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PAPILLARY ADENOCARCINOMA OF THE LUNG

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Abstract

***Background**: Lung cancer is the most common cause of cancer-related deaths worldwide. Mortality and incidence rates are generally highest in high-income countries, especially the United States and European countries. In the United States, it is estimated that there were 234,030 diagnosed cases of lung cancer in 2018. Adenocarcinoma is the most common type of lung cancer, with the rare subtype of papillary adenocarcinoma. **Case Report**: A case is reported of a 66-year-old male with slide number B/4903/19. Macroscopic examination revealed gray, elastic biopsy tissue with a volume of approximately 0.2 cc. Microscopic examination showed a tumor mass forming a papillary arrangement with a fibrovascular core, and a small portion appeared solid. It consisted of cells with pleomorphic nuclei, coarse chromatin, hyperchromatic nuclei, some with intranuclear vacuoles, pale cytoplasm, and prominent nucleoli. Mitosis was present. The stroma consisted of fibrous connective tissue infiltrated by tumor cells and scattered lymphocyte inflammatory cells. Blood vessels were dilated and congested. Areas of necrosis and lymphovascular invasion were observed. **Discussion and Conclusion:** Based on the histopathological findings, the patient was diagnosed with papillary adenocarcinoma of the lung with characteristic histological features that facilitate the diagnosis. The prognosis is poor.*

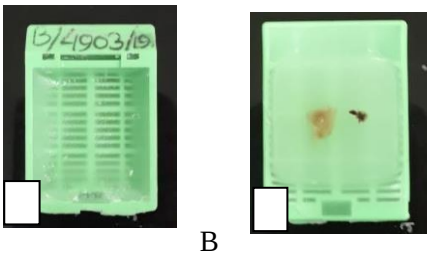
Keywords**: **Lung cancer, adenocarcinoma, papillary adenocarcinoma

INTRODUCTION

Lung cancer is the most common cause of cancer deaths throughout the world.[1] Incidence and death rates generally occur in high-income countries, such as the United States and European countries.[2] Estimated new cases of lung cancer in the US for 2018 were 121,680 for men and 112,350 for women, with a total of 234,030 cases equivalent to 641 lung cancer cases diagnosed per day, with estimated deaths in 2018 being 83,550 deaths for men and 70,500 cases for women, approximately 25% of deaths occur due to cancer each year. In Indonesia alone, lung cancer is the third highest cancer with 30,023 new cases every year, with a death rate of 26,095 cases in 2018 and this is in the first position as the cause of death due to cancer. This lung cancer is most often diagnosed in men (14.5% of total cases occur in men and 8.4% in women)[1-4] Lung cancer is classified into two primary groups, small cell lung carcinoma and non-small cell lung carcinoma. These groupings were progressively determined using histopathological features and immunohistochemical markers. Adenocarcinoma is a non-small cell lung carcinoma that often occurs, with one of the rare histological subtypes of papillary adenocarcinoma.[3]

CASE REPORT

We present a case involving a 66-year-old male who underwent a transbronchial lung biopsy (TBLB) due to a suspected right lung tumor, as diagnosed by the attending clinician. The biopsy specimen was subsequently forwarded to the Anatomical Pathology Laboratory at Haji Adam Malik Hospital in Medan, with reference to slide number B/4903/19.



A B

Figure 1. A, B macroscopic image of tissue mass from paraffin blocks

Upon macroscopic examination, the biopsy specimen displayed a grayish color and had a volume of approximately 0.2 cc. Microscopic analysis revealed that the predominant pattern within the tumor mass was papillary, characterized by a fibrovascular core, with a smaller solid component. The tumor cells exhibited enlarged round and oval nuclei with coarse chromatin, some of which were hyperchromatic and featured vacuolated intranuclear spaces. Additionally, the cells had pale cytoplasm with prominent nuclei and mitotic activity was observed. Focal areas of necrosis were evident. The stromal component was composed of fibrous connective tissue infiltrated by tumor cells and inflammatory lymphocytes. Notably, blood vessels displayed dilation and congestion, and lymphovascular invasion was identified.

