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RESEARCH ARTICLE

A Case of Extensive Pneumonitis in Typical Bronchial Carcinoid Tumor Ending with Total Pneumonectomy

Julius Tanoto[1,2] Isnin Anang Marhana[1,2]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Airlangga University, Surabaya, Indonesia.
[2]Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

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***Corresponding Author**

isnin.anang@fk.unair.ac.id

ABSTRACT

Carcinoid tumors are uncommon malignant neuroendocrine epithelial neoplasms, accounting for around 0.4–3% of all lung cancers. Based on their distinct histological and biological features, as well as their anatomical distribution, they are categorized into atypical (AC) and typical carcinoid (TC) tumors. A young man aged 17 came with shortness of breath since early 2022, and progressed to coughing blood since May 2023. Clinically diagnosed as lung tuberculosis. ATD (Anti Tuberculosis Drug) treatment for 6 months showed no clinical improvement. Bronchoscopy and forceps biopsy were done for tissue sampling. Subsequently immunohistochemistry examination were done, with the result confirmed the mass is a TC tumor. The results of CT scan evaluation revealed an enhancing solid intrabronchial mass measuring +/- 2.20 x 1.83 x 2.76 cm. Patient planning for surgery and during operation there were adhesions in pleura and right lung parenchyma with diaphragm, chest wall and mediastinum. Finally, patient had to undergo a total pneumonectomy.

INTRODUCTION

Based on the WHO classification from 2015 regarding neuroendocrine tumors (NET), bronchopulmonary carcinoid tumors are rare, well-differentiated NETs, making up roughly 1-2% of the overall cases of lung cancer. Carcinoid tumors are most frequently found in the digestive system, with 80-90% of those occurring in the segmental or subsegmental bronchi, while only 10% develop in the bronchopulmonary area. [1,2]

Carcinoid tumors mostly occur in young adults and have a low incidence of metastasis. Histologically, they can be classified into two subtypes: atypical and typical. Central airway obstruction is the leading cause of symptoms, while less common symptoms include carcinoid syndrome and crises. [2]

CT scans are the primary diagnostic tool, as they provide information on tumor size, mediastinal lymph node enlargement, endobronchial nodules, hilar or perihilar masses, or can indicate peripheral nodules and bronchial obstruction. Bronchoscopy is one of the primary tools for obtaining histopathological samples, evaluating bronchial wall invasion, and addressing endobronchial manifestations that can resolve atelectasis. To exclude lymph node metastasis, an endobronchial ultrasound is required. [3]

Surgery is the main treatment for carcinoid tumors; however, in recent years, pneumonectomy for central tumors has become rare because the current standard of care now favors bronchoplasty and sleeve lobectomy, which prioritize lung parenchyma preservation. [4]

Case Report

A 17-year-old male, Javanese, high school student, with a BMI of 16.5 (underweight), presented with chief complaint of shortness of breath. The shortness of breath is intermittent, particularly during heavy activity. He has experienced shortness of breath and easy fatigue since 2022, often diagnosed with pneumonia and treated with repeated courses of antibiotics. Since May 2023, the patient has experienced hemoptysis and underwent a CT scan, which resulted atelectasis and pneumonia. Sputum Genexpert results were negative, and he received a clinical diagnosis of pulmonary tuberculosis. Despite undergoing treatment for six months, the patient's symptoms have not improved. There is no history of contact with TB, no family history of TB, and no history of asthma or allergies in either the patient or family. The patient does not smoke and has no history of COVID-19.

