

Papillary Adenoma of Type 2 Pneumocytes in the Lung

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Recent developments in radiologic imaging and thoracoscopic excision techniques have increased the possibility of encountering small, benign or premalignant tumors in the lung. In this report, we describe a rare case of papillary adenoma of type 2 pneumocytes. A 51-year-old Japanese woman was hospitalized following a traffic accident. Helical CT scan of the chest incidentally detected a nodular ground-glass opacity measuring 8 mm in diameter at the subpleural region of left lung. The nodule was thoracoscopically resected out. Light microscopic examination demonstrated a noninfiltrative tumor consisting of cuboidal cells covering fibrovascular cores; thus, the tumor exhibited a branching papillary appearance. The cuboidal cells showed little nuclear atypia. Mitotic figures, necrosis, and intercellular mucin were absent. The cytoplasm was immunohistochemically stained for surfactant apoprotein A and cytokeratin, though not for carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), or S100 protein. The morphologic and immunohistochemical findings fulfilled the criteria of papillary adenoma of type 2 pneumocytes.

Key Words: papillary adenoma of type 2 pneumocytes, surfactant apoprotein A

Introduction

Although most bronchioloalveolar tumors are malignant, apparently benign or potentially malignant forms have been described as the following types; papillary adenoma, mucinous cystadenoma, bronchioloalveolar adenoma, also referred to as atypical alveolar hyperplasia, and alveolar adenoma¹⁾. Recent develop-

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ments in radiologic imaging and thoracoscopic excision techniques have increased the possibility of encountering such benign or premalignant tumors in the lung. In this report, we describe a case of papillary adenoma of type 2 pneumocytes in the lung. We also discuss the pathologic differentiation among those benign or premalignant tumors.

Case Report

A 51-year-old Japanese woman was hospitalized in July 1998 following a traffic accident. The patient was generally bruised. Radiologic examination was performed to evaluate possible internal injuries. Helical computed tomography (CT) of the chest incidentally found a nodular ground-glass opacity measuring 8 mm in diameter at the subpleural region of the left lung (B¹⁺²); no other lesion was noted in the lung itself. After recovering from the bruise, the patient underwent CT of the chest on December 1998, which demonstrated that the size of the lesion remained unchanged (Fig. 1). Physical and laboratory examinations

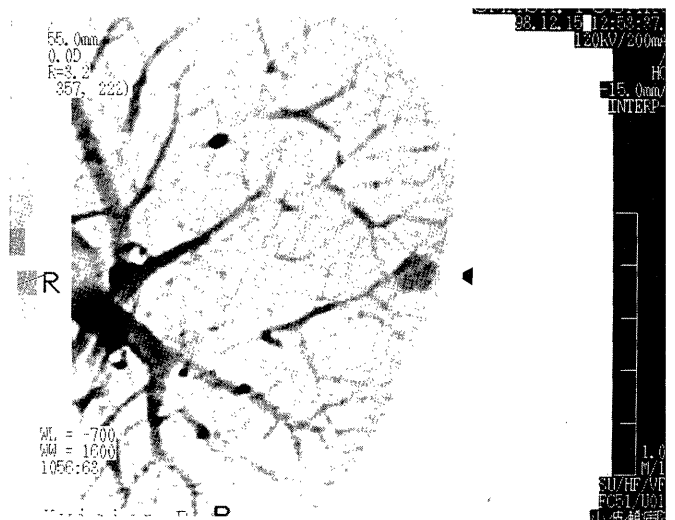


Figure 1. Computed tomography of the chest. Note a nodular ground-glass opacity in the subpleural region of left lung (B¹⁺², arrowhead).

were within normal limits. The patient underwent thoroscopic excision biopsy of the nodule. She has been well for 4 months after the operation. She has no history of smoking or exposure to known occupational or environmental toxins.

Pathologic Examination

The biopsy specimen was fixed in 10%-buffered formalin. The tumor, 5 x 3 mm in size at the cut surface and located at the subpleural region without any pleural indentation, was circumscribed, but nonencapsulated

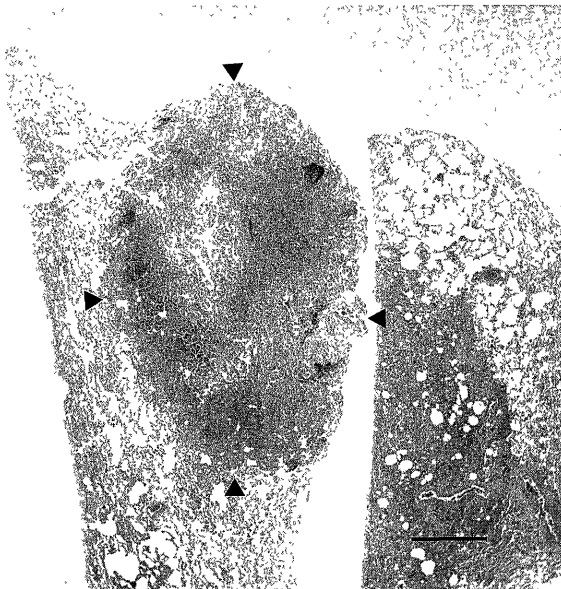


Figure 2. Low power view of the nodule. The tumor is circumscribed but not encapsulated (arrowhead, bar: 1 mm).