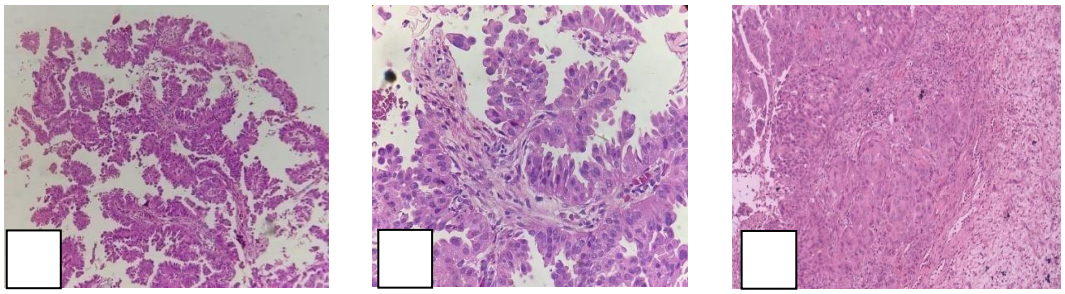
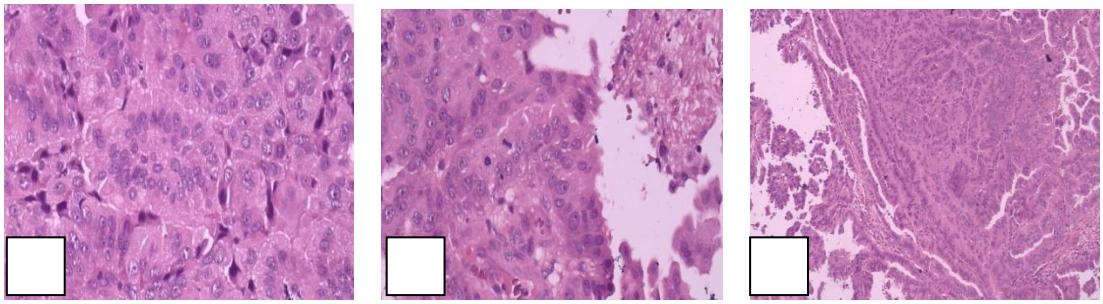


Figure 2. **A** & **B** The tumor mass forms a papillary structure with a fibrovascular core (H&E, 40x, 400x) C. Tumor mass that forms a solid structure (H&E, 200x).



Gambar 3. **A.** The nuclei are enlarged, round and oval in shape, the chromatin is rough, the nuclei are prominent, the cytoplasm is pale and there is vacuolated intranuclear. **B.** Mitosis is found (H&E, 400x) **C.** Tumor cells have invaded the stroma, and infiltration of inflammatory cells by lymphocytes (H&E, 400x)

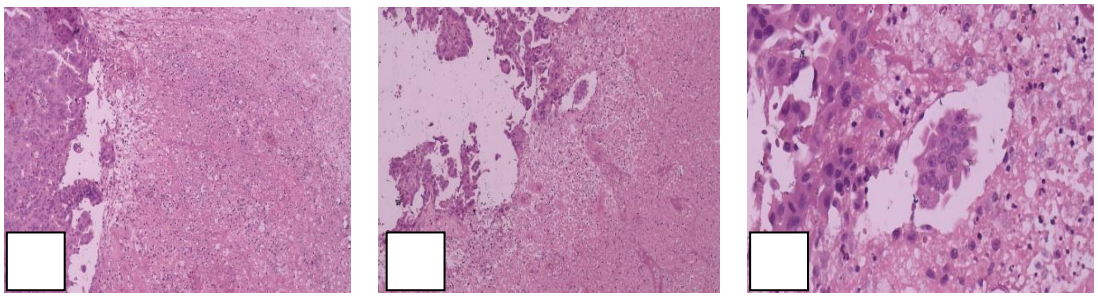


Figure 4. A. Nekrosis (+) (*H&E*, 400x). **B** & **C.** LVI (+) (*H&E*, 100x & 400x)

Based on the histopathological examination results, which revealed a predominant papillary pattern, the diagnosis for this patient was determined to be papillary adenocarcinoma of the lung, with the corresponding ICD-O code: 8260/3.