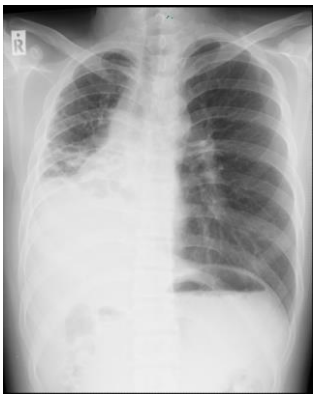

Fig. 1. Chest X-ray before operation

On physical examination the patient was in stable condition but slightly short of breath. On chest examination there were signs of right lung atelectasis. The electrolyte levels and the results of the liver function test, renal function test, and complete blood count test all fell within the normal range. Arterial blood gas analysis showed respiratory acidosis with mild hypoxemia. The patient then underwent bronchoscopy and found an intrabronchial mass that bled easily in the right main bronchus and obstruct the entire right main bronchial lumen. After a forceps biopsy was performed, the histopathology results showed suspicion of a neuroendocrine tumor, so immunohistochemistry was performed with CK, CD56, Chromogranin, Synaptophysin, and Ki67 antibodies. The Immunohistochemistry results confirmed a typical carcinoid tumor. Hormonal tests, such as ACTH levels, were within normal limits.

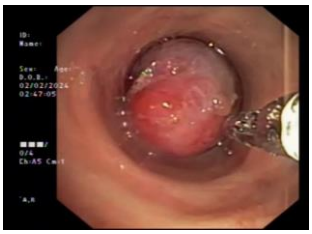

Fig. 2. Mass on right main bronchus

After confirming a grade 1 typical carcinoid tumor, the patient was planned for surgery. Patient underwent another CT scan before surgery with the results a solid intrabronchial mass (47 HU) measuring approximately 2.20 x 1.83 x 2.76 cm, located about 1.05 cm from the carina. Upon contrast administration, there was contrast enhancement (78 HU), and the mass appeared to infiltrate and narrow the right upper lobe bronchus, with a smallest caliber approximately 0.23 cm; it also narrowed the right intermediate bronchus with a smallest caliber approximately 0.3 cm, accompanied by atelectasis and superior retraction of the right hemidiaphragm. The mass was attached to the right pulmonary artery with clear borders. There was panlobular emphysema in the superior lobe; the superior and posterobasal segments of the right inferior lobe. Lymph

nodes measuring approximately 0.7 cm in the lower right paratrachea and 0.9 cm in the upper right paratrachea were noted. No nodules were observed in the liver or either adrenal gland.

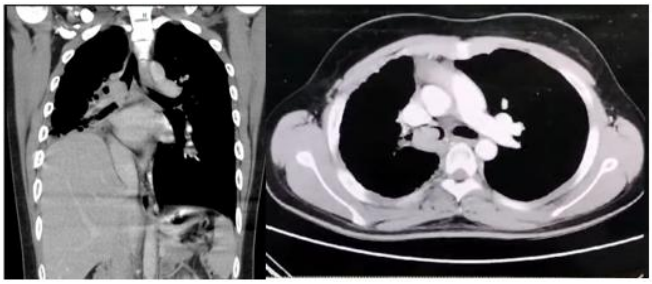

Fig. 3. Thorax CT scan before surgery

The patient was scheduled for lobectomy and signed the informed consent. Surgery was performed using a posterolateral approach, during surgery adhesions were found between the pleura and the parenchyma of the right lower, middle, and upper lobes, as well as the diaphragm, chest wall, and mediastinum. The patient then underwent pneumonectomy accompanied by removal of lymph nodes from stations 2 until 9, revealing an intrabronchial tumor in the right main bronchus, approximately 2x3 cm. A 28 Fr chest tube was subsequently positioned in the right hemithorax after the surgical procedure, along with a modified Indwelling Pleural Catheter (IPC) 16 Fr inserted beneath the chest tube insertion. The patient was then transferred to High Care Unit for postoperative care. Pain management was provided with ketorolac injection. After 2 days, the chest tube was removed, but the IPC was maintained until May 13, 2024, until the fluid production was minimal.

