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## 세침흡인 세포검사에서 양성 질환을 닮은 폐의 고분화 샘편평 암종 - 1예 보고 -

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= Abstract =

### Well Differentiated Adenosquamous Carcinoma of Lung Mimicking Benign Lesions in Fine Needle Aspiration Cytology -Report of a Case -

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Fine needle aspiration (FNA) cytological examination is an appropriate method for the evaluation of pulmonary nodules. In major types of lung cancer, its diagnostic accuracy is quite high. However, it is sometimes difficult, using this technique, to differentiate between some unusual phenotypes including adenosquamous carcinoma, bronchioloalveolar carcinoma (BAC), neuroendocrine tumor, mucoepidermoid carcinoma, and sclerosing hemangioma. Here, we present a case involving extremely well differentiated adenosquamous carcinoma, mimicking benign lesions, such as pulmonary scar and adenomatoid malformation with squamous metaplasia. The patient was a 68-year-old man presenting with a solitary pulmonary nodule (1.6×1.6 cm), which was incidentally found at the periphery of the right lower lobe. FNA revealed some clusters of glandular cells with minimal atypia, in addition to squamous cells at a nearly full maturational state. Histological examination verified the cytological diagnosis on a lobectomy specimen. The tumor exhibited a well differentiated adenocarcinoma component, mimicking the bronchioles in scarred lung tissue, and a well differentiated squamous cell carcinoma component, mimicking the squamous cell nests of adenoacanthoma, in the other organs. In the present case, the possibility of adenosquamous carcinoma should have been considered if squamous cells were seen in the FNA from the peripheral pulmonary nodule, even though they appeared to be benign.

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**Key words** : Adenosquamous carcinoma, Bronchioloalveolar carcinoma, Sclerosing hemangioma,  
Adenomatoid malformation, Cytology

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## INTRODUCTION

Fine needle aspiration (FNA) cytological examination is an appropriate method for evaluating pulmonary nodules.<sup>1,2</sup> In major types of lung cancer, its diagnostic accuracy is quite high. However, it is difficult, using this technique, to differentiate between some unusual phenotypes, including adenosquamous carcinoma, neuroendocrine tumor, mucoepidermoid carcinoma and sclerosing hemangioma.

Carcinoma is an uncommon form of lung cancer. It comprises about 3.4% of primary lung malignancies, and is known to be aggressive.<sup>3</sup> Most adenosquamous carcinomas exhibit both adenocarcinoma and squamous cell carcinoma components, each evidencing histologic anaplasia. The cytological findings of the usual adenosquamous carcinoma in the lung are expected to be similar to that found in other organs, such as the pancreas and the breasts. However, due largely to its rarity, its cytological properties in the lung have yet to be adequately described. Here, we present a case involving extremely well differentiated adenosquamous carcinoma, which mimics benign lesions, such as pulmonary scar and adenomatoid malformation with squamous metaplasia.

## CASE

A 68 year-old man was admitted, with the chief complaint of an itching sensation throughout his entire body, which had persisted for 4 days. The patient's smoking history was 40 pack year. Ultrasonographic examination demonstrated stones in the gallbladder. Dynamic computed tomography revealed an incidental solitary pulmonary nodule in the right lower lobe, measuring 1.6 × 0.6 cm (Fig. 1). After FNA and percutaneous needle core biopsy, a right lower lobectomy was performed.

### Cytologic findings

The smears, stained with Papanicolaou and hematoxylin-eosin stains, exhibited many clusters of epithelial

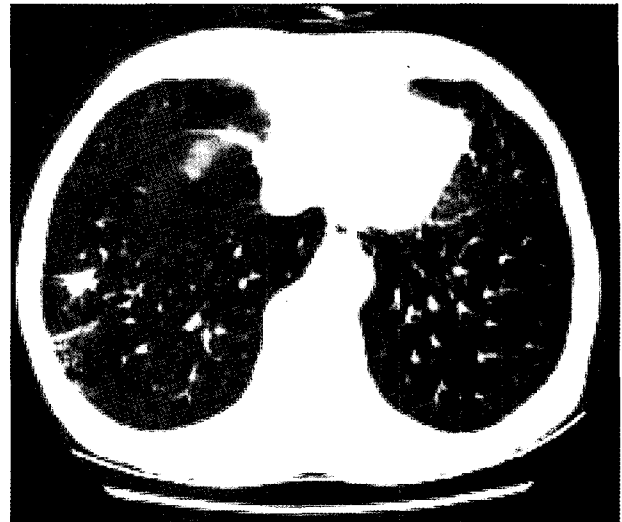


Fig. 1. Radiological Findings. Computed tomogram shows a solitary pulmonary nodule in the right lower lobe.

