Papillary Lung Carcinoma With Prominent "Morular" Component

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Abstract

Three cases of primary pulmonary papillary carcinomas with a prominent "morular" component involved 2 women and 1 man (age range, 25-68 years). The patients had symptoms related to the pulmonary mass, including chest pain, cough, and dyspnea. Radiographic evaluation of the thorax revealed the presence of a pulmonary mass. Surgical biopsies were obtained and reported as non–small cell carcinoma. All patients underwent lobectomy. Two tumors were located in the right upper lobe and 1 in the left upper lobe. The tumors were soft, white to tan, without evidence of necrosis or hemorrhage, and 2.5 to 3.5 cm in greatest diameter. The tumors were characterized predominantly by papillary architecture containing numerous "morules" composed of spindle cells without nuclear atypia or mitotic activity. Some morules were floating freely within papillary spaces; others seemed to detach from the papillary structures. Immunohistochemical studies of 2 tumors showed positivity for thyroid transcription factor-1, keratin, and carcinoembryonic antigen and negativity for thyroglobulin. The morules showed positive thyroid transcription factor-1 staining, weak keratin staining, and negative staining for smooth muscle actin, desmin, and HMB-45. These cases highlight an unusual phenomenon, that of primary papillary carcinomas of the lung with a prominent morular component.

Primary lung carcinomas composed predominantly of papillary features are relatively unusual. The majority of lung carcinomas in which papillary features are present are well-differentiated adenocarcinomas with a bronchioloalveolar growth pattern or bronchioloalveolar carcinomas.[1] In contrast, the presence of "morules" in primary lung neoplasms generally is associated with pulmonary blastoma.[2,3]

Herein we report 3 cases of primary pulmonary papillary carcinoma with a prominent "morular" component. These cases highlight an unusual phenomenon, which requires special attention to properly classify the neoplasms.

Cases

Clinical Findings

The patients were 2 women and 1 man between the ages of 25 and 68 years. Clinically, all patients had symptoms of chest pain, cough, and dyspnea. Radiographic evaluation showed the presence of a pulmonary mass. Two tumors were located in the right upper lobe, and 1 tumor was located in the left upper lobe. The specimen from the initial biopsy in the 3 cases was interpreted as non–small cell carcinoma. All patients underwent lobectomy. The pathologic staging was T1 N0 M0 for 2 patients and T2 N0 M0 for 1 patient.

Gross Features

The tumors were described as well circumscribed, soft, white to tan, and without necrosis or hemorrhage. The tumors measured from 2.5 to 3.5 cm in greatest diameter.

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Histologic Features

Scanning magnification revealed that the tumors were characterized by prominent papillary architecture with branching papillary projections of different sizes. In addition, within empty spaces, there were small to medium-sized buds of tumor cells **Image 1**. At closer magnification, the dual cell population present in these tumors became apparent **Image 2**. The papillary component was composed of branching papillary projections lined by cuboidal cells with moderate cytologic atypia and scattered mitotic figures. The cords of these papillary projections were present in some areas with a discrete vascular component and inflammatory cells. Meanwhile, the morular component present within empty spaces was composed of tightly packed spindle cells without evidence of nuclear atypia or mitotic activity **Image 3**. In some areas, these morules seemed to detach from the epithelium lining the papillary neoplasm.

Foci of conventional well-differentiated adenocarcinoma were present in all cases. However, the papillary component made up more than 75% of the tumor.

Immunohistochemical Features

Immunohistochemical studies were performed in 2 cases using antibodies for smooth muscle actin, desmin,