The histopathological results showed bronchial tissue and lung parenchyma, with tumor growth in the bronchial lumen organized in an organoid and partially trabecular pattern, consisting of round-oval tumor cells that are generally uniform. Some nuclei were prominent, with chromatin that was partially fine and coarse, and moderate to abundant eosinophilic cytoplasm. A single instance of mitosis was recorded per 2 mm^2. There were no indications of lymphangioinvasion, perineural invasion, or spread via air spaces (STAS). In other areas, dilatation of bronchus and alveoli lumen was seen and accompanied by extravasation of erythrocytes. No necrosis was found, and the margins of the lung, bronchus, and pleura were free of tumor cells, leading to a final diagnosis of typical carcinoid tumor.

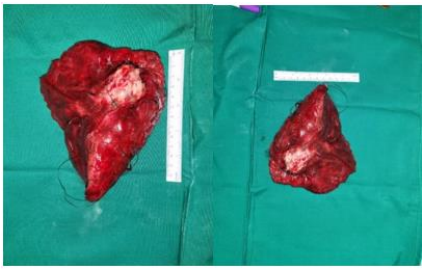

Fig. 4. A cut section of post-operative tissue revealing a firm, lobulated mass that completely fills the bronchial lumen.

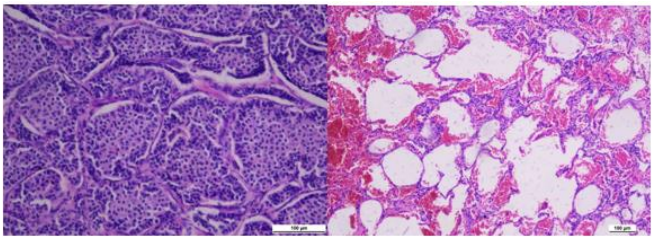

Fig. 5. Histologic section revealing uniform round cells, prominent nuclei, with partially fine and coarse chromatin, and abundant eosinophilic cytoplasm and no STAS

The discharge occurred on the fourth day following the surgical procedure. A follow-up CT scan at the showed no residual mass, and a repeat bronchoscopy yielded no malignant cells.

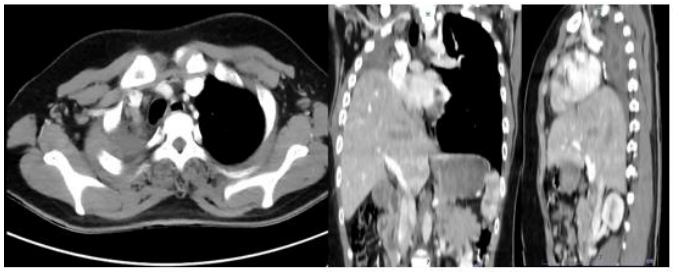

Fig. 6. Follow up CT scan after pneumonectomy

DISCUSSION

According to the 2015 classification by WHO and the International Association for the Study of Lung Cancer (IASLC) regarding neuroendocrine tumors (NET), bronchopulmonary carcinoid tumors are classified as uncommon, well-differentiated NETs, accounting for about 1-2% of lung cancers cases. Within this category, typical carcinoid tumors comprise approximately 76-90%. Bronchial mucosal cells, specifically enterochromaffin cells or Kulchitsky cells, are the source of pulmonary neuroendocrine tumors and are considered part of the diffuse neuroendocrine system (DNES). The production of adrenocorticotropic hormone (ACTH) and serotonin is a function of these specialized cells, and their secretion into the blood could lead to the development of carcinoid syndrome. [3]

The classification of neuroendocrine tumors (NET) according to the WHO 2015 includes large cell neuroendocrine carcinoma (LCNEC), small cell lung carcinoma (SCLC), and carcinoid tumors, which are then divided into two subtypes: atypical and typical. Another classification categorizes tumors into several grades: grade 1 represents tumors previously classified as TC, grade 2 represents AC, and grade 3 represents poorly differentiated tumors, which are divided into small cell and large cell types. This grading system allows for a pathological classification that aligns more closely with clinical outcomes. [3,5] In this case, the diagnosis is grade 1 typical carcinoid tumor.

