Salivary gland-type neoplasm of the lung

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Abstract

Salivary gland-type tumours of the lung, which include adenoid cystic carcinoma and mucoepidermoid carcinoma, are rare entities. Histologically, they show morphologies that are similar to those of salivary gland origin. For classification purposes, the terminology applied to tumours of salivary gland origin is also applied to their pulmonary counterparts. Of these types of tumours, adenoid cystic carcinoma is the most common followed by mucoepidermoid carcinoma. Epithelial-myoepithelial carcinoma and pleomorphic adenoma are uncommon. The possibility of metastasis from the salivary glands is important to exclude through careful examination of patients' medical history because low-grade salivary cancers can metastasize after long latencies. A gene rearrangement analysis is helpful in making a definitive diagnosis, particularly in cases with an unusual morphology. Molecular-based classification may be useful to understand the nature of morphologically varied tumours. The immunohistochemical profile of the tumours is also a valuable tool for an accurate diagnosis in difficult cases.

Keywords adenoid cystic carcinoma; epithelial-myoepithelial carcinoma; lung; mucoepidermoid carcinoma; pleomorphic adenoma; salivary gland-type tumour

Introduction

Salivary gland-type tumours of the lung are a rare type of neoplasm, and submucosal exocrine glands in the central airways are considered to be the origin of such neoplasms. In adults, the vast majority of all tracheal tumours are malignant, while the majority of those are benign in children. Primary tracheal malignant tumours are uncommon, accounting for up to 0.2% of all respiratory malignancy in the United States.[1,2] Of those, squamous cell carcinoma comprises the majority in population-based studies,[1] but in our experience and others based on pathological examinations, adenoid cystic carcinoma (ACC), a salivary gland-type tumour, is equally or more prevalent than squamous cell carcinoma.[2] Among other tumours of exocrine gland origin, mucoepidermoid carcinoma (MEC) is much less common than ACC, but is more prevalent than benign ones in the trachea. Similarly, ACC and MEC are relatively common types of primary salivary gland-type tumours of the bronchus, whereas epithelial-myoepithelial carcinoma (EMC) is very rare and pleomorphic adenoma (PA) or mixed tumour is also very uncommon.[1]

Salivary gland-type tumours of the trachea, main stem or lobar bronchus show the similar histology to those of salivary gland origin. Therefore, the terminology applied to salivary gland tumours is also applied to their lung counterparts. One of the important issues for surgical pathologists is to exclude the possibility of metastasis from major or minor salivary glands, especially when a tumour is encountered in the peripheral lung. Careful examination of the patients' past medical history is recommended because low-grade cancer of salivary gland origin can be indolent with a long time period before metastasis.

The pathological classification of tumours of the salivary glands was extensively revised with many new entities in 2005. The current WHO classification of head and neck tumours (published in 2005) recognizes 24 malignant and 10 benign epithelial tumours.[3,4] Of those, several entities are unique to the salivary glands, such as basal cell adenocarcinoma and polymorphous low-grade adenocarcinoma. In the current WHO classification of lung tumours (published in 2004),[5] only three malignant salivary gland-type tumours, i.e., ACC, MEC and EMC, along with two benign tumours, i.e. mucous gland adenoma and PA are described, reflecting the low prevalence of salivary gland-type tumours in the lung. Since there have been additional insights into the tumours of salivary gland origin even after the publication of the WHO classification of head and neck tumours,[6] the updated criteria and information are also applied to lung counterparts.

For tumours of salivary gland origin, grading is recommended for ACC and MEC but is not recommended for other entities because their diagnoses already reflect the level of malignant potential. For instance, some entities are acknowledged as low-grade malignancy (polymorphous low-grade adenocarcinoma, basal cell adenocarcinoma, acinic cell adenocarcinoma) and others as high-grade malignancy (salivary duct carcinoma).[4] A similar grading system may be applicable to lung counterparts, although there is currently not enough evidence to support its role, given the fact that high-grade MEC is rarely encountered.

Salivary gland-type tumours in general exhibit various morphologies, thus differentiation of one entity from another can be problematic. In such cases, molecular testing, in particular, a gene rearrangement analysis including cytogenetic approach and fluorescence in-situ hybridization (FISH) may be helpful in making a definitive diagnosis. The application of genetic approaches as a basis for classification is still controversial but molecular techniques may help in understanding the nature of morphologically varied tumours. Immunohistochemistry may also be a valuable tool in some diagnostically-challenging cases.

In this review, we will focus on three malignant tumours (ACC, MEC and EMC) and one benign tumour (PA), which are most commonly encountered in the lung, and will describe their cytomorphologic features, immunohistochemical findings and molecular alterations.

Adenoid cystic carcinoma

ACC, one of the most common malignant salivary gland-type tumours in the lung, consists of epithelial and myoepithelial

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cells, which show variable morphological configurations including tubular, cribriform and solid patterns. Alternative names are cylindroma and adenocystic carcinoma, although their use is not recommended because of erroneous impression such as natures of a benign tumour or real adenocarcinoma.

ACCs comprise 1% or less of all lung tumours,[7] ranging from 14% to 42% of pulmonary salivary gland-type carcinomas[8,9] with no gender predominance. The average age at presentation is 50 years. ACC does not seem to be associated with tobacco smoking.

