG positron emission tomography (PET) was not performed. Since the nodule was clinically suspected to be primary lung cancer (cT1aN0M0, Stage IA), segmentectomy with hilar lymph node dissection was performed with curative intent for early lung cancer.

The resected tumor was approximately 1.0 × 1.0 × 0.8 cm in size. The details of macroscopic findings and histology

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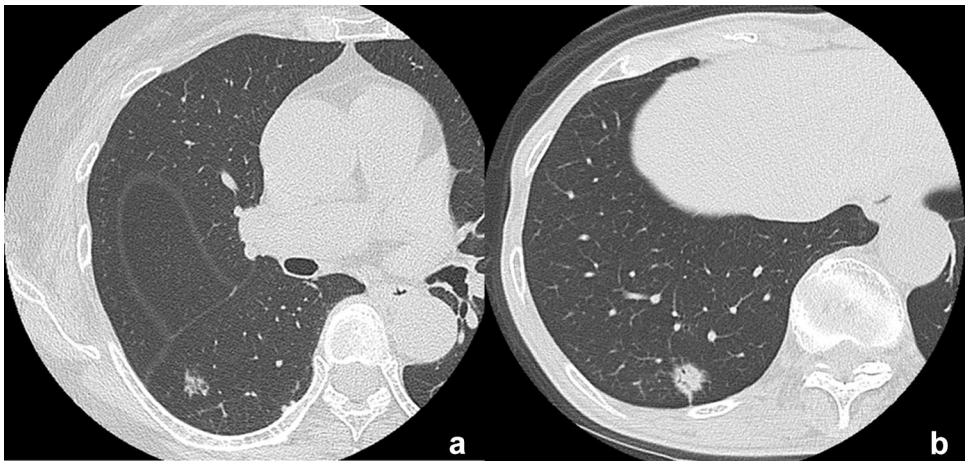

Fig. 1 CT images from case 1 (**a**) and case 2 (**b**)

are shown in Fig. 2. No lymph node metastasis was present. Since dilated bronchioles were present in the lesion (Fig. 2b), the final pathological diagnosis was peribronchiolar metaplasia.

Case 2

A 79-year-old Japanese woman was referred to our hospital due to early gastric cancer. Preoperative chest CT found a sub-solid nodule (1.7 × 1.7 cm in size) with an irregular margin and pleural retraction in the right lower lobe (Fig. 1b). The size of consolidation was 1.6 cm. ^{18}F-FDG PET revealed no abnormal accumulation of ^{18}F-FDG in the tumor. Transbronchial lung biopsy was performed, but failed to retrieve the tumor tissue. The patient had never smoked. Her laboratory data showed no abnormalities in serum tumor markers. The tumor was clinically diagnosed as lung cancer, with a clinical stage of cT1aN0M0 (Stage IA). 2 months after surgery for early gastric cancer, segmentectomy without lymph node dissection was performed for conservative reasons in consideration of her comorbidities.

The size of the tumor was 1.5 × 1.2 × 1.2 cm. The details of macroscopic findings and histology are shown in Fig. 3. Since ciliated and non-ciliated tumor cells with bronchioloalveolar growth are closely associated with dilated