The common clinical symptoms of typical carcinoid tumors include hemoptysis, atelectasis, post-obstructive pneumonitis, fever, wheezing, dyspnea, recurrent pulmonary infections, and cough. In certain cases, patients may not exhibit any symptoms, leading to incidental findings of the tumors. [6] Other symptoms may arise from carcinoid syndrome due to the secretion of serotonin, histamine, and bombesin, leading to bronchoconstriction, flushing, hemodynamic instability, tachycardia, and digestive disturbances. Cushing's syndrome can also be caused by carcinoid tumors due to increased ACTH (adrenocorticotropic hormone) levels. A lack of adequate arginine vasopressin (AVP) secretion may give rise to various syndromes associated with diminished sodium and water retention. [7] In this case, the patient presented with clinical symptoms, including shortness of breath, hemoptysis, recurrent pneumonia, cough, and atelectasis leading to post-obstructive pneumonitis. Hormonal tests showed normal ACTH levels, and no additional symptoms were found.

Nearly 80% of bronchial carcinoid tumors are located centrally, predominantly occurring in the segmental bronchi, lobar bronchi, or main bronchi. The tumors appear central, round or oval in shape, with well-defined margins on CT scans. Tumor sizes range from 2 to 5 cm. Mass can cause narrowing or total obstruction of the bronchi, resulting in partial or total atelectasis, post-obstruction pneumonitis, mucus impaction, and potential formation of lung abscesses. Emphysema may occur if expiratory air cannot escape due to total atelectasis. Tumors can show diffuse or punctate calcification, and direct invasion into the mediastinum or cavities is rare. Not all carcinoids exhibit uniform contrast enhancement, especially atypical carcinoids, which may show uneven enhancement. Contrast enhancement cannot differentiate carcinoid tumors from

bronchogenic lung tumors. [8] In this case, the tumor was centrally located, measuring approximately 2.20 x 1.83 x 2.76 cm, with contrast enhancement of 78 HU, atelectasis, and superior retraction of the right hemidiaphragm. Emphysema was noted, and no nodules were found in the liver.

The primary technique for diagnosing pulmonary carcinoid tumors is bronchoscopy because 75-77% are centrally located. In 75% of bronchoscopy cases, lesions are well-defined, well-vascularized, round, and red in color, posing a potential bleeding risk when sampled for biopsy. In the context of atypical bronchial carcinoids, pre-operative CT scans can effectively assess lymph node metastasis, exhibiting a specificity between 90 and 93%. In the evaluation of mediastinal lymph nodes, Utilizing endobronchial ultrasound (EBUS) alongside transbronchial needle aspiration shows advantages over CT. If the tumor is >3 cm or if histopathology indicates atypical carcinoid, EBUS with a convex probe is recommended for tumor management evaluation. EBUS with a radial 20 MHz probe facilitates a more specific examination of tumor invasion into the bronchial wall compared to CT, especially in lesions causing atelectasis. [2,9]

Patients diagnosed with carcinoid tumors exhibit histopathological characteristics indicative of neuroendocrine differentiation. Organoid and trabecular configurations are the patterns most frequently encountered. There may be other observed growth patterns, which encompass follicular development, pseudo-glandular patterns, papillary growth, and rosette formation. Tumor cells usually have a consistent appearance, featuring finely granular nuclear chromatin, cytoplasm that is moderately to abundantly eosinophilic, and nucleoli that are not prominent. [10] Carcinoids generally exhibit fewer than two mitotic events per 2 mm^2 and lack any signs of necrosis. Although atypical carcinoids share certain histological traits, they are specifically identified by the presence of 2 to 10 mitoses per 2 mm^2, along with necrosis. Rather than relying on a designated number of high-power fields, counts should be reported for each 2 mm^2. [11]

For immunostaining, it is advised to use an antibody panel that includes CD56, synaptophysin, and chromogranin A. Evaluating biopsy or cytology samples benefits greatly from the Ki67 labeling index, especially in cases where crush artifacts obscure the assessment of the mitotic index. This index measures the percentage of cells undergoing active division. The Ki67 index typically ranges from 35% to 50% (mean 42.5%) in large cell neuroendocrine carcinoma, 10% to 30% (mean 19%) in atypical carcinoids, and 1% to 10% (mean 2.6%) in typical carcinoid tumors. [12,13] The findings indicated positive results for synaptophysin, chromogranin, and CK, with a Ki67 index of 5%.

