Human Pathology (2016) **49**, 22–26

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Human PATHOLOGY

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Case study

Ciliated muconodular papillary tumor: a solitary peripheral lung nodule in a teenage girl☆

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Received 8 August 2015; revised 23 September 2015; accepted 25 September 2015

Keywords:
Glandular papilloma;
Ciliated muconodular papillary tumor;
Papillary adenocarcinoma;
Mucinous adenocarcinoma;
Peripheral lung tumor

Summary Papillary tumors of the peripheral lung containing ciliated cells and extracellular mucin include solitary peripheral ciliated glandular papilloma, ciliated muconodular papillary tumor, and well-differentiated papillary adenocarcinoma with cilia formation. We report the case of a 19-year-old woman who was a nonsmoker and presented with an incidental small peripheral lung nodule. The resection specimen showed a soft grayish nodule. Histologic examination further revealed a relatively circumscribed mucinous nodule featuring a tubulopapillary tumor composed of ciliated columnar cells and goblet cells, accompanied with abundant extracellular mucin. No lepidic growth pattern was evident. The tumor cells were immunoreactive for cytokeratin 7, thyroid transcription factor-1, and carcinoembryonic antigen, whereas p63 and cytokeratin 5/6 highlighted the presence of basal cells. Next-generation sequencing did not identify any genetic alterations in targeted regions and mutational hotspots of a panel of 22 genes commonly implicated in lung and colon cancers. Taken together, our case was most likely a ciliated muconodular papillary tumor.
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1. Introduction

Papillary tumors of the peripheral lung, which contains ciliated cells and extracellular mucin, encompass benign neoplasms such as solitary peripheral ciliated glandular papilloma (SPCGP) [1–4] and ciliated muconodular papillary tumor (CMPT) [5–9] at one end to well-differentiated papillary adenocarcinoma with cilia formation [10,11] at the opposite end of the spectrum. Distinguishing these entities on small biopsies and frozen sections can be challenging. Here, we report a case of a 19-year-old teenager with a small peripheral lung nodule who was otherwise asymptomatic. Histologic examination showed a circumscribed mucinous tumor with a papillary architecture, composed of ciliated cells, goblet cells, and basal cells.

2. Case report

A 19-year-old Chinese female student presented with an incidental finding of a small 1.2-cm right lung lower-lobe

☆ Disclosures: No financial support was needed for the preparation of this manuscript. There was no conflict of interest.

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http://dx.doi.org/10.1016/j.humpath.2015.09.038
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nodule (Fig. 1A) during workup for a large left paraovarian cyst in June 2013. She underwent emergency cystectomy for torsion in July 2013, and histology showed a papillary serous cystadenoma. Intraoperatively, both ovaries and uterus were normal. Follow-up serial computed tomography of the thorax (Fig. 1B) in October 2013 and April 2014 showed a stable solitary right lower-lobe nodule with no new masses or thoracic lymphadenopathy. Radiologically, the nodule contained an eccentric lucent area suspicious for cavitation.

The patient had a medical history of childhood asthma, but was not on any medication. She was a nonsmoker. There was a strong family history of malignancies; her maternal grandfather had lung cancer, her paternal grandfather had liver cancer, and her paternal aunt had breast cancer.

She underwent right video-assisted thoracoscopic surgery (VATS) lower-lobe wedge resection in August 2014. Macroscopic examination of the resection specimen showed a soft grayish nodule measuring 1.3 × 1.2 × 1 cm in the lung parenchyma. It was diagnosed as a mucinous neoplasm on frozen section during intraoperative consultation. The paraffin sections showed a relatively circumscribed mucinous nodule featuring a tubulopapillary tumor composed of ciliated columnar cells and goblet cells (Fig. 2A-D). No lepidic growth pattern was evident. The nuclei were regular, euchromatic with inconspicuous nucleoli, and about 1.5 times bigger than the size of normal bronchiolar counterparts. No mitotic figures were seen. Pools of abundant basophilic extracellular mucin distended the nodule's crevices and surrounding alveolar spaces. The margin of resection was free of tumor.

