Ciliated muconodular papillary tumour of the lung: a newly defined low-grade malignant tumour

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Abstract

We present two cases of ciliated muconodular papillary tumour (CMPT) in this report. CMPT is a newly defined low-grade malignant tumour with ciliated columnar epithelial cells, occurring in the peripheral lung. Both patients underwent pulmonary resection due to an enlarged solitary pulmonary nodule. Pathological findings in both cases confirmed a papillary tumour with a mixture of ciliated columnar and goblet cells. The tumours were rich in mucous and had spread along the alveolar walls, as observed in bronchioloalveolar carcinoma. Nuclear atypia was mild, and no mitotic activity was observed. Immunohistochemically, tumour cells stained positive for carcinoembryonic antigen, thyroid transcription factor-1 and cytokeratin 7 but not for cytokeratin 20. The immunohistochemical staining patterns were almost identical to those of pulmonary adenocarcinoma. We definitively diagnosed as CMPT. Both patients remained relapse-free.

Keywords: Ciliated muconodular papillary tumour; Low-grade malignancy; Peripheral lung

1. Introduction

Lung tumours with ciliated cells are considered benign, and most of these tumours occur in the central airway [1, 2]. Herein we report two cases of ciliated muconodular papillary tumour (CMPT), which is considered a low-grade malignant tumour with ciliated epithelial cells, occurring in the peripheral lung.

2. Case presentation

2.1. Case 1

A 67-year-old man, a smoker (20 pack/year) having no remarkable medical history, was referred to us with flu-like symptoms. Computed tomography (CT) revealed a lung tumour, 5 mm in diameter in the right S3 segment. Follow-up CT 18 months later revealed that the tumour had slightly enlarged to 6 mm in diameter. The patient desired follow-up observation. Follow-up CT 10 months later revealed that the tumour had further enlarged to 9 mm in diameter with ground glass opacity (GGO) surrounding the tumour (Fig. 1a). Primary lung cancer was suspected, and video-assisted right S3 partial resection was performed. Frozen sections revealed papillary tumours with a mixture of ciliated epithelial and goblet cells. We considered it a low-grade malignant tumour because of the presence of ciliated cells and performed partial resection with wide tumour-free margins. Microscopic analysis revealed that the tumour cells were composed of ciliated columnar and goblet cells with papillary growth (Fig. 1b,c). Some tumour cells had spread along the alveolar walls, as observed in bronchioloalveolar carcinoma. Nuclear atypia was mild, and no mitotic activity was observed. Immunohistochemically, the tumour cells stained positive for carcinoembryonic antigen (CEA), thyroid transcription factor-1 (TTF-1) and cytokeratin 7 (CK7) but not for cytokeratin 20 (CK20) (Fig. 1d,e). These immunohistochemical findings were almost identical to those observed for adenocarcinoma, which is a typical primary lung cancer of the peripheral lung. We diagnosed the tumour as CMPT. After surgery, the patient remained relapse-free for 10 months.

2.2. Case 2

Following a medical check-up, a 59-year-old woman with no previous medical and smoking history was referred to our institution for further examination of GGO in the right S9 segment, which was revealed by chest CT. We suspected the lesion to be a benign lung tumour and placed the patient under observation. Follow-up CT six months later revealed a tumour 7 mm in diameter with a central cavity (Fig. 1f). We suspected primary lung cancer and performed video-assisted right S9 partial resection. Analysis of the frozen sections revealed a papillary tumour with a mixture of ciliated epithelial and goblet cells, similar to case 1. Based on these findings, we suspected CMPT and performed partial resection. Light microscopic and immunohistochemical findings were also similar to case 1 (papillary tumour...
with ciliated columnar and goblet cells, mild nuclear atypia, lack of mitotic activity and positive staining for CEA, TTF-1 and CK7 but not for CK20. Therefore, this tumour was also confirmed to be CMPT. There was no local and distant failure 18 months after surgery.

3. Discussion

CMPT is a papillary tumour with cilia occurring in the peripheral lung. It is a rare tumour, with few reported cases [3, 4]. The tumour is not classified according to the 2004 fourth edition of the World Health Organization classification pathology and genetics of tumors of the lung, pleura, thymus, and heart [5]. Lung tumours with cilia are rare and are considered benign. Most of them occur in the central airway [1, 2, 6]. A unique feature of CPMT, besides developing in the peripheral lung, is the presence of columnar ciliated epithelial cells. Additionally, although morphological findings revealed few malignant characteristics, immunohistochemical findings suggested it to be malignant. The two cases reported here have mild nuclear atypia and no mitotic activity. Immunostaining was positive for CEA, TTF-1 and CK7 and negative for CK20, and these findings were similar to those observed in case of peripheral lung adenocarcinoma.