RESULTS AND DISCUSSION

Invasive adenocarcinoma is a malignant epithelial tumor with glandular differentiation, mucin production, or expression of pneumocyte markers. This tumor has 5 different histological growth patterns: lepidic, acinar, papillary, micropapillary, and solid. Most invasive adenocarcinomas (>80%) consist of a heterogeneous mixture of different patterns of histologic subtype..[1,5-7,11] Most cases are diagnosed in patients over 55 years of age. However, some authors have stated that the average age of diagnosis for men and women is approximately 59 years.[9] Risk factors for lung cancer come from smoking habits, exposure to carcinogenic substances in workers such as asbestos, radon, mining, air pollution, chemicals, certain dietary supplements, and underlying chronic lung disease. There are known reports of families with an inherited genetic predisposition to lung cancer associated with germline EGFR mutations or ERBB2 mutations.[1,8] The risk in smokers increases with the duration of smoking and the number of cigarettes smoked per day and gradually decreases in smoking cessation. Lung cancer can also occur among those who have never smoked. Lung cancer can occur anywhere in the lungs. The most common localization of invasive adenocarcinoma subtypes occurs in the lung periphery, from the bronchi, bronchioles, and alveolar cells, with or without mucin production. The clinical picture of patients presents with various symptoms such as coughing and shortness of breath or no symptoms at all, this really depends on the location of the tumor; tumor size, clinical stage at diagnosis. Initial evaluation of patients with suspected lung cancer may include imaging to determine the extent of the disease; such as *CT, PET, MRI,Bronchoscopy, Transthoracic Needle Biopsy (TNB), Fine Needle Aspiration Biopsy (FNAB), Mediastinoscopy, and Endobronchial Ultrasound-Transbronchial Needle Aspiration (EBUS-TBNA)*.[1,9]

Macroscopically, the majority of invasive adenocarcinomas are single or multiple, solid, well-defined white-gray nodules with fibrosis. In some cases, the tumor may show necrosis and/or hemorrhage.[1,5,9] Histologically, the World Health Organization (WHO) divides invasive adenocarcinoma into 5 subtypes based on their dominant pattern.[1]

Tabel 1. *WHO Classification of tumours of the lung.*[1]

Epithelial tumours	
Adenocarcinoma	8140/3
Lepidic adenocarcinoma	8250/3*
Acinar adenocarcinoma	8551/3*
Papillary adenocarcinoma	8260/3
Micropapillary adenocarcinoma	8265/3
Solid adenocarcinoma	8230/3

Lepidic Adenocarcinoma

This variant usually consists of a number of pneumocyte II cells (clara cells) / tumor cells that proliferate / grow along the surface of the alveolar wall which is similar to the morphology found in minimally invasive adenocarcinoma and adenocarcinoma in situ. There is an invasive component with at least one focus measuring > 5 mm in the largest dimension. If there are multiple foci of invasion, or the size of the invasiveness is difficult to measure in discrete (separate) foci, recent data suggest another way to estimate the size of the invasiveness is to sum the percentages of the invasive components and multiply them by the overall tumor diameter. If the result is > 5 mm, then the diagnosis of lepidic adenocarcinoma must be made. Say invasive here is defined as: 1) Histological subtype other than lepidic pattern (i.e. acinar, papillary, micropapillary, or solid); 2) Myofibroblastic stroma associated with invasive tumor cells; 3) Vascular or pleural invasion; 4) Spread through air space.[1,3,5]