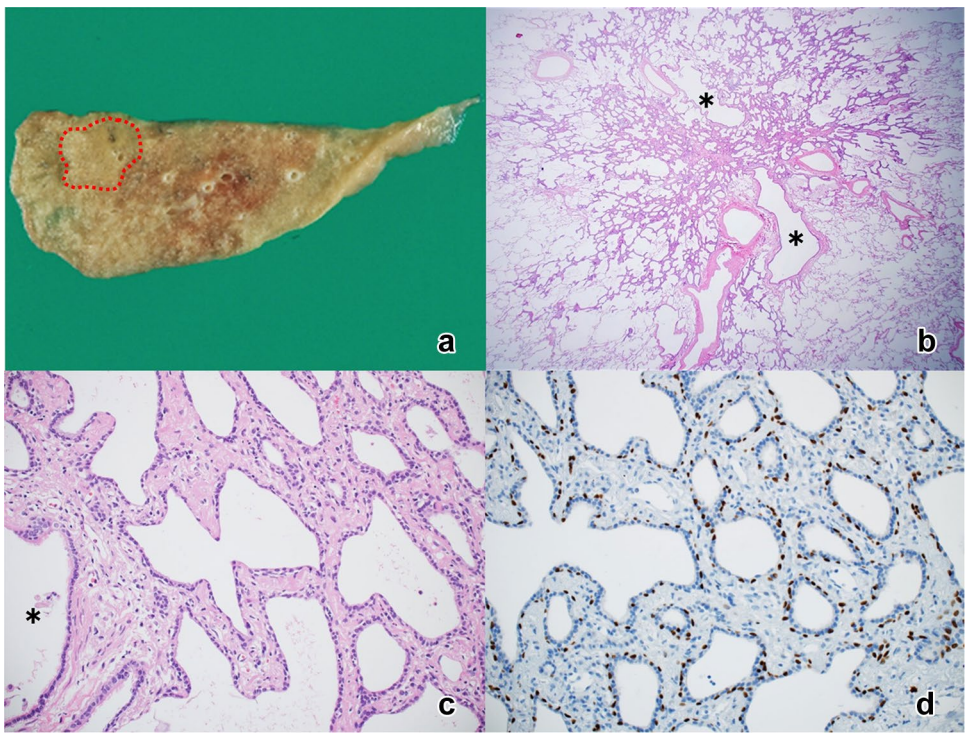

Fig. 2 Macroscopic findings and histology for case 1. The tumor was yellowish-white in color at the cut surface, and the consistency increased at an indistinct margin surrounded by dot line (**a**). A low-power view of the tumor showed prominent lepidic growth resembling adenocarcinoma in situ (**b**). A high-power view showed that the alveolar structure was slightly fibrotic and was lined mostly with non-ciliated cuboidal bronchiolar cells and a few mucus cells (**c**). Immunohistochemistry showed non-ciliated cuboidal bronchiolar cells to be positive for CAM5.2, but negative for TTF-1, and p40-positive cells were present underneath the cuboidal bronchiolar cells (**d**). Furthermore, the mucus cells were positive for MUC5AC. **b, c** Hematoxylin & eosin staining. The asterisk (*) shows a dilated bronchiole

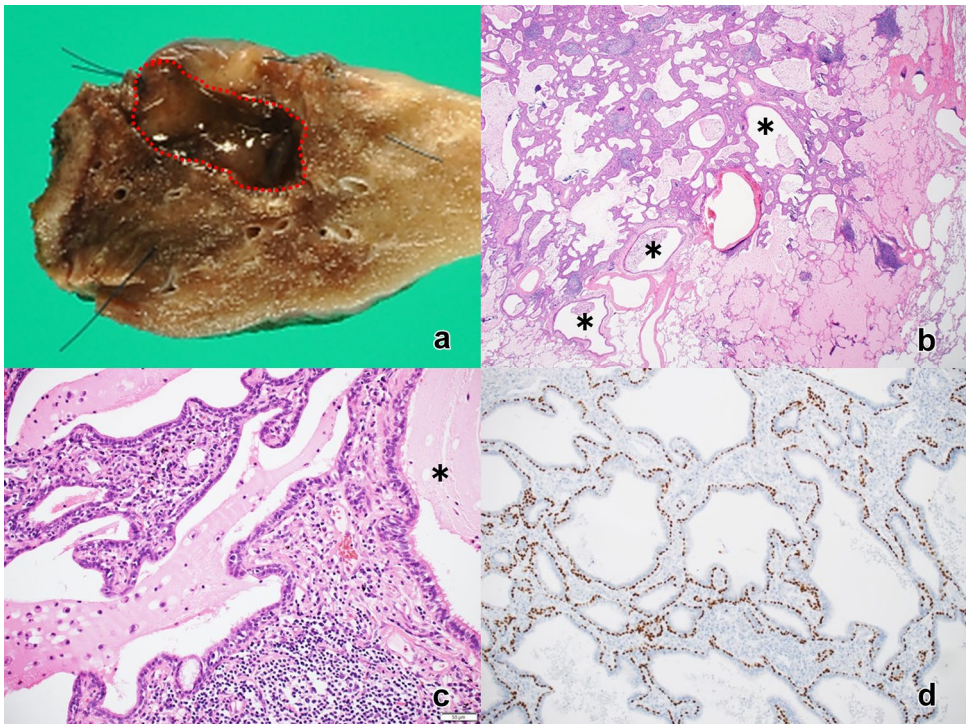

Fig. 3 Macroscopic findings and histology for case 2. The tumor was a solid nodule with a clear border, and when cut, the surface was glittering brown in color surrounded by dot line (**a**). The tumor histology showed bronchioloalveolar growth containing dilated bronchioles surrounded with mucus-filled alveoli (**b**). The tumor cells formed two cell patterns; columnar or cuboidal in the upper layer and basal-like cells in the lower layer (**c**). The columnar cells had cilia on the cell surface, but these were absent on the cuboidal cells. In some areas, the tumor-contained mucus cells. The non-ciliated and ciliated cells were positive for CAM5.2, but negative for TTF-1, while the basal-like cells were positive for p40 (**d**) and keratin 5/6. Carcinoembryonic antigen (CEA) was not detected. **b, c** Hematoxylin & eosin staining. The asterisk (*) shows a dilated bronchiole

bronchioles, the final pathological diagnosis was peribronchiolar metaplasia.

Discussion

In 2002, Henschke et al. proposed a new terminology of solid and sub-solid nodules instead of the previously used term ground-glass opacity (GGO) in CT screening for lung cancer [4]. Sub-solid nodules are localized forms of GGO, which is subclassified into part-solid or non-solid nodules based on the presence or absence of a solid area. Mirtcheva et al. revealed that bronchioloalveolar carcinoma and adenocarcinoma with bronchioloalveolar features were histologically presenting as GGO on CT [5]. In CT lung cancer screening, sub-solid nodules are usually regarded as malignant, but they may also be benign lesions such as focal interstitial fibrosis, inflammation and hemorrhage [6].

The size and shape and their changes during follow-up of sub-solid nodules are important factors in evaluating malignancy [7]. About 75% of persistent pulmonary GGO nodules were reported to be bronchioloalveolar carcinoma or adenocarcinoma with predominant bronchioloalveolar components [8]. Increased or persistent sub-solid nodules are more likely to be malignant, specifically in primary lung adenocarcinoma, so it is reasonable to clinically diagnose case 1 as adenocarcinoma. Larger nodule size is an important predictor of malignancy in sub-solid nodules [9]. In case 2, the tumor size was 1.7×1.7 cm and the nodule was associated with pleural retraction, resulting in the clinical diagnosis of adenocarcinoma. In case 2, the ^{18}F-FDG PET study was negative. In lung cancers, ^{18}F-FDG PET is preoperatively helpful to detect lymph node metastasis, but its clinical usefulness in small sub-solid nodules remains controversial [10].

In this study, two small nodules were clinically diagnosed as malignant, and resected, but the pathological diagnosis of both lesions was peribronchiolar metaplasia. Peribronchiolar metaplasia or lambertosis is a non-specific reaction to injury that results in the extension of bronchiolar type epithelial cells along the alveolar walls adjacent to the airways [11]. In general, peribronchiolar metaplasia is a common pathological finding for various chronic interstitial lung diseases [12]. However, our cases were not associated with interstitial lung fibrosis. To date, no case has been reported of large solitary peribronchiolar

metaplasia appearing as a sub-solid nodule on CT and clinically misdiagnosed for adenocarcinoma.

The histology of large peribronchiolar metaplasia in our cases showed great diversity. Case 1 resembled the histology of atypical adenomatous hyperplasia or adenocarcinoma in situ. However, the proliferating epithelium was immunohistochemically negative for TTF-1 and positive for p40. Case 2 morphologically resembled ciliated muconodular papillary tumors, but differed immunohistochemically with negative results for TTF-1 and CEA in the proliferating ciliated columnar epithelium [13, 14]. Moreover, the proliferating epithelia were characteristically composed of ciliated columnar cells lined with p40-positive basal-like cells. Previous studies indicated that p63 or p40 immunohistochemistry was useful in distinguishing reactive and neoplastic glandular proliferations in bronchioloalveolar epithelium [15]. As solitary peribronchiolar metaplasia is a tumor-like lesion showing various histology from case to case, pathological diagnosis should be carefully performed using immunohistochemistry.

Conclusion

In summary, we report two cases of solitary peribronchiolar metaplasia clinically misdiagnosed as malignant. In terms of reduction of overdiagnosis and overtreatment, solitary peribronchiolar metaplasia should be noted as one type of benign pulmonary lesion showing as a sub-solid nodule on CT.

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Compliance with ethical standards

Conflict of interest None declared.

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