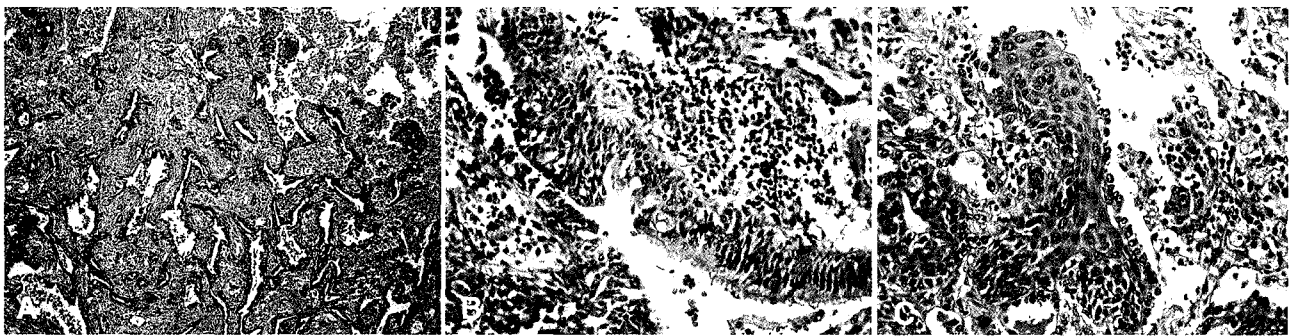
cells on the clean background. The cellular clusters were divided into three groups. Most of the clusters were composed of glandular epithelial cells. These cells evidenced minimal cytological atypia, with fine chromatin and inconspicuous nucleoli (Fig. 2A). Some of these clusters were interspersed with central squamous cells (Fig. 2B). They exhibited a moderate amount of eosinophilic cytoplasm and bland nuclei. A cluster was composed of a full thickness of squamous epithelial cells arranged in nearly normal orientation (Fig. 2C), mimicking a desquamated metaplastic epithelium.

### Histologic findings

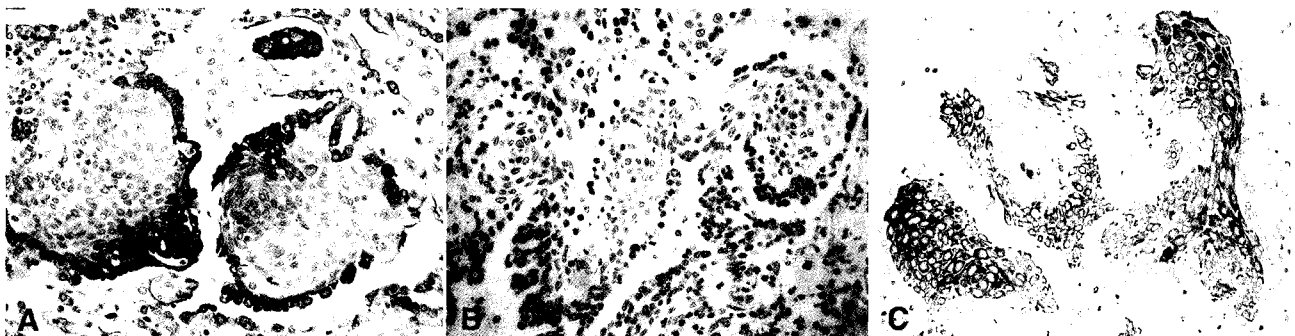
A percutaneous needle core biopsy, which was performed concomitantly with FNA, failed to detect any neoplastic lesions. A right lower lobectomy was performed. The cut surface displayed an ill-defined gray-white fibrotic tumor, measuring 1.6×1.6 cm around its periphery. Upon histological examination, the tumor was composed largely of acinar structures. The lining cells were single-layered cuboidal to low columnar, with minimal atypia (Fig. 3A). The intervening stroma was fibrotic, with mild to moderate cellularity, mimicking an early scar reaction. Overall features mimicked adenomatoid malformation or scarred lung tissue. In larger



**Fig. 2.** Cytological Findings. Many clusters of glandular cells show minimal atypia (A) (Papanicolaou). A few clusters are composed of squamous cells lined by cuboidal cells (B) (Papanicolaou). A cluster of full thickness of squamous epithelial cells shows minimal atypia (C) (H & E).