Surgery is the primary treatment for carcinoid tumors, focusing on preserving lung tissue to the greatest extent. A study by Wilkins et al. involving 111 patients with bronchial carcinoid from 1931 to 1981 divided the research into two periods: before and after 1963. The study concluded that the number of pneumonectomies and bilobectomies meaningfully diminished in the second period, coinciding with an increase in sleeve resections. The adoption of lobectomy as the conventional surgical intervention for central tumors underscores the necessity of regular lymph node dissection, as lymph nodes are often sites of metastasis. [14] García-Yuste et al. reported on 661 patients treated in Spain from 1980 to 2002, performing 63 (11%) pneumonectomies, 57 sleeve lobectomies, and 9 bronchial sleeve resections. The findings indicated no significant survival difference between patients who had sleeve resections and those who underwent pneumonectomy or lobectomy, regardless of whether they had typical or atypical carcinoids. [15]

Indications for pneumonectomy in bronchial carcinoid tumors are decrease, except in cases of vascular accidents or intraoperative complications. Specific indications include central tumors with extensive pneumonitis or destroyed lung, very large central tumors where bronchoplastic procedures are not feasible, and tumor recurrence after bronchial sleeve resection or lobectomy. Alternative procedure such as endobronchial treatment (EBT) may be used, especially for central tumors causing bronchial obstruction and post-obstructive pneumonitis. However, the effectiveness of this technique is heavily influenced by tumor type, lymph node metastasis, and tumor size, which should be evaluated before proceeding. [4] Carcinoid tumors generally had

poor responses to chemotherapy and radiotherapy, making surgical resection of the tumor along with regional lymph nodes were the primary treatment, unless contraindications to surgery exist. [16] In this case, there was noted adhesion of the pleura and parenchyma of the right lower, middle, and upper lobes to the diaphragm, chest wall, and mediastinum due to extensive pneumonitis.

The five-year and ten-year survival rates for patients with typical carcinoid tumors are between 87–100% and 82–95%, respectively. In contrast, patients with atypical carcinoid tumors have survival rates of 40–93% and 31–67%. Atypical histology, the presence of lymph node metastasis at diagnosis, advanced disease stage, and the occurrence of tumorlets are all considered poor prognostic factors. [17]

CONCLUSION

Typical bronchial carcinoid tumors are rare lung tumors, and their symptoms can vary, mimicking conditions like asthma or infections such as TB, which may lead to misdiagnosis and inappropriate treatment. Diagnostic procedures such as CT scans and bronchoscopy should be performed for patients with respiratory symptoms, even if adequate therapy has been provided. Histopathological examination followed by immunohistochemistry is essential to differentiate the tumor grade and type before deciding on the appropriate therapy. Treatment options for this tumor include resection via bronchoscopy, lobectomy, or pneumonectomy. While total pneumonectomy has become less common, in this case, it was necessary due to extensive tumor adhesion to surrounding tissues due to extensive pneumonitis.

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Figure Legends

Fig. 1. Chest X-ray before operation.

Fig. 2. Mass on right main bronchus.

Fig. 3. Thorax CT scan before surgery.

Fig. 4. Post-operative tissue cut section showing lobulated, firm mass filling bronchial lumen.

Fig. 5. Histologic section showing uniform round cells, prominent nuclei, with partially fine and coarse chromatin, and abundant eosinophilic cytoplasm and no STAS.

Fig. 6. Follow up CT scan after pneumonectomy.

Note:

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