CASE REPORT

Pulmonary Papillary Adenoma: Report of Two Cases

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ABSTRACT
Pulmonary papillary adenoma is a rare tumor. Two cases without any clinical symptoms were enrolled in our hospital. Both cases were incidentally detected in pulmonary area by imaging. Pathological examination revealed well-circumscribed nodules consisting of papillary growth of cuboidal to low columnar epithelial cells lining the surface of the fibrovascular stroma. Immunohistochemistry (IHC) staining showed that the lining cells were diffusely positive for TTF-1, CK, p63, CK7, and Napsin A. The Ki-67 proliferation index was approximately 2%. The morphological features and the IHC profile of the tumor were in agreement with that of pulmonary papillary adenoma. Both patients are doing well without recurrence or metastasis of the tumor.

Key Words: Pulmonary. Papillary adenoma. Differential diagnosis.

INTRODUCTION
Pulmonary papillary adenoma is a rare tumor of the lung. Since 1980, when Spencer et al.1 first described two cases of papillary adenoma of the lung, 25 cases have been reported worldwide.2 These tumors are benign and can occur over a broad age range, including children. Some scientists speculated their malignant potential owing to the microinvasive characteristics.3 Two cases of pulmonary papillary adenoma, together with a review of the related literature, will be discussed.

CASE REPORT

Case 1: A 64-year female without any significant past medical history presented a 17 x 15 mm sized mass in the upper lobe of the right lung on a computed tomography (CT) scan prescribed for an unrelated purpose. A malignant tumor was suspected, and hence, a lobectomy was performed; a 15 x 15 x 12 mm, well-encapsulated, brownish-white tumor was observed with some hemorrhagic areas. Currently, the patient is alive without tumor recurrence or metastasis at 6 months of follow-up.

Case 2: A 41-year female, without a previous history of admission to our hospital, complained about a left pulmonary nodule incidentally detected on CT scan. The patient was asymptomatic. The results of physical examination and routine laboratory studies were within the normal limits. Chest CT showed a well-defined, 20 mm, homogeneous nodular shadow in the left lobe. The radiologist considered it as a metastatic tumor. The patient received thoracoscopic wedge resection.

Microscopically, the tumor was observed with well-circumscribed margin, but no capsule was apparent. It was a branching papillary growth with slender fibrovascular cores (Figure 1). The surface of the cores was covered by columnar epithelium and a small amount of cuboidal epithelium. Focally, some adenoid structures were appreciated. Cytoplasmic eosinophilia, few vacuoles, and no intracellular mucus were observed. The nucleus was oval or circular, localized in the basal region or away from the basal surface, harbored small nucleoli, with mild atypia, grooves were not obvious. Mitotic activity and necrosis were not recorded. Glandular lumens showed eosinophilic secretions. The focal aggregation of cells formed multinucleated giant cells. Papillary axis showed visible lymphocytes, plasma cells, few mast cells, histiocytes, and focal lymphoid follicle formation.

Immunohistochemistry (IHC) was performed using the labeled streptavidin-biotin method and overnight incubation. IHC demonstrated that the tumor cells were stained moderately or strongly for cytokeratin7 (CK7), thyroid transcription factor-1 (TTF-1), Napsin A, and carcinoembryonic antigen (CEA). A few tumor cells (2%)

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Received: December 21, 2016; Accepted: July 07, 2017.

Figure 1: A dense branching papillary growth with slender fibrovascular cores.
were positive for Ki-67 (Figure 2). However, the staining was found to be negative for vimentin, synaptophysin, CD56, and Thyroglobulin (TG).

Subsequently, we assessed the EGFR and K-ras genes and failed to find any mutations. We used AMRS assay for this purpose.

**DISCUSSION**

Pulmonary papillary adenoma is rare. Since the initial description of papillary adenoma by Spencer et al., fewer than 25 cases have been reported in the literature. Patients’ age ranged from 2 months to 70 years, with an average of 34.67 years. The number of males were slightly more than the females. Moreover, no clinical symptoms were noted. The tumors were observed incidentally on imaging, in the left lower lobe of lung, followed by right upper lobe and lower lobe. Adenoma was rare in the left upper lobe and right lobe of the lung. Majority were solitary tumors with occasional multiple nodules. Light microscopy displayed a branching papillary growth of the tumor; few cases demonstrated solid areas, and occasional cases showed micro glandular structure. The surface of the tumor was covered with cuboidal or columnar epithelium with occasional ciliated cells. The cytoplasm was eosinophilic or clear, the nucleus round or oval, and eosinophilic inclusions were found in the nucleus. Fukuda et al. and Krodo et al. found fibro vascular cores lacked elastic fibers, which is characteristic of the tumor. Interstitial fibrosis was found in some cases. In the current cases, several papillary processes were seen covered by cuboidal and columnar epithelium. No ciliated cells were seen. Interstitial alterations in the vascular core were similar to those found in the literature. IHC staining showed that the lining cells were diffusely positive for TTF-1, EMA, CK, CK7, SPA, p63, and Napsin A, and negative for vimentin, synaptophysin, and CD56. The stromal cells were negative for TTF-1. Ki-67 was expressed in about 2% of all the tumor cells.

Electron microscopy of the epithelial cells revealed secretory granules of high electron density and osmiophilic lamellar bodies. Ultrastructural features favored type II alveolar epithelium and Clara cell differentiation. Hence, the tumor is also known as Clara cell adenoma, bronchiolar adenomas, and type II alveolar papillary tumor.

The pathogenesis of papillary lung tumor is yet unclear. Some authors suggest that it originates from the bronchioalveolar epithelial stem cells. Other studies suggest that it may be associated with inflammation. Dessy et al. reported 2 cases with undetermined malignant potential: one case showed infiltration of lung parenchyma and pleura while the second one showed capsular invasion. Kondo et al. reported one case of infiltration of bronchioles and adjacent lung tissue and small veins. Spencer et al. reported one case wherein the tumor invaded the capsule and invaded the adjacent alveolar region. Knodo et al. reported a case of infiltrating bronchial with a malignant potential. EGFR gene mutations are early events in pulmonary adenocarcinoma. EGFR and K-ras gene mutations were not found in both our cases. Case 2 demonstrated along with papillary lung tumor, a splenic tumor and uterine fibroids; splenic tumor underwent pathological examination as hamartoma. However, whether the patient harbors a genetic alteration that causes these tumors is not yet clarified.

The differential diagnosis of the tumor includes pulmonary sclerosing pneumocytoma, alveolar adenoma, and papillary adenocarcinoma. It is critical to differentiate among these, as these have different therapeutic implications.

Pulmonary papillary adenoma is an extremely rare tumor characterized by widespread papillary structures. Such cases challenge the pathologists necessitating several considerations and careful diagnosis.

**REFERENCES**