Pulmonary mixed squamous cell and glandular papilloma mimicking adenocarcinoma: a case study and literature review

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ABSTRACT

Mixed squamous cell and glandular papilloma of the lung is an extremely rare benign neoplasm. Here we present another case of mixed squamous cell and glandular papilloma in a 64-year-old female nonsmoker. Histologically, the tumor was composed of mainly papillary structures covered with squamous, glandular and transitional epithelium. Some glandular structures extending into adjacent bronchiolar and alveolar spaces with mucus were similar to adenocarcinoma. Immunohistochemical analysis showed the different kinds of epithelia had similar immunophenotype. The different components were positive for cytokeratin (CK) 7, CK19, CAM5.2, CK5/6, CK34βE12, and TTF-1, but negative for CK20. The transitional morphology and immunohistochemistry indicate the different components likely come from a same kind of progenitor in the bronchiolar wall.

KEY WORDS

Lung; pulmonary; mixed squamous cell and glandular papilloma


Case report

A 64-year-old female nonsmoker was admitted to our hospital because of chest pain without cough, hemoptysis, and other systemic symptoms. A chest CT scan revealed a peripheral solid nodule with a diameter of 13 mm in the lower lobe of the right lung (Figure 1A). The lesion did not present lobulated sign or spiculated sign, however, focal pleural indentation was observed (Figure 1B). From the CT scan, the diagnosis of lung cancer could not be excluded. Following wedge resection was performed. On gross examination, the tumor itself varied from grey to pale yellow. Microscopically, squamous and glandular epithelium could be observed, and in some area transitional epithelium like urothelium with morphology between the two kinds of epithelium was also present. Including transitional epithelium, all kinds of epithelium displayed papillary growth architectures (Figure 2A-C). The glandular epithelium consisted of non-ciliated columnar cells with eosinophilic cytoplasm and some mucin-filled cells (Figure 2B). In addition, the different epithelium showed no significant atypia, while some glandular tumor cells extended into adjacent bronchiolar and alveolar spaces with mucus which is similar to adenocarcinoma with lepidic-like pattern (Figure 2B). Further Immunohistochemical analysis showed these different components were diffusely positive for cytokeratin (CK) 7 (Figure 3A), CK19, CAM5.2,
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Figure 1. A. CT revealed a peripheral lump in the right lower lobe of the lung; B. Focal pleural indentation (arrow).

Figure 2. Hematoxylin and eosin (HE) staining (original magnification ×100). A. Papillary structure composed of squamous epithelium; B. Papillary structure composed of glandular epithelium consisted of non-ciliated columnar cells and some mucin-filled cells. Some glandular tumor cells extended into adjacent bronchiolar and alveolar spaces with mucus which is similar to adenocarcinoma; C. Papillary structure composed of urothelium-like epithelium.

Discussion

Solitary pulmonary papillomas are rare tumors (1-3). The recent World Health Organization classification of lung tumors subdivides papillomas into three separate categories: squamous cell papilloma, glandular papilloma and mixed papilloma, of which mixed papilloma is the most extremely rare entity which accounted for 15.85% of all cases (3).

All mixed papillomas occurred in middle-aged and old people with a male preponderance (14 males and 5 females). Most patients are smokers, suggests smoking be a causative factor for that. Initial symptoms could be hemoptysis, syndromes of pneumonia or chest pain, but some cases was found by chance and showed no significant symptoms (1-7). Most cases were central endobronchial type arising from the wall of a stem bronchus or its major subdivisions (1-3,5-7). Of the 18 reported cases,
only 3 were peripheral type which arose within the peripheral small bronchus (4,8,9). The present case is an additional case of peripheral mixed papilloma in the lung. HPV DNA was detected in most cases of squamous cell papilloma, indicating HPV may be a cause of that (2), however, HPV DNA has not been found yet in mixed papilloma and glandular papilloma of the lung (2,5-8,10). Although HPV ISH was not investigated in this case, the negative p16 staining indirectly suggests there is no existence of HPV.

Microscopically, the tumor was composed of squamous and glandular epithelium, and transitional urothelium-like morphology between the two kinds of epithelium was also present, which suggested the different kinds of epithelium come from the same origin. Some cases showed malignant transformation including focal squamous cell carcinoma in situ, adenocarcinoma (1-3) and spindle and squamous cell carcinoma (9). But it seemingly didn’t have influence to the favourable prognosis (1-3). In this case, the epithelium showed no significant atypia, however, some of its glandular tumor cells extended into adjacent bronchiolar and alveolar spaces with abundant mucus. This growth pattern could be confused with bronchoalveolar carcinoma or adenocarcinoma with papillary or micropapillary features. In fact, this morphology had been mentioned in a few cases of mixed papilloma, glandular carcinoma with papillary or micropapillary features. We consider that different kinds of tumor cells lacking atypia can assist pathologists to make the correct diagnosis.

Interestingly, the immunohistochemical analysis showed these different kinds of epithelia had similar immunophenotype. Our findings were similar to that of Inamura et al. reported (7): all kinds of epithelia were diffusely positive for CK7, CK19, CAM5.2, CK5/6 (the staining of the mucous cells were weak) and CK34βE12, but negative for CK20. All kinds of epithelia were positive for TTF-1, which was strongly immunostained in the basal cells of squamous component, while became weaker as the maturity of squamous epithelium, and finally disappeared in the surface layer of the squamous epithelium. In consideration of aboving histological and immunohistochemical findings, we consider the tumor’s different components arise from the same kind of progenitor cells which can differentiate into different components, including glandular, squamous and urothelium-like epitheliums.

Herein, we reported a case of mixed papilloma in the lung. Since this tumor is extremely rare, the etiology and pathological characteristics are still unclear. In a few cases of mixed papilloma, glandular tumor cells can extend into bronchiolar and alveolar spaces with mucus, therefore, pathologists need to watch for it to avoid misdiagnosis. To our knowledge, recurrence has not been reported in mixed papilloma, and complete resection appears to be a curative treatment for this rare tumor.

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References

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