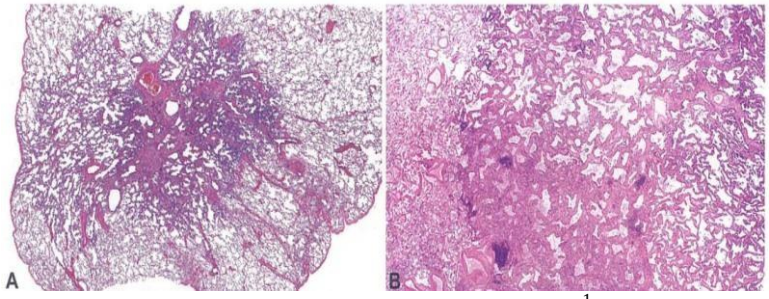


Figure 5. A &B *Lepidic adenocarcinoma*. [1]

Adenocarcinoma

This variant shows mostly glandular components, round to oval in shape with a luminal center surrounded by tumor cells. Neoplastic cells and / or glandular space may contain mucin. Acinar structures can also be round aggregates of tumor cells with polarized nuclei at the periphery and central cytoplasm without a clear lumen. When the lepidic pattern forms nests, the glandular morphology may be difficult to distinguish from the acinar pattern. The cribriform pattern is considered an acinar pattern of adenocarcinoma, although it is associated with a poor prognosis.[1]

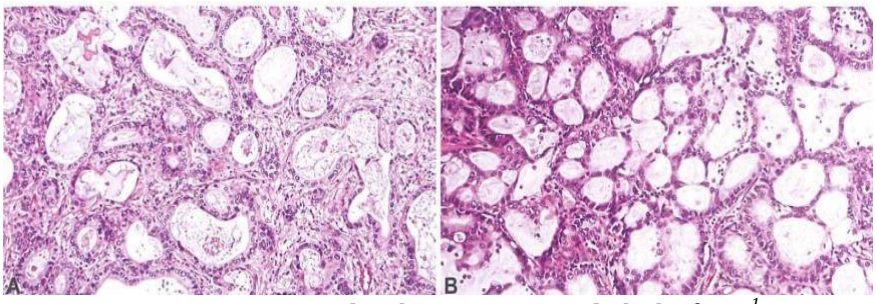


Figure 6. A. A*cinar adenokarsinoma* B. Pola *kribriform.*[1]

Papillary Adenocarcinoma

The main component shows the growth of glandular cells with a *fibrovascular core*, replacing the alveolar layer.[5] *The fibrovascular core* is lined by neoplastic cells with cuboidal to columnar epithelium. psammoma may be present. Myofibroblastic stroma is not necessary to diagnose this pattern.[1] Pure pulmonary papillary adenocarcinoma is only found in 3-10% of all

cases. Papillary components generally occur with other histologic subtypes. necrosis and invasion may occur.[5,6,10]

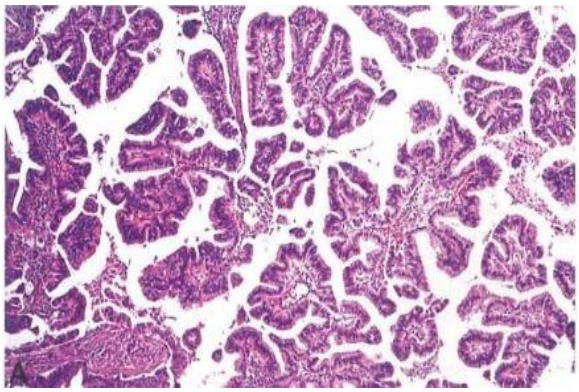


Figure 7. *Papillary adenocarcinoma* consists of tumor cells with cuboidal to columnar epithelium visible on the surface *fibrovascular core*.[1]

Micropapillary adenocarcinoma

Tumor cells that grow in papillary bundles form florets that do not have a fibrovascular core. It may appear detached from and/or connected to the alveolar wall. Tumor cells are usually small and cuboidal, with variable nuclear atypia. Ring-like glandular structures can float in the alveolar space. Vascular and stromal invasion is common. Psammoma bodies can be found.[1]

Solid adenocarcinoma

The main component of polygonal tumor cells that form sheets that do not have a recognizable adenocarcinoma pattern, such as lepidic, acinar, papillary, micropapillary. If the tumor is 100% solid, intracellular mucin should be visible in ≥ 5 tumor cells in each of two large fields, and confirmed by histochemical staining for mucin.[1]

