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Case Report

Multiple Pulmonary Carcinoids and The Importance of Differential Diagnosis: A Case Report

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Abstract

Introduction: Pulmonary carcinoid tumors (PCTs) are a rare group of neoplasms, representing 1-2% of lung cancers in adults and 20-30% of neuroendocrine tumors (NETs). They primarily occur in women during the fifth and sixth decades of life. These tumors are classified as typical carcinoid (low-grade) and atypical carcinoid (intermediate-grade), and can present with respiratory symptoms or be discovered incidentally. Diagnosis is typically made via bronchoscopy, transthoracic biopsy, or, less frequently, by mediastinoscopy and endobronchial ultrasound (EBUS).

Case report: Describes a case of multiple neuroendocrine pulmonary nodules in a 68-year-old female patient, presenting with clinical symptoms of weakness and occasional fatigue, dyspnea on moderate exertion, and cough with little sputum, in addition to an unintentional weight loss of 2kg over three months.

Conclusion: This case report documents the rare occurrence of multiple foci of pulmonary carcinoid tumors, a less common phenomenon compared to the predominantly unifocal cases reported in the literature. The diagnostic approach, which included biopsy and immunohistochemical analysis, together with pulmonary segmentectomy treatment, proved to be largely effective.

Keywords: carcinoid tumor; pulmonary neoplasm; multiple foci

Introduction

Carcinoid tumors, also known as neuroendocrine tumors (NETs), are a rare group of pulmonary neoplasms accounting for approximately 1-2% of adult lung cancers and about 20-30% of all diagnosed NETs [1,2]. They occur primarily in women between the 5th and 6th decades of life [3]. These tumors originate from neuroendocrine cells that produce peptides and amines and can occur in several parts of the body. The gastrointestinal tract is the most frequent site of these tumors, accounting for 52-58% of cases, while the lung is the second most common site, with an incidence of 21-32% [4,5].

Pulmonary NETs are classified into four categories, but the two principal types are: typical carcinoid (TC), a low-grade tumor with generally indolent behavior, and atypical carcinoid (AC), an intermediate-grade tumor with greater aggressive potential [6,7]. According to the World Health Organization (WHO) classification, tumors such as small-cell lung cancer and large-cell neuroendocrine carcinoma of the lung are categorized as high-grade neoplasms, distinctly separate from pulmonary NETs [7,8].

Pulmonary carcinoid tumors (PCTs) may present with nonspecific respiratory symptoms, with central forms being more common, or they may be incidentally detected on imaging studies, particularly in peripheral forms. The most common presentation is a solitary lesion, with the occurrence of multiple lesions being rare. Less frequently, these tumors present with symptoms of hormonal hypersecretion, such as carcinoid syndrome (CS). Diagnosis is typically established through bronchoscopy or transthoracic biopsy. Histopathological diagnosis of PCTs is based on identifying specific morphological features and demonstrating the neuroendocrine nature of the tumor via immunohistochemistry for markers such as chromogranin A (CgA) and synaptophysin, which are expressed in most carcinoids [3,9]. This case report explores a rare presentation of multiple carcinoid tumor foci in the lung, discussing the diagnostic and therapeutic challenges encountered during the clinical management of the patient, given that the initial diagnostic hypothesis was pulmonary metastases from an occult primary site.

Case Report

A 68-year-old female patient was referred to a specialized oncology center for suspected pulmonary metastases following imaging performed after a SARS-CoV-2 infection. She reported asthenia, dyspnea upon moderate exertion, cough with scant secretion, and an unintentional weight loss of 2 kg over three months. She was neither a smoker nor an alcohol consumer. Her family history included lung, esophageal, and intestinal cancers in first-degree relatives. The initial chest computed tomography (CT) scan revealed scattered pulmonary nodules, with the largest measuring 16x9 mm. A subsequent CT scan at the specialized center confirmed multiple solid, well-demarcated nodules scattered in both lungs, the largest measuring 16x10 mm

in the anteromedial basal segment of the left lower lobe, raising suspicion of metastatic disease.

A percutaneous biopsy of the nodule was performed, revealing a well-differentiated neuroendocrine neoplasm with a Ki-67 index of 0.2%, grade 1. The CT scan performed for biopsy guidance showed bilateral non-calcified pulmonary nodules with a random distribution, including a 14-mm nodule in the anteromedial basal segment of the left lower lobe and a 5-mm nodule in the lingula. Mild mosaic attenuation in the left lower lobe suggested air trapping (Figure 1).

The patient underwent non-anatomical pulmonary segmentectomies of the left lung through an open posterolateral thoracotomy, with resection of all palpable nodules in May 2024. Histopathological and immunohistochemical analysis (Figure 2) of the surgical specimens confirmed a well-differentiated neuroendocrine tumor, grade 1, with a Ki-67 index of 0.2%, positive in 7 out of 8 resected pulmonary nodules. A postoperative CT scan showed stability of the small residual pulmonary nodules bilaterally. An expectant approach was adopted for the remaining lesions due to their stability and small size.

