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The Necessity of Histology

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Introduction

The overwhelming majority of primary lung malignancies are secondary to smoke inhalation and occur in the older adult population in the presence of symptoms that are usually suspicious for an underlying malignancy. A chest radiograph is the initial imaging modality of choice to diagnose a lung cancer. However, a small percentage of lung cancer occurs despite a lack of smoking history whatsoever and in asymptomatic individuals.

This case outlines an example of a rare type of primary lung cancer found to be metastatic at diagnosis in a young adult despite the patient being virtually asymptomatic and not having a smoking history. It demonstrates the absolute necessity in considering primary lung cancer as a diagnosis even in younger patients without a smoking history who are asymptomatic if there is no definite etiology for an abnormal chest radiograph.

Case Summary

A 42-y-old lifetime non-smoking female presented with a 3-month history of a cough, with a chest radiograph revealing innumerable bilateral pulmonary nodules with a basal predominance. There were also significant interstitial opacities (Fig. 1). She was completely asymptomatic except for a mild nonproductive cough. There were no B symptoms (ie, fevers, night sweats, or weight loss). Her appetite was normal, and she was exercising regularly with no limitations. There were no symptoms of connective tissue disease. Travel and occupational history were negligible. She was not on any medications and denied illicit drug use. She had no allergies.

A computed tomography scan of the chest was completed and revealed randomly scattered bilateral nodules with a basal predominance. Some nodules demonstrated central cavitation (Fig. 2), and there were regions of bronchiectasis (Fig. 3).

Fig. 1. Frontal chest radiograph demonstrating innumerable poorly defined pulmonary nodules with a basal predominance. Some appear to have cavitation.

The differential was broad. Even though the radiographic pattern was not classical for sarcoidosis, the clinical-radiographic disparity suggested that sarcoidosis was a possible etiology. Screening blood work was completed and found to be normal. A bronchoscopy was performed but did not elicit results. Thus, she underwent a video-assisted thoracoscopy for a lung biopsy.

The histology with immunohistochemical staining revealed stage IV adenosquamous carcinoma (Figs. 4–6). Because a portion of her lung cancer was adenocarcinoma, the samples were sent for epidermal growth factor receptor mutations and found to be positive. A subsequent com-

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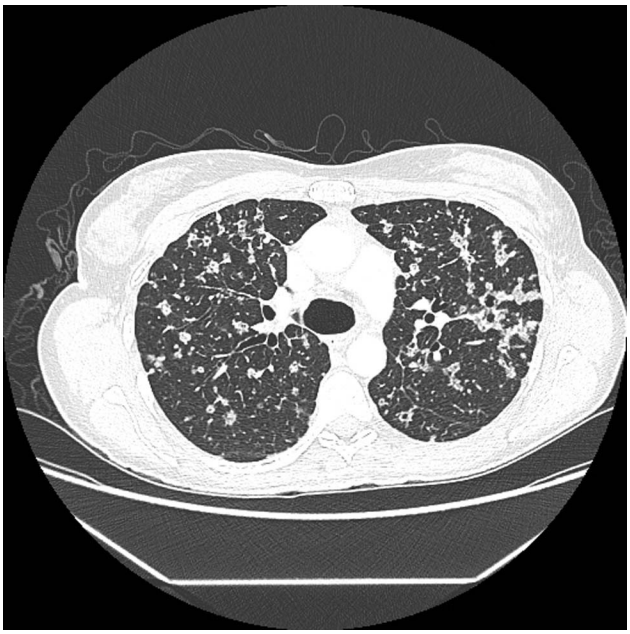

Fig. 2. High-resolution computed tomography of the chest confirming poorly defined cavitating nodules.

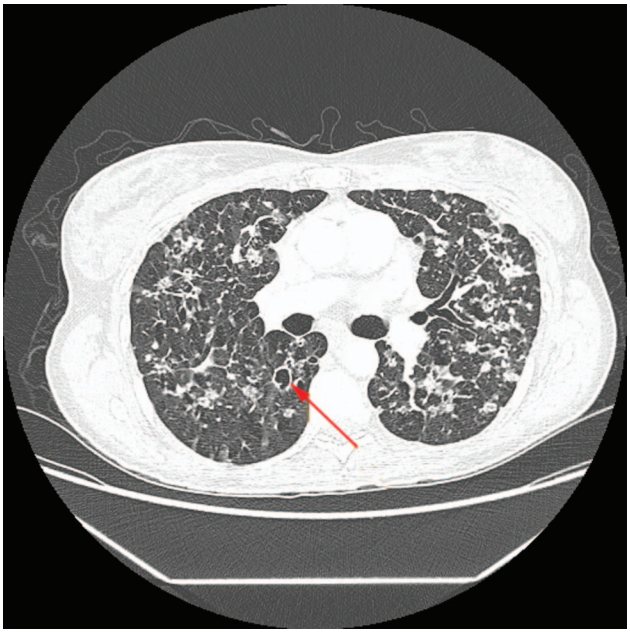

Fig. 3. High-resolution computed tomography of the chest demonstrating cavitating nodules and focal bronchiectasis (arrow).

puted tomography scan of the abdomen (including the adrenal glands) was negative for malignancy.