The ciliated columnar cells, goblet cells, and basal cells were all immunoreactive for cytokeratin (CK) 7 and thyroid transcription factor-1 (TTF-1) (Fig. 3A and B), with patchy positivity for carcinoembryonic antigen (CEA) at the luminal aspect of the ciliated columnar cells and goblet cells (Fig. 3C). Some of the goblet cells also showed strong staining for napsin-A, which was not noted in the ciliated columnar cells and basal cells (Fig. 3B). Focal weak delicate staining for MUC5AC was seen in rare ciliated columnar cells (Fig. 3D) and goblet cells (Fig. 3E), but not in basal cells. All 3 cell types were negative for CK20 (Fig. 3F) and MUC2 (data not shown). Ki-67 immuno-labeling highlighted scattered basal cells at a rate comparable to normal bronchiolar counterparts (Fig. 3G). Immunohistochemistry for CK5/6 and p63 showed positive staining in basal cells (Fig. 3H).

Tumor DNA was extracted from macrodissected sections prepared from paraffin-embedded tissue and was subjected to next-generation sequencing with Ion AmpliSeq Colon and Lung Cancer Panel (Life Technologies, Carlsbad, CA) (which included *KRAS*, *EGFR*, *BRAF*, *PIK3CA*, *AKT1*, *ERBB2*, *PTEN*, *NRAS*, *STK11*, *MAP2K1*, *ALK*, *DDR2*, *CTNNB1*, *MET*, *TP53*, *SMAD4*, *FBXW7*, *FGFR3*, *NOTCH1*, *ERBB4*, *FGFR1*, and *FGFR2*). No genetic alterations were detected in targeted regions and mutational hotspots of all the genes evaluated in this assay.

Taking into account the histomorphology, immunophenotype, and molecular profile, we proposed a diagnosis of CMPT.

3. Discussion

SPCGP is an extremely rare lesion arising from peripheral bronchioles in older adults who are mostly nonsmokers [1,2]. This tumor is composed of fibrovascular cores covered by ciliated or nonciliated columnar cells with varying number of cuboidal and goblet cells. The presence of basal cells is highlighted by immunohistochemistry for CK17 [2]. As opposed to papillary adenocarcinoma, the tumor cells in SPCGP do not display any cytologic or architectural atypia, mitoses or necrosis. CMPT is another extremely rare tumor of the peripheral lung in middle-aged to elderly adults of East

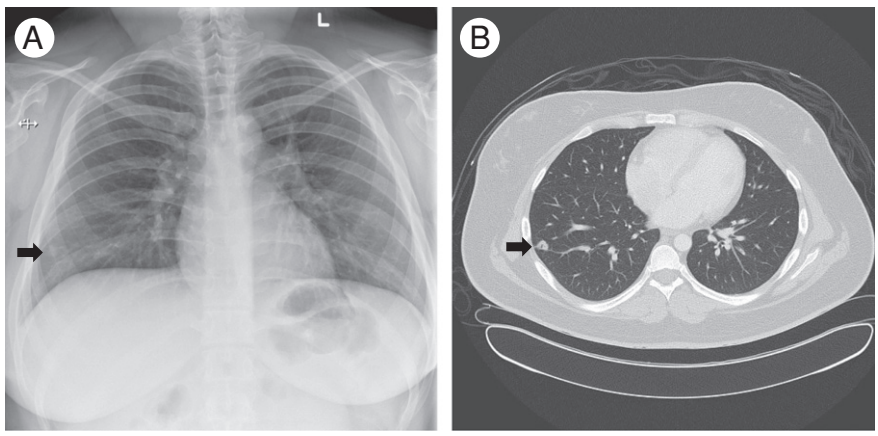

Fig. 1 A, Chest x-ray showing nodular opacity (black arrow) in right lower zone. B, Computed tomography of the thorax showing well-defined 1.2-cm nodule (black arrow) in the laterobasal segment of the right lower lobe with eccentric lucent area suspicious for an area of cavitation.

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