Common symptoms of ACC include shortness of breath, coughing, wheezing and haemoptysis due to airway obstruction. Radiologic imaging typically shows a centrally located mass that may have an endobronchial component. When compared to MEC, ACC is larger in size and more frequently involves the central airways, and has a higher median uptake of FDG.[10]

ACC deceptively infiltrates peribronchial soft tissue, insidiously grows, and sometimes extends into the lung parenchyma and mediastinum. Perineural invasion, frequently found in ACC, renders complete surgical resection difficult, and results in relatively frequent local recurrence. Metastases to distant organs are uncommon. It is recommended that the TNM system of lung tumours be used for staging of ACC.

Cytologic findings

ACC is cytologically characterized by three-dimensional microacinar pattern with pale opaque globules corresponding to intraluminal hyalinized or myxoid material. It should be noted that the myxoid matrix is positive not only for PAS, but also for other mucin stains such as alcian blue and mucicarmine. The matrix should also be differentiated from collagen of the basal membrane. The latter is positive for glycogen (that is positive for PAS and negative for PAS/d), but not for mucin.

Macroscopic findings

ACC typically arises as an endobronchial mass within central bronchi or in the trachea. Tumours may show a well-delineated grayish-white, homogeneous cut surface, but frequently infiltrate beyond the visible macroscopic margins. The peribronchial soft tissues and any surgical margins should therefore be extensively sampled and analyzed, both at frozen section and in resection specimens.

Histopathologic findings

ACC consists of small-sized cells with scant cytoplasm and usually small, homogeneous hyperchromatic nuclei that infrequently exhibit mitoses (Figures 1 and 2). The tumour often shows perineural invasion (Figure 3). Characteristic architecture includes cribriform, tubular and solid patterns. The most characteristic cribriform pattern consists of cells surrounding cylinders of connective tissue with variably myxoid and hyalinized material, from which the term "cylindroma" originated (Figure 1). When forming tubules lined by two to three cells, the luminal cells are cuboidal and the peripheral cells form a myoepithelial layer (Figure 2). Both ductal and myoepithelial natures can be demonstrated by their immunoreactivity to cytokeratin, and vimentin, actin and S-100, respectively. Immunohistochemically the matrix, which is positive for type IV collagen, laminin and heparin sulphate, recapitulates basement membrane-like material.

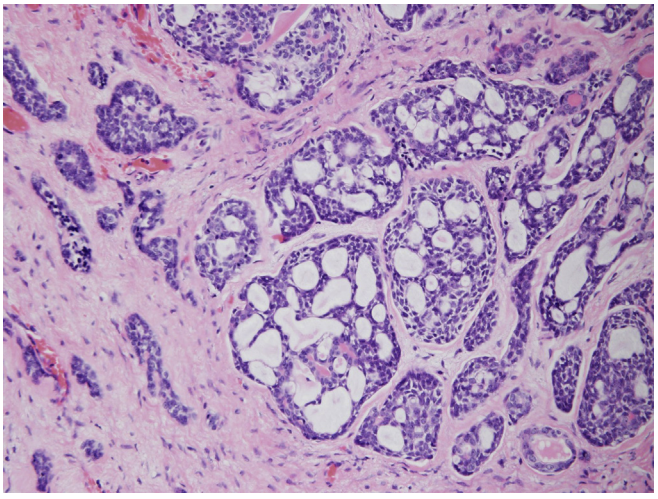

Figure 1 Adenoid cystic carcinoma showing a cribriform pattern and characteristic eosinophilic cylinders.

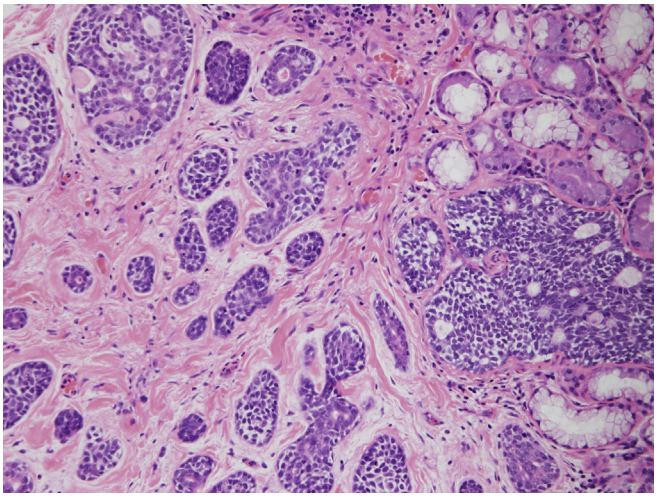

Figure 2 Adenoid cystic carcinoma showing a tubular pattern with inner and outer layers, involving bronchial glands.

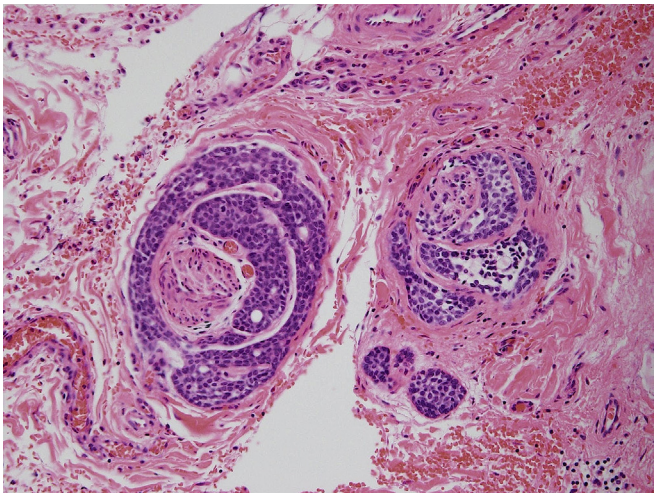

Figure 3 Perineural invasion is frequent in adenoid cystic carcinoma.