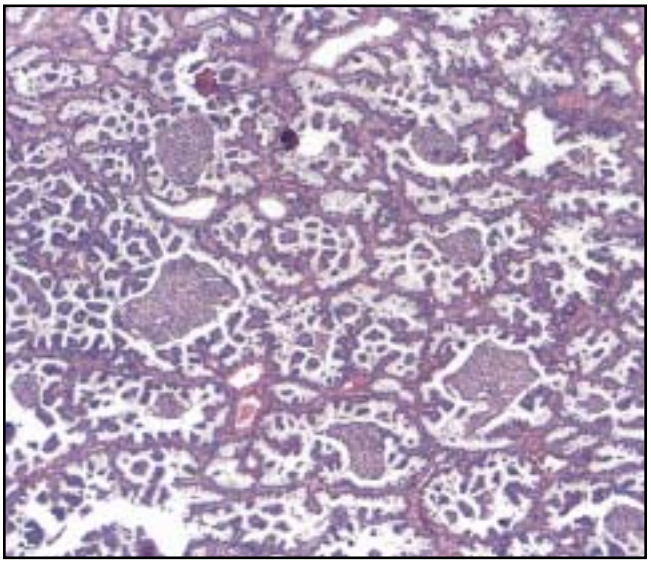

Image 1 Low-power view of a predominantly papillary carcinoma of the lung containing small buds within empty spaces (H&E, ×20).

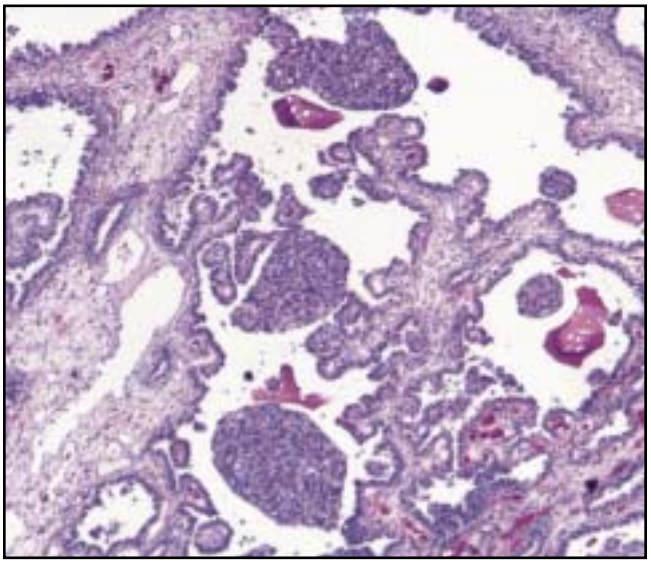

Image 2 Intermediate-power magnification showing 2 distinct cellular populations (H&E, ×25).