The differential diagnoses were (i) hyperplasia, (ii) papilloma and (iii) extremely well-differentiated adenocarcinoma. Hyperplasia is unlikely in CPMT because histology of

<table>
<thead>
<tr>
<th>Author</th>
<th>Age/ gender</th>
<th>Location</th>
<th>CT finding</th>
<th>Preoperative diagnosis</th>
<th>Size (mm)</th>
<th>Immunohistochemical findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ishikawa [3]</td>
<td>30 F</td>
<td>RUL</td>
<td>GGO, Central density</td>
<td>(Papilloma)</td>
<td>15</td>
<td>+ n/a n/a n/a n/a n/a n/a n/a –</td>
</tr>
<tr>
<td>Harada [4]</td>
<td>62 M</td>
<td>LLL</td>
<td>N, High</td>
<td>–</td>
<td>9</td>
<td>+ – + – – n/a – –</td>
</tr>
<tr>
<td>Present case</td>
<td>67 M</td>
<td>RLL</td>
<td>Y (margin), High</td>
<td>–</td>
<td>8</td>
<td>+ + + (10%) – + + –</td>
</tr>
<tr>
<td>Present case</td>
<td>59 F</td>
<td>RUL</td>
<td>Y (pure), Low</td>
<td>–</td>
<td>5</td>
<td>+ + + (3%) + – + – –</td>
</tr>
</tbody>
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CMPT, ciliated muconodular papillary tumour; CT, computed tomography; GGO, ground glass opacity; CEA, carcinoembryonic antigen; TTF-1, thyroid transcription factor-1; CK, cytokeratin; MUC, mucin; rec, recurrence; prg, prognosis; n/a, not applicable; RUL, right upper lobe; RLL, right lower lobe; LLL, left lower lobe.
the background lung was normal. Papilloma, particularly solitary glandular papilloma, is a rare and benign lung tumour that generally occurs in the central airway [6]. Recently, Aida et al. reported solitary glandular papilloma of the peripheral lung [7]. Although light microscopy revealed that glandular papilloma is most similar to CMPT, immunohistochemical details of malignant characteristics were unclear, and the authors evaluated the glandular papilloma to be benign. Nakamura et al. reported an extremely well-differentiated adenocarcinoma with ciliated epithelial and goblet cells [8]. However, nuclear atypia and mitosis were prominent in this adenocarcinoma.

There are four reported cases of CMPT including the two cases presented here [3, 4]. The clinical and immunohistochemical features are shown in Table 1. The incidence rate has not been described previously. At our institution, only two (0.05%) among 4200 cases of lung cancer or suspected lung cancer have been diagnosed as CMPT in the past 20 years. In all four cases, the patients were in their 50s and 60s. Additionally, the tumour might occur in any pulmonary lobe, and there was no correlation of tumour occurrence with smoking. CT findings revealed pure GGO to high-density depending on the amount of mucous and fibrosis. Preoperative pathological diagnosis was not available because the tumour was small and located in the peripheral lung region, except in one case diagnosed with papilloma, where the tumour had spread to the subsegmental bronchus [4]. Immunohistochemically, all cases were positive for CEA. The immunostaining findings of these cases, including our cases, were almost similar to the staining pattern of adenocarcinoma, which is a representative lung cancer of the peripheral lung. All reported cases survived without recurrence. Based on these clinical and pathological observations (light microscopy and immunohistochemistry), we consider that CMPT is a newly defined well-differentiated pulmonary tumour with malignant potential, although it has ciliated epithelial cells.

Malignant tumours with cilia have been reported in other organs [9, 10]. Ciliated carcinoma is a variant of endometrial carcinoma and a representative malignant tumour with cilia. This tumour is also a low-grade malignant tumour with a good prognosis; however, careful distinction from benign lesions must be made because of the presence of myometrial or lymphatic invasion [10]. For practical purposes, differential diagnosis of CMPT from peripheral lung cancer is important. Surgical intervention, in particular, would be necessary to distinguish CMPT from mucous-rich bronchioalveolar carcinoma showing high-density on CT. CMPT should be considered in cases where ciliated tumour cells are recognized in frozen sections.

Based on previous reports and our observations, for tumours with low-grade malignant features and no recurrences, partial resection with wide tumour-free margins seem an appropriate treatment. We have reported two cases of CMPT. Further investigation is required to clearly determine the clinical and pathological features of this tumour.

References