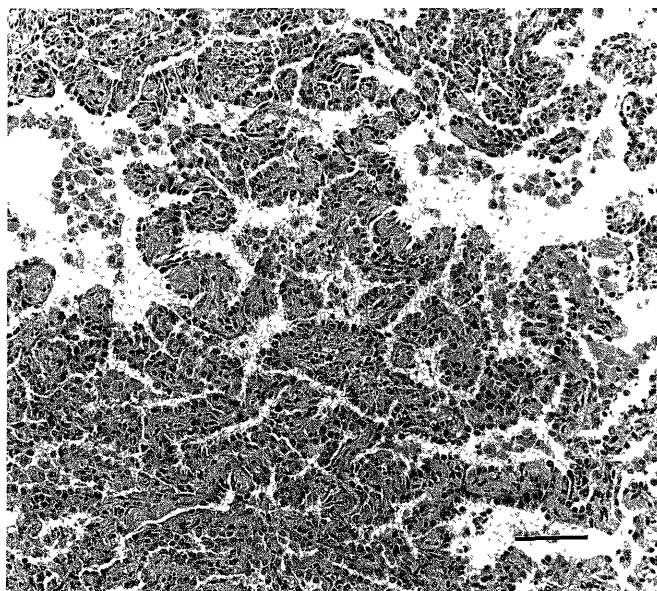


Figure 3. Cuboidal cells cover the papillae containing fibrovascular cores (Hematoxyline Eosin Stain, bar: 100 μ m).

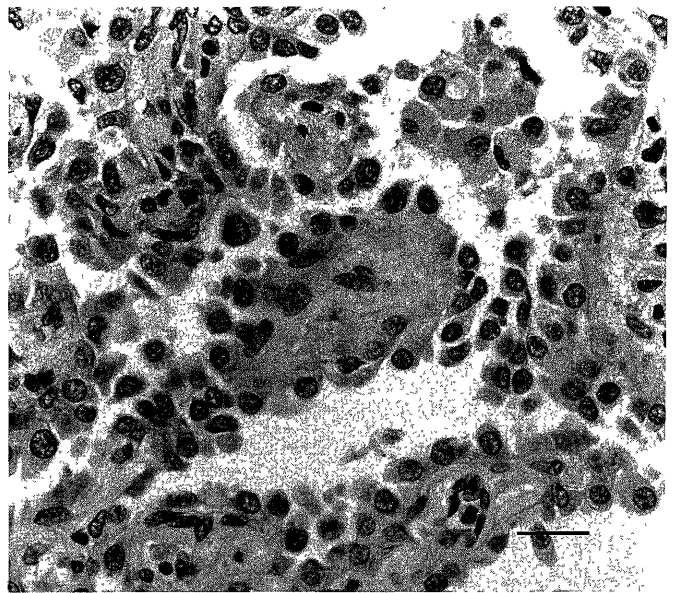


Figure 4. The nuclei of cuboidal cells contain delicate chromatin and nuclear membranes. No cellular atypia or mitoses is present (Hematoxyline Eosin Stain, bar: 25 μ m).

(Fig. 2). These sectioned specimens were embedded in paraffin and cut into 4 μ m-thick sections for routine stains and immunohistochemistry. The antibodies used for immunohistochemistry were as follows: anti-surfactant apoprotein A (DAKO JAPAN, Co. Ltd., Tokyo), cytokeratin (DAKO Corporation, Carpinteria, CA), carcinoembryonic antigen (CEA; Immuno-Biological Laboratories, Fujioka, Gunma, Japan), epithelial membrane antigen (EMA; Nichirei Co. Ltd., Tokyo), and S100 protein (DAKO A/S, Glostrup, Denmark). Light microscopic examination revealed papillary structures in the tumor (Fig. 3). Cuboidal cells with round to oval nuclei containing delicate chromatin and nuclear membranes covered fibrous cores (Fig. 4). We noted no histologic features of carcinoma such as cellular atypia, necrosis, or mitoses. The cytoplasm was immunohistochemically stained for surfactant apoprotein A and cytokeratin, though not for CEA, EMA or S100 protein (Figure 5). The histologic and immunohistochemical findings fulfilled the diagnostic criteria of papillary adenoma of type 2 pneumocytes^{2,3}.

