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## Case Report

# Primary lung carcinoid metastatic to the breast

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### ABSTRACT

Lung carcinoid tumors account for approximately 2% of lung cancers, with 10% of the tumors represented by the atypical type. While atypical carcinoids are metastatic to intrathoracic lymph nodes in approximately half of the cases on the initial presentation, distant metastases are seen in only 20% of the patients and are found most frequently in bones, liver, adrenal glands, and brain. We present a case of an unusual metastatic disease to the breast in 51-year-old female who developed a new breast mass 2 years after left lower lobectomy due to atypical carcinoid tumor. Atypical pulmonary carcinoid metastases to the breast are exceptionally uncommon, yet they are important considerations for appropriate management, especially with an anamnesis of this neoplasm.

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## Introduction

Pulmonary neuroendocrine tumors arise from Kulchitsky cells that are found in the bronchial mucosa and responsible for production and storage of neuroendocrine peptides [1]. Pathologic proliferation of these cells can lead to formation of small tumorlets, low- and intermediate-grade neoplasms, or more aggressive tumors [1]. The biological behavior of these proliferated cells reflects their histologic aggressiveness and ranges from asymptomatic lesions to nefarious malignancies such as small cell lung cancer and large cell neuroendocrine tumors with 5-year survival rate of 21% [2]. Typical carcinoid tumors represent low-grade lung neuroendocrine neoplasms, accounting for 90% of all carcinoid lung tumors [3]. These

tumors usually present as an incidentally discovered or symptomatic noncalcified or partially calcified solid peribronchial or partially or completely obstructing endobronchial lesion in a young individual [4]. The 5-year survival rate is approximately 97%, and the metastatic potential is low: 5%–15% to intrathoracic lymph nodes and only 3% to distant sites [3]. Conversely, atypical carcinoids are considered intermediate neoplasms and account for 10%–20% of bronchopulmonary neuroendocrine tumors [3]. Atypical carcinoids are much more likely to have systemic manifestations and significantly lower 5-year survival rate of 57% [3]; 40%–50% of patients present initially with metastases to intrathoracic lymph nodes, and approximately 20% have distant disease [3]. Both typical and atypical carcinoids occasionally can present with

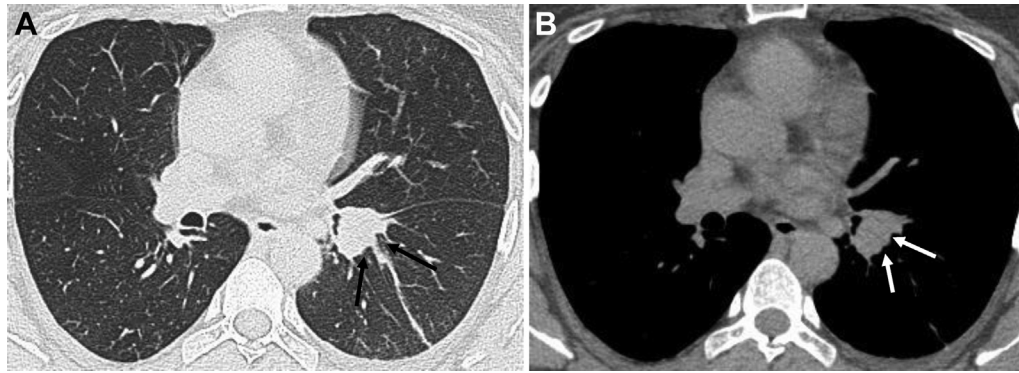
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**Fig. 1** – Axial chest CT in lung (A