CASE REPORT

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A case of peribronchiolar metaplasia of the lung appearing as a solid nodule on computed tomography

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ABSTRACT

Peribronchiolar metaplasia is an uncommon lesion characterized by fibrosis and bronchiolar epithelial cell proliferation along the peribronchiolar alveolar walls, primarily in response to bronchiolar and peribronchiolar injuries. Peribronchiolar metaplasia usually appears as ground glass nodules or sub-solid nodules on computed tomography. However, we present an exceptional case of peribronchiolar metaplasia that appeared as a solitary solid nodule on computed tomography. A 62-year-old woman with conjunctival icterus was diagnosed with ampullary cancer and nodal metastasis. A solid predominant nodule (0.7 cm maximum diameter) in the left lower lobe was identified on computed tomography, requiring accurate differentiation between primary lung cancer and pulmonary metastasis. Due to the location, histological confirmation via transbronchial biopsy was not feasible. Hence, the patient underwent surgery for both diagnosis and treatment. The pathological findings revealed the growth of columnar epithelium containing ciliated cells replacing alveolar epithelium in the bronchioloalveolar wall with no malignant component. The final pathological diagnosis of the lesion was peribronchiolar metaplasia. This unique case highlights an atypical presentation of peribronchiolar metaplasia as a solitary solid nodule on computed tomography. Recognizing that peribronchiolar metaplasia can also manifest as solid nodules, as illustrated in our current case, is essential.

Keywords: peribronchiolar metaplasia, PBM, lung neoplasms, epithelial cell proliferation

Abbreviations:
PBM: peribronchiolar metaplasia
CT: computed tomography
BA: bronchiolar adenoma
CMPT: ciliated muconodular papillary tumor

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INTRODUCTION

Peribronchiolar metaplasia (PBM) is characterized by fibrosis and the proliferation of bronchiolar epithelium along the peribronchiolar alveolar walls, often occurring in response to bronchiolar and peribronchiolar injuries.[1] PBM typically presents as ground glass opacity lesion on computed tomography (CT)[1-3] and rarely manifests as a solitary nodule. This unique presentation necessitates careful discrimination between PBM and primary lung cancer and metastatic lung tumors. In this report, we describe a case of PBM appearing as a solid nodule on CT imaging and the diagnostic challenges this presentation posed.

CASE PRESENTATION

A 62-year-old woman presented at Daido Hospital with conjunctival icterus as her chief complaint. Upon thorough examination, the patient was diagnosed with ampullary cancer accompanied by nodal metastasis. Pretreatment CT revealed a pulmonary nodule in the left lower lobe. The nodule appeared as a solid predominant nodule with a maximum diameter of 0.7 cm (Figure 1). No significant lymph node enlargement in the hilar and mediastinal regions was detected. Diffusion-weighted whole-body imaging with background body signal suppression showed no abnormalities, aside from the duodenal lesion.

The pulmonary nodule was suspected to be primary lung cancer or pulmonary metastasis of ampullary cancer. Accurate diagnosis of the nodule was important for staging the ampullary cancer and for treatment. If the nodule was a primary lung cancer, radical surgery was necessary, and if the nodule was metastasis of the ampullary cancer, the ampullary cancer would be diagnosed as stage IV. A transbronchial biopsy to determine the histology of the pulmonary nodule was difficult to obtain due to the location of the nodule. Consequently, a surgical procedure was planned to determine the diagnosis and treat the nodule.

The patient's preoperative history included nonsmoking status and a history of hypertension and dyslipidemia. Her laboratory results revealed elevated CA19-9 levels but no abnormalities in other serum tumor markers. Video-assisted thoracic surgery under general anesthesia was performed to diagnose the nodule. Based on the location of the nodule, an anatomical pulmonary resection was planned. The patient underwent left basal segmentectomy for the nodule to enable

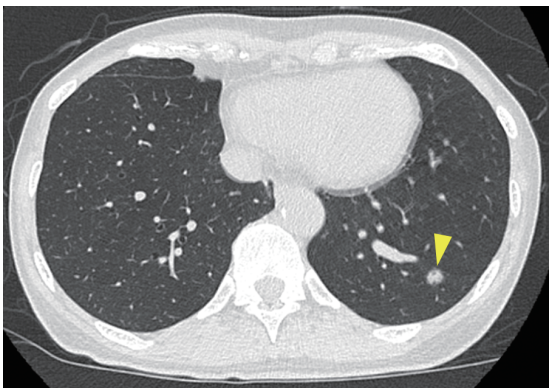

Fig. 1 Chest computed tomography image shows a solid nodule, presenting as a solid predominant nodule with a maximum diameter of 0.7 cm.

radical resection in case of primary lung cancer and resection with adequate margins in case of metastatic lung tumors. Intraoperative histopathological diagnosis was performed using the frozen section technique. A diagnosis of primary lung cancer or metastasis of ampullary carcinoma could not be confirmed.