**Fig. 3.** Histological Findings. Adenocarcinomatous areas mimic adenomatoid malformation or scar tissue on lower power view (A). A large airway is partly lined by stratified atypical cuboidal cells (B). Squamous cell carcinoma components are lined by single cuboidal cells in the periphery (C).



**Fig. 4.** Immunohistochemical stain. Cytokeratin 7 (A) and thyroid transcription factor (TTF)-1 (B) are positive in the adenocarcinoma and the lining cells of squamous cell carcinoma nests. Cytokeratin 5/6 is positive in the squamous cell carcinoma nests (C).

irways within the tumor, the lumina were lined by stratified atypical cells and their outermost layers were covered with single cuboidal cells (Fig. 3B), similar to the lining cells of the adenocarcinomatous areas. These areas had merged from the pseudostratified columnar respiratory epithelia, and were thus regarded as initiating foci or in situ lesions of this tumor. Squamous cell

components were mainly present at the periphery of the tumor (Fig. 3C). They formed squamous morular structures. Some of the morules were covered by single cuboidal cells on their surfaces. Immunohistochemical stains for cytokeratin-7 (Fig. 4A) and thyroid transcription factor (TTF)-1 (Fig. 4B) were positive in the adenocarcinoma cells and surface-lining cells on the stratified

atypical cells, as well as in the large airways and squamous morules. However, cytokeratin 5/6 was only positive in the squamous component (Fig. 4C). These findings were consistent with extremely well differentiated adenosquamous carcinoma. Lymph node metastasis was not identified.

## DISCUSSION

Percutaneous FNA biopsy for the cytological examination of lung lesions is an accepted and safe diagnostic procedure, particularly when dealing with major malignant lung tumors.<sup>1,2</sup> The diagnostic specificity of this technique is 100%, and it is 99.1% sensitive.<sup>2</sup> However, it is sometimes difficult to diagnose benign tumors, including carcinoid and sclerosing hemangiomas, and unusual or rare types of malignancy, such as bronchioloalveolar carcinoma (BAC) and mucoepidermoid carcinoma.

Prudent examination is required to make a diagnosis of BAC and even minimal cytological atypia in glandular cells should not be overlooked. Sclerosing hemangioma is notorious for mimicking well differentiated adenocarcinoma on FNA, particularly BAC.<sup>4</sup> Hyalinized stroma, two cell types, and hemosiderin-laden macrophages are important findings with regard to sclerosing hemangioma.<sup>4</sup> Carcinoid tumor smears exhibit uniform round cellular populations and neuroendocrine cell type-stippled chromatin patterns.<sup>5</sup> The cytological findings associated with mucoepidermoid carcinoma have been well-documented in lung and salivary glands, both of which represent more common primary sites. These findings include an intimate admixture of polygonal intermediate cells, and well-differentiated mucinous and squamous cells.<sup>6</sup> Adenosquamous carcinoma is defined as a mixture of adenocarcinoma and squamous cell carcinoma, in which both components are malignant. Lung is a primary site of adenosquamous carcinoma, as are the uterus, pancreas, and even the breast. Most adenosquamous carcinomas, regardless of their location, exhibit prominent atypia upon both cytological and histological examinations, and are clinically more aggressive.<sup>3</sup>

Therefore, making a diagnosis of adenosquamous carcinoma is quite straightforward when both malignant components are identified.

However, in this case, cytological atypia of the glandular cells was minimal and, moreover, the squamous cells mimicked the squamous morules of adenoacanthoma in other organs. In this situation, ordinary examination often overlooks these findings, as adenoacanthoma is clearly not yet established in the lung. We also overlooked these findings at first glance, and were considering scarred lung tissue or adenomatoid malformation. During an intradepartmental consultation, minimal cytological atypia and unusual cellularity were detected, and thus a descriptive diagnosis was rendered: 'a few clusters of glandular cells with minimal atypia, suspicious for well differentiated adenocarcinoma', and a biopsy was recommended. The cytological findings associated with adenomatoid malformation may be assumed to be similar to the glandular components of this case, but have not been described in any of the literature in English. However, squamous epithelial components have been only sparsely mentioned with regard not only to adenomatoid malformation, but also in reference to BAC and sclerosing hemangioma.

Squamous cell nests are largely neoplastic in the peripheral lung, although they appear bland under cytological examination. Therefore, we should consider the possibility of well differentiated adenosquamous carcinoma whenever squamous cells are associated with atypical glandular cells.

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