Discussion

This case highlights the rare presentation of multiple pulmonary carcinoid tumor foci in a 68-year-old female patient. The diagnosis was established through imaging studies and confirmed by biopsy and immunohistochemical analysis. As previously demonstrated, pulmonary carcinoid tumors account for a small fraction of lung tumors and are categorized as typical or atypical carcinoids [1,2,6]. Most cases reported in the literature involve a single focus, making the presentation of multiple foci a rare phenomenon [10], often differentiated from diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) or, primarily, from pulmonary metastases originating from other sites, such as the gastrointestinal tract or pancreas, which are the most common primary sites [5,7,11].

Pulmonary metastases are typically the result of malignancies at other sites, with the lung being a common site of hematogenous spread due to its extensive capillary system [11]. Gastrointestinal carcinomas, especially those originating in the pancreas, small intestine, and colorectum, frequently metastasize to the lungs, often presenting as multiple bilateral nodules. Radiologically, pulmonary metastases are typically multiple, variable in size, and randomly or centrifugally distributed, without lobe-specific predilection [9,11]. This pattern can initially obscure the diagnosis, particularly in patients with a history of malignancy or significant risk factors, such as the familial history of lung, esophageal, and intestinal cancer observed in this patient [9]. Differentiating between a primary pulmonary carcinoid and metastases from gastrointestinal NETs is crucial for management and prognosis.

Studies suggest that the presence of multiple foci may be associated with genetic or environmental factors, though the etiology is not fully understood [7,10]. Tumor location and diameter are crucial for predicting treatment success. Approximately 70% of carcinoids are central, often detectable by bronchoscopy, and have a better prognosis than peripheral tumors, which tend to be larger and more associated with atypical carcinoids [7,12]. Central tumors generally present with symptoms related to bronchial obstruction (e.g., pneumonia, cough, wheezing) and are presumed to be diagnosed earlier than peripheral tumors, which are more often asymptomatic [2,13].

The nonspecific clinical presentation, such as cough, dyspnea, and weight loss, often delays diagnosis. In this patient, the symptoms were nonspecific and may also be attributable to the prior COVID-19 infection. Beyond imaging studies, diagnostic methods rely on histopathology with neuroendocrine morphology and immunohistochemistry, including cellular morphology, nuclear divisions, and the Ki-67 index. The WHO 2015 classification for pulmonary tumors recommends synaptophysin (Syn), chromogranin A (CgA), and CD56 as neuroendocrine markers, with Syn and CgA being the first options [8,14].

An unusual feature leading to this report was the presence of multiple carcinoid tumor foci in the lung. Surgical resection revealed that 7 of the 8 resected nodules were positive for well-differentiated grade 1 neuroendocrine tumors (Ki-67 index of 0.2%). This multifocal presentation underscores the rarity of this condition and necessitates an individualized diagnostic and therapeutic approach. A key concern was whether these could be metastases from other sites or coexist with tumors of different histologies synchronously.

Current therapeutic approaches for tumor treatment include chemotherapy, radiotherapy, immunotherapy, targeted therapy, and surgery. Treatment choice may vary depending on the subtypes of pulmonary neuroendocrine tumors (PNETs). For pulmonary carcinoids (PCs), surgery is considered the preferred therapeutic option [5,9,14]. Extensive retrospective studies have shown that adjuvant therapy provides no additional benefits for typical carcinoids (TCs) or atypical carcinoids (ACs) [15]. The primary goal is tumor removal while preserving as much pulmonary tissue as possible. For peripheral pulmonary tumors, the ideal surgical approach is complete anatomic resection, such as lobectomy or segmentectomy. In patients with limited pulmonary function, standard segmental resection often results in better outcomes than a wide wedge resection. For atypical pulmonary carcinoids, limited sublobar resection may increase the risk of local recurrence postoperatively [9,14].

In this patient, considering the good pulmonary reserve and the well-differentiated nature of the previously biopsied tumor, the decision was to perform multiple non-anatomical segmentectomies, aiming for greater preservation of pulmonary parenchyma given the number of lesions. Postoperative chest CT revealed stability of the small residual pulmonary nodules and the absence of new lesions. Therefore, an expectant approach was adopted for the remaining lesions.

Adjuvant chemotherapy following the complete resection of pulmonary neuroendocrine tumors is not generally recommended, as no randomized controlled trials support this practice. While several retrospective studies have explored the efficacy of adjuvant chemotherapy, most have not demonstrated clear advantages with its administration [5,15].

Conclusion

This report documents the rare presentation of multiple pulmonary carcinoid tumor foci, highlighting the effectiveness of pulmonary segmentectomy and the importance of a personalized diagnostic and therapeutic approach.

Statement of Ethics

This study protocol was reviewed and approved by the ethics committee of Erasto Gaertner Hospital on October 30, 2024 (approval reference number: 82620824.0.0000.0098) for the publication of the case and complied with current regulations on human research. Written informed consent was obtained from the patient for the publication of their medical case details and accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Luis Pereira: writing – original draft, conceptualization, visualization. Fernanda Bomfati: writing – review and editing, visualization, conceptualization. Milena Kozonoe: writing – original draft, visualization. Sergio Ioshii: writing – original draft, visualization. Gerardo Valladares: writing – review and editing, supervision. Vinicius Preti: writing – review and editing, supervision.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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