The nodule was 0.5 × 0.5 cm. The microscopic findings are shown in Figure 2. The nodule was difficult to identify in the excised specimen because it was elastic, soft, and difficult to palpate. Upon histopathological examination, the tumor displayed characteristics consistent with PBM, including growth of ciliated columnar epithelium, replacing the alveolar epithelium of the bronchioloalveolar wall, without any malignant components (Figure 2a-2c). Immunostaining confirmed a bilayer structure with epithelial cells positive for TTF-1 and lined by p40 positive basal cells (Figure 2d, 2e). Thus, the final pathological diagnosis was PBM.

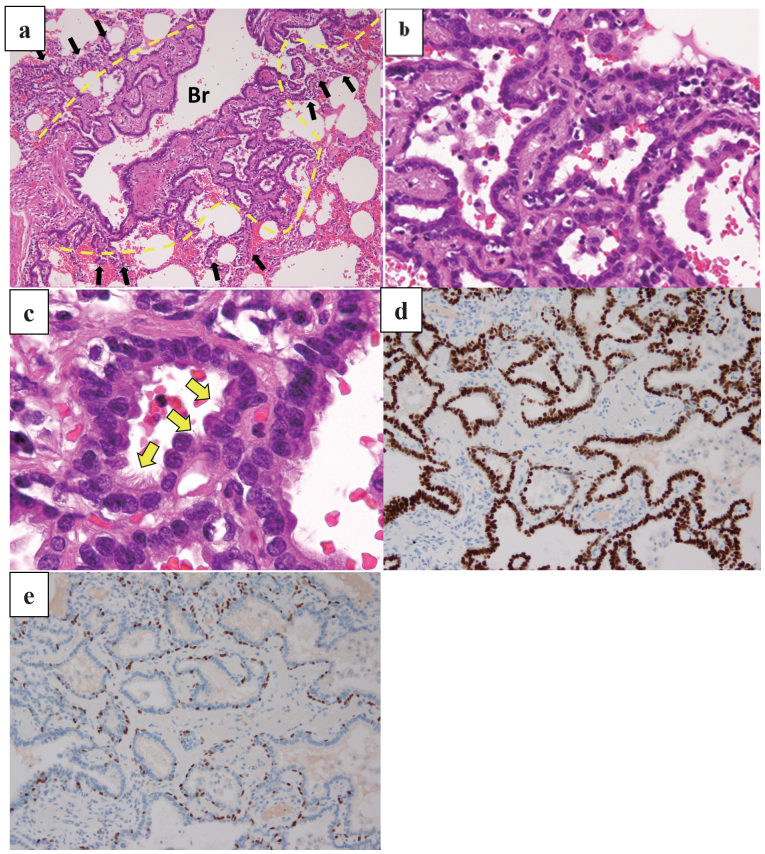

Fig. 2 Histopathological findings (Hematoxylin-Eosin and immunostaining)

Fig. 2a: The area inside the yellow dotted line is the peribronchiolar metaplasia (PBM) area. The lesion was 0.5 cm in maximum diameter. It showed proliferation of bronchiolar epithelium along the alveolar wall. The black arrows around PBM show an area of hyperplasia of type II alveolar epithelium, which have transitioned from the PBM. (×100) Br: bronchioles

Fig. 2b: Columnar epithelium containing ciliated cells were growing with replacing alveolar epithelium of bronchioloalveolar wall. Macrophage infiltration was observed in a part of the alveoli. (×400)

Fig. 2c: Ciliated cells are indicated by triangles. (×1000)

Fig. 2d: Epithelial cells are positive for TTF-1. (×200)

Fig. 2e: Basal cells are positive for p40. (×200)

The patient's postoperative course was uneventful, and the patient was discharged seven days after surgery. The patient was subsequently diagnosed with ampullary carcinoma (cT2aN1M0, cStage IIIA) and underwent pancreatoduodenectomy one month after the pulmonary resection. The patient is currently under observation and no signs of ampullary carcinoma recurrence have been detected six months postoperatively.

DISCUSSION

We present a case of PBM in the lung, which manifested as a solid nodule on CT. Diagnosis required careful differentiation from primary lung cancer and metastatic lung tumors. PBM is a nonspecific reaction to bronchiolar and peribronchiolar injury, resulting in fibrosis and proliferation of bronchiolar epithelium along the peribronchiolar alveolar walls. Fukuoka et al reported the features of 15 patients with clinical evidence of interstitial lung disease (ILD) in whom PBM was the primary histologic finding. The designations of PBM and PBM-ILD were suggested in this report. High-resolution CT images and CT images taken during exhalation were effective in diagnosing PBM, and mosaic attenuation or mild lobular air trapping were characteristic CT image features of PBM-ILD.[4]

Based on previous reports, the presentation of PBM as a solitary nodule, as observed in the current case, is rare. Most previously documented cases of PBM exhibited ground glass nodule or sub-solid nodule characteristics on CT imaging. These nodules exhibited progressive growth or the emergence of a solid component within the nodule on CT scans over time, eventually prompting heightened suspicion of malignancy.[1-3] Matsui et al reported the case of a 7 mm ground glass nodule that was monitored biannually; a solid component surfaced fifty-three months after the initial detection. Over the next six months, the nodule's size gradually increased to 11 mm. This progression led to suspicions of early-stage lung adenocarcinoma, resulting in partial resection and the ultimate diagnosis of PBM.[2]