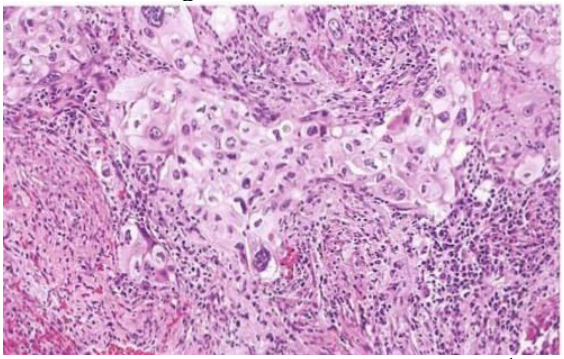


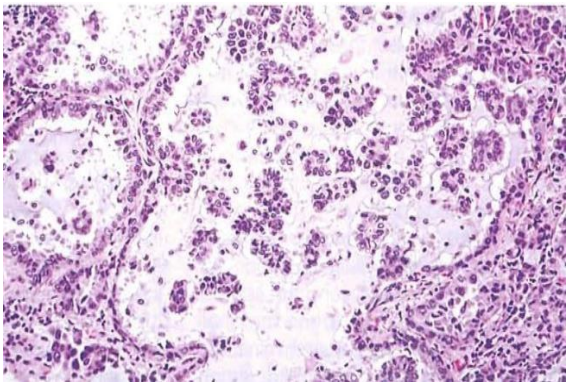
Figure 8. Mikroskopis *solid adenocarcinoma*.[1]

From several descriptions of the histological subtypes that have been described previously and their dominant patterns, the histological picture of the case report is very suitable for the papillary predominant adenocarcinoma subtype because it shows more papillary components with a very typical fibrovascular core. Currently the most commonly used pneumocyte markers are TTF-1 (positive in the nucleus) and Napsin-A (positive in the cytoplasm). TTF-1 and Napsin-A had a sensitivity/specificity of 84.5%/96.4%, and 92.0%/100%, respectively.[5] Approximately 75% of invasive adenocarcinomas are positive for TTF-1. The discovery of epidermal growth factor (EGFR) and anaplastic lymphoma kinase (ALK) mutations is an effective target for EGFR tyrosine kinase inhibitors or ALK inhibitors in patients with advanced lung adenocarcinoma in revolutionizing clinical practice therapeutic strategies.[1,11]

Differential diagnosis of metastatic papillary thyroid carcinoma (PTC), clinical history of thyroid cancer, Psammoma bodies, presence of PTC (orphan Annie) nuclei, positive for PAX8 and thyrogobulin.[12] The other most frequent differential diagnosis is *squamous cell carcinoma*. Some solid subtypes have a dense eosinophilic cytoplasm appearance that is similar to squamous cells.

carcinoma.

Poorly differentiated tumors may have squamous morphology, but lack diagnostic squamous features such as keratinization, *keratin pearl*, or *intercellular bridges*, and can be correctly diagnosed using immunohistochemistry *squamous marker* such as p40 or p63 (positive). Observing the morphological features or immunohistochemical staining is usually sufficient. However, a multidisciplinary approach that correlates clinically, radiologically, morphologically and molecularly may be necessary for difficult cases.[1,11] Several studies have been conducted to determine the clinical importance of these histological subtypes of lung adenocarcinoma by assessing the presence and extent of various histological growth patterns.[6] Different histological subtypes have different prognostic significance. The stage I lepidic subtype shows a good prognosis, but most recurrent tumors have several high risk factors, such as close margins in limited resection, or the presence of a micropapillary component, or vascular and/or pleural invasion. Micropapillary and solid growth patterns are associated with a poor prognosis.[1,5,11]



CLOSING

A case has been reported of a man, aged 66 years, who was diagnosed by a clinician with a right lung tumor and underwent *TBLB* treatment. Based on the clinical information and histopathological picture, it shows a *papillary adenocarcinoma of the lung*, and these tumors have a poor prognosis.

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