Discussion

Histologic evaluation and immunohistochemical staining played a pivotal role in the diagnosis and management

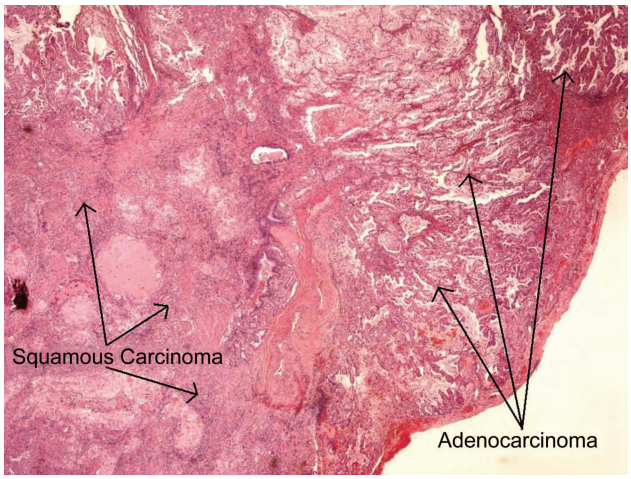

Fig. 4. Photomicrograph of a lung biopsy with hematoxylin and eosin staining at medium power magnification showing areas of both adenocarcinoma and squamous cell carcinoma.

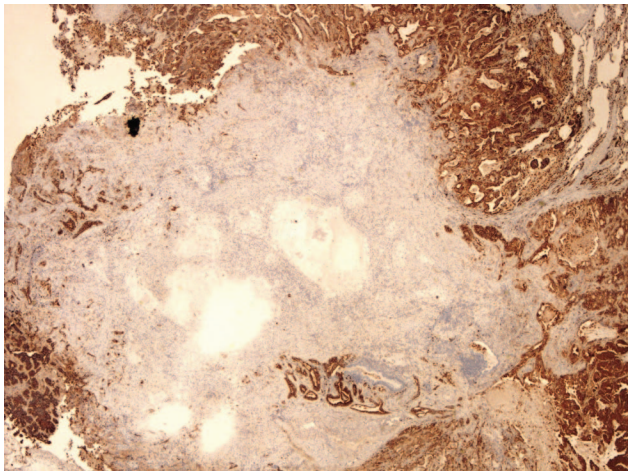

Fig. 5. Photomicrograph of a lung biopsy at low power magnification with napsin A staining (dark areas) positive for adenocarcinoma.

this patient's metastatic lung disease. Given that the prognosis and management of the various types of lung cancer continue to diverge, histologic criteria have become the foundation for a new classification system.[1] Immunohistochemical stains have also become more pertinent than ever before. Napsin A, for example, is a useful antibody with high specificity in diagnosing primary lung adenocarcinoma.[2] Moreover, a diagnosis of primary adenocarcinoma of the lung usually leads to testing for the epidermal growth factor receptor gene mutation, which, if positive, leads to novel targeted therapy with tyrosine kinase inhibitors.[3]

The immunohistochemical stains in this case were not only positive for napsin A but also for cytokeratin-5. Cytokeratin-5 staining is both sensitive and specific for squa-

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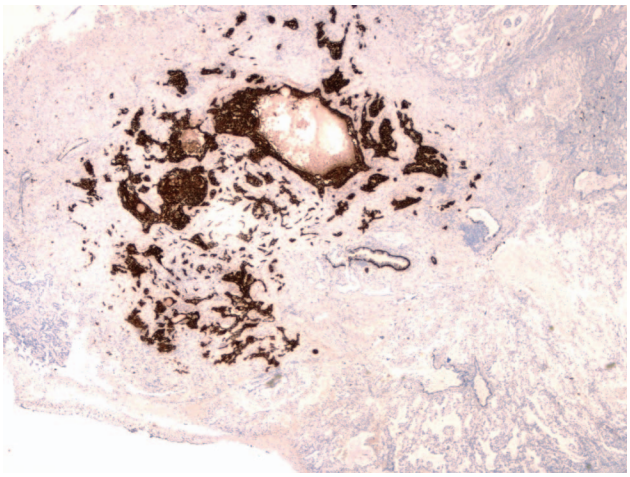

Fig. 6. Photomicrograph of a lung biopsy at low power magnification with cytokeratin-5 staining (dark areas) positive for squamous cell carcinoma.

mous cell carcinoma.[2] This is equally important given that some treatment regimens, such as pemetrexed, have shown significant benefit in only non-squamous cell lung cancers.[4]

The most recent classification system categorizes adenosquamous carcinoma of the lung as its own entity.[5] The defining characteristics of adenosquamous carcinoma are dependent on a biopsy revealing components of adenocarcinoma and squamous cell carcinoma, with each comprising at least 10% of the tumor.[6] Adenosquamous carcinoma comprises 0.3–0.5% of non-small cell lung cancers, appears to be clinically distinct from either adenocarcinoma or squamous cell carcinoma of the lung, and carries a worse prognosis than either of these as well.[7,8] Clinically, these types of lung cancer are more commonly associated with younger adults. Radiographically, they may present with significant cavitating lung nodules.[9]

This case underscores the idea that primary lung cancer can occur in various age ranges with or without risk factors. The physician must be aware of this, and the significant variation in prognosis and treatment modalities of primary lung cancers relies heavily on an initial histological assessment.

Teaching Points

- Despite clinical impression, histological evaluation is pertinent in evaluating chest radiographic abnormalities of unknown etiology.
- Immunohistochemical staining techniques are necessary to further classify and manage pulmonary malignancies using the most recent classification system.
- Adenosquamous carcinoma of the lung is a rare type of non-small cell lung cancer with a poor prognosis.

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