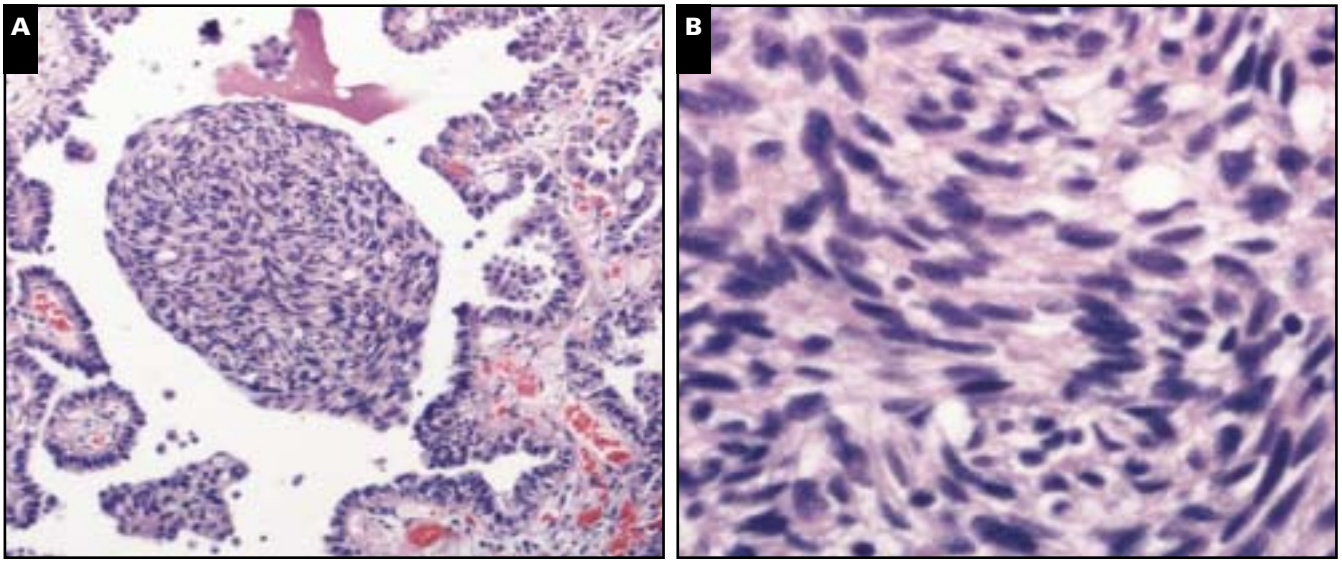

Image 3 **A**, Closer view of a small "morule" surrounded by a papillary carcinoma (H&E, ×35). **B**, High-power view of a morule showing a spindle cell proliferation lacking nuclear atypia and/or mitotic activity (H&E, ×60).

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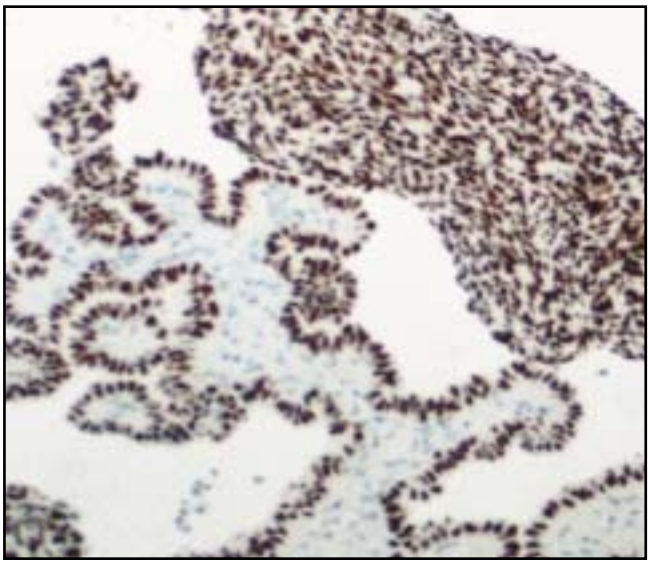

Image 4 Immunohistochemical stain showing a strong positive reaction not only in the papillary component but also in the morular component (thyroid transcription factor-1, ×35).

HMB-45, keratin, carcinoembryonic antigen, and thyroid transcription factor (TTF)-1. The papillary component showed strong positive staining for keratin, carcinoembryonic antigen, and TTF-1, whereas the morular component showed a strong positive reaction only with TTF-1 **Image 4** and a weak positive reaction for keratin. The stains for smooth muscle actin, desmin, and HMB-45 were all negative.

Follow-up

Two patients were alive 6 months after surgical resection of the tumor; 1 patient was lost to follow-up.

Discussion

The vast majority of primary lung carcinomas are of the non–small cell type, namely squamous cell carcinoma and adenocarcinoma.[1] The World Health Organization panel for the classification of lung tumors modified the criteria for the diagnosis of bronchioloalveolar carcinoma. Thus, these tumors are becoming less common.[4] Nevertheless, features such as mucinous, nonmucinous, and papillary features are well known to be associated with well-differentiated adenocarcinomas with bronchioloalveolar growth pattern or with bronchioloalveolar carcinoma.[1]

The existence of "true papillary" carcinomas of the lung has been recognized for some time. In 1997, Silver and Askin[5] described a series of primary lung neoplasms, which they classified on the basis of histologic features alone as true papillary carcinomas. According to them, these tumors are composed of at least a 75% papillary growth pattern. In their experience, papillary carcinoma has considerably worse morbidity and mortality than conventional bronchioloalveolar carcinoma. Some later reports seem to support such an analysis. Householder et al[6] reported a case of lung papillary carcinoma with metastases to the ovary, and Chang et al[7] reported an additional case of papillary lung carcinoma with cutaneous metastases.