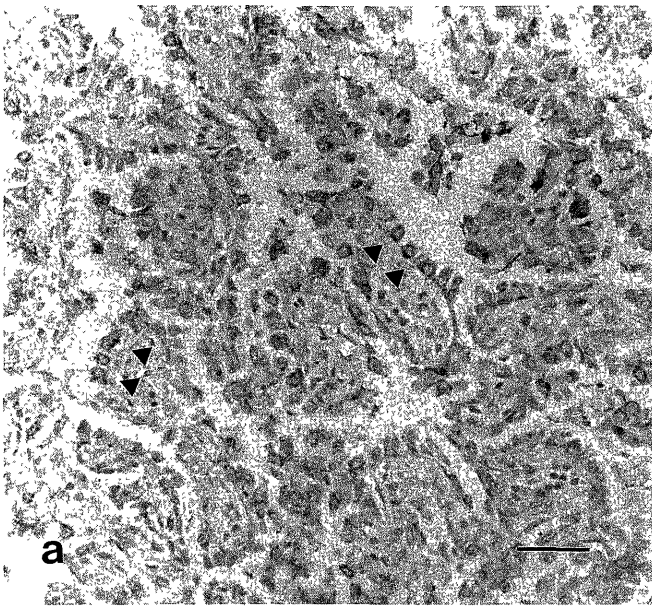


Figure 5. a) Tumor cells are positive for surfactant apoprotein A (arrowhead, bar; 50 μ m).

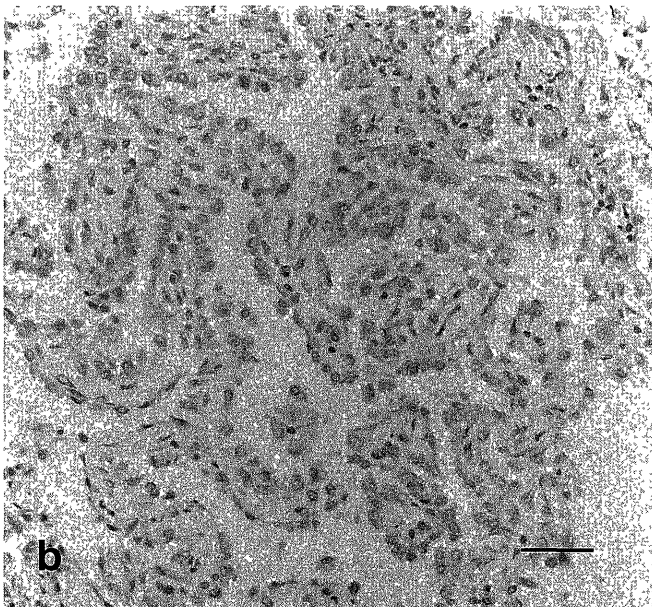


Figure 5. b) Tumor cells were negative for CEA (bar; 50 μ m).

Comments

Spencer et al.⁴⁾ have noted unusual, benign, non-invasive papillary tumors in which the lining cells resemble Clara cells. An ultrastructural study⁵⁾ demonstrates concentric lamellar inclusions in the cytoplasm of tumor cells, indicating their similarity to Clara cells or type 2 pneumocytes. Subsequent immunohistochemical

studies have also shown that the tumor cells exhibit a Clara cell-specific antigen⁶⁾ or surfactant apoproteins in the cytoplasm²⁷⁾. Although most authors have regarded this type of tumor as benign, Mori et al.⁸⁾ report one case in which tumor cells invaded into the surrounding lung tissues and a small vessel.

The differential diagnosis of papillary adenoma of type 2 pneumocytes includes bronchioloalveolar adenoma, bronchioloalveolar carcinoma, alveolar adenoma, and sclerosing hemangioma³⁾. Bronchioloalveolar adenoma, a possible precursor lesion of bronchioloalveolar carcinoma, exhibits a lepidic growth rather than a papillary pattern, and greater cytologic atypia than papillary adenoma³⁾. Most cases are found in the lung adjacent to bronchioloalveolar carcinoma or bronchogenic adenocarcinoma¹⁾. Alveolar adenoma, first identified by Yousem and Hochholzer⁹⁾, presents as a solitary subpleural nodule. Microscopically, it is composed of multiple cystic spaces filled with serous or floccular material or by blood. The lining of the cysts is largely inapparent or consisting of flattened cells that are immunohistochemically uncertain in the cell origin. Sclerosing hemangioma, originally described by Liebow and Hubbell¹⁰⁾, has been thought to represent epithelial neoplasms derived from bronchiolar epithelial cells, type 2 pneumocytes, or Clara cells. It shows a greater diversity of histopathologic patterns that Katzenstein et al.¹¹⁾ have categorized as solid, hemorrhagic, papillary, and sclerotic patterns.

The histologic and immunohistochemical findings in the present case favor the diagnosis of papillary adenoma of type 2 pneumocytes, although some parts of the tumor might mimic the pattern of bronchioloalveolar adenoma.

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