PBM requires pathological differentiation from bronchiolar adenoma (BA)/ciliated muconodular papillary tumors (CMPT). BA/CMPT is a peripherally nodular tumor that first described as CMPT, the tumor showing papillary proliferation of abundant mucinous and ciliated cells, by Ishikawa et al[5] in 2002. The concept of BA which includes CMPT as one subtype was proposed by Chang et al[6] in 2018. Those lesions were listed in the 2021 WHO classification.[7] The defining features of BA/CMPT is nodular proliferation of bland bilayered bronchiolar-type epithelium with a continuous basal cell layer. Genomic alternations have detected involving BRAF V600E, EGFR exon 19 deletions, EGFR exon 20 insertions, KRAS, HRAS, ALK, and AKT1.[8] BA classified into proximal type which containing abundant ciliated and mucinous cells and distal type which containing predominantly cuboidal cells and only scant or absent ciliated and mucinous cells. PBM and distal-type BAs share many histologic features including peribronchiolar localization, bilayered proliferation, and scarce mucinous cells.[6] According to a report by Chang et al, TTF-1 was negative or weakly-focally positive in proximal-type BAs similar to proximal bronchiolar epithelium, but in distal-type BAs, TTF-1 showed diffuse positivity in both luminal and basal cells similar to respiratory bronchioles. They also reviewed staining of lung tissue with interstitial lung disease and PBM, which shows frequent positivity for TTF-1. Although there is a report that TTF-1 is negative in PBM,[1] there is a report of TTF-1 positive in PBM. Therefore, it could be recognized that TTF-1 positivity or negativity is not useful for differential diagnosis between PBM or other lesions.[9] In the present case, the luminal cells were positive for TTF-1. The differential points between PBM and BA/CMPT are that BA include a solitary, well-circumscribed lesion with a distinctly nodular contour and presence of ciliated cells on micropapillary tufts or

in peculiar outpouchings, in contrast, PBM tend to show ill-defined borders and they present as discrete nodules.[6,8] Han et al discussed the differentiation between BA and PBM. They noted that PBM typically presents as multiple lesions, each measuring ≤1 mm, and is often associated with a history of chronic interstitial lung disease.[9] Conversely, Yasuura et al reported two cases of solitary lesions measuring ≥1 cm, which were not linked to interstitial lung disease.[1] PBM lesions can occasionally appear as solitary lesions large enough to be differentiated from malignancies on CT imaging,[1-3] as was observed in the current case. Although Han et al have reported an association between PBM and interstitial lung disease,[4,9] it is not invariably linked to such conditions, as PBM is essentially a reactive change to bronchiolar and peribronchiolar injury. Previous reports of solitary PBM cases also did not reveal any interstitial lung disease,[1-3] and no interstitial shadows or other abnormal findings were observed in the background lung of the current case. Han et al recommended genomic testing for differentiating between BA and PBM due to identified mutations such as KRAS, HRAS, ALK, and AKT1 in BA cases. However, Chang et al reported that 14% of patients with BA (3 out of 21 cases) lacked any genetic mutations, suggesting that the absence of genetic mutations cannot be the sole criterion for diagnosing PBM. Therefore, the critical distinction between BA/CMPT and PBM primarily relies on histopathological morphology, with immunostaining and genetic testing serving as supplementary diagnostic tools. In the present case, PBM was diagnosed based on morphological features of ill-defined borders. Therefore, the critical distinction between BA/CMPT and PBM primarily relies on histopathological morphology, with immunostaining and genetic testing serving as supplementary diagnostic tools. In the present case, PBM was diagnosed based on morphological features of ill-defined borders. Prior reports have consistently depicted PBM nodules as ground glass nodules (GGNs) on CT images, a consequence of the proliferation of bronchiolar epithelium along the alveolar wall. When the interstitium exhibits fibrotic changes, these nodules may manifest as partially solid components on CT imaging. Consequently, PBM often presents as pure-GGN or partially solid nodules, posing a challenge in distinguishing PBM from lung adenocarcinoma with a lepidic growth pattern.[1-3] In most cases described in the literature, PBM lesions have been distinguished from pulmonary malignancies by the GGN appearance on imaging. In contrast to these previous reports, the PBM in the current case manifested as a solid nodule on CT imaging. Microscopic examination revealed macrophage infiltration within certain alveoli of the lesion, indicative of an inflammatory response in the subacute phase. During the CT imaging, the substantial presence of inflammatory cell infiltration and the accumulation of exudate within the nodule may have contributed to the solid nodule appearance.

CONCLUSIONS

We present a case of PBM that appeared as a solitary nodule on CT, necessitating differentiation from pulmonary malignant tumors. While PBM often appears as a GGN on CT imaging, recognizing that PBM can also manifest as a solid nodule, as illustrated in the current case, is important.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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