These true papillary lung carcinomas should be separated from another entity labeled as *lung adenocarcinomas with micropapillary component* by Amin et al.[8] In this latter neoplasm, the tumors are adenocarcinomas with areas resembling the micropapillary features seen in other tumors such as of the ovary, breast, and bladder. In none of the cases described as true papillary carcinoma or adenocarcinoma with micropapillary component has the presence of morules been described focally or as a major component as in our cases. The presence of morules in lung neoplasia generally has been associated with unusual tumors such as pulmonary blastomas with monophasic or biphasic histologic features.[2,3] These tumors represent less than 1% of primary lung neoplasia, and the presence of morules is a distinctive feature, which helps to properly diagnose these tumors.[2,3] The morules are small buds of spindle cell proliferation, which generally do not show nuclear atypia or mitotic activity. The morules have been shown to have positive staining for immunohistochemical markers, including epithelial and neuroendocrine markers.[2]

The cases described herein represent an unusual phenomenon. In all of our cases, the histologic features of the neoplasm were those of a predominantly papillary carcinoma of the lung. However, the presence of small buds of spindle cells might raise a wider differential diagnosis. Perhaps more important is the differentiation from pulmonary blastoma. In such cases, the presence of morules is in association with a complex glandular pattern that resembles "embryonal" fetal lung. Thus, the mere presence of morules does not make any tumor a blastoma. On the other hand, the presence of morules in blastomas usually is adjacent to glandular structures or discretely placed in the interstitium. In the cases herein described, the morules were floating in the papillary spaces or, in a few instances, almost detaching from the lining of the papillary structures.

Other considerations would include the presence of a smooth muscle component or even lymphangioleiomyomatosis. However, in the former, the negative reaction of the spindle cells for muscle markers would make such a possibility unlikely, whereas in the latter, the radiologic evidence of a pulmonary mass and the negative staining of the spindle cell for muscle markers and HMB-45 also would make such a possibility unlikely. Another consideration would be that of meningothelial proliferation or

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meningioma.[9] Both of these conditions would manifest with a small pulmonary nodule or a pulmonary mass. However, these entities are not characterized by the presence of floating spindle cells in the papillary spaces. The morular component might be a diagnostic challenge in a small biopsy specimen. However, in the 3 cases reported herein, that component was not present in the initial biopsy specimen. Awareness of this feature in other tumors unrelated to pulmonary blastomas is important to properly classify these neoplasms.

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References

1. Colby TV, Koss MN, Travis WD. *Tumors of the Lower Respiratory Tract*. Washington, DC: Armed Forces Institute of Pathology; 1995. *Atlas of Tumor Pathology*; Third Series, Fascicle 13.
2. Koss MN, Hochholzer L, O'Leary T. Pulmonary blastomas. *Cancer*. 1991;67:2368-2381.
3. Berho M, Moran CA, Suster S. Mixed epithelial and mesenchymal tumors of the lung. *Semin Diagn Pathol*. 1995;3:67-72.
4. Travis WD, Colby TV, Corrin B, et al. *Histological Typing of Lung and Pleural Tumours*. 3rd ed. Berlin, Germany: Springer; 1999. *World Health Organization International Histological Classification of Tumours*.
5. Silver SA, Askin FB. True papillary carcinoma of the lung: a distinct clinicopathologic entity. *Am J Surg Pathol*. 1997;21:43-51.
6. Householder J, Han A, Edelson MMI, et al. Immunohistochemical confirmation of pulmonary papillary adenocarcinoma metastatic to ovaries. *Arch Pathol Lab Med*. 2002;126:1101-1103.
7. Chang SE, Choi JC, Moon KC. A papillary carcinoma: cutaneous metastases from lung cancer [letter]. *J Dermatol*. 2001;28:110-111.
8. Amin MB, Tamboli P, Merchant SH, et al. Micropapillary component in lung adenocarcinoma: a distinctive histologic feature with possible prognostic significance. *Am J Surg Pathol*. 2002;26:358-364.
9. Moran CA, Rush W, Hochholzer L, et al. Primary meningiomas of the lung: a clinicopathologic and immunohistochemical study of 10 cases. *Cancer*. 1996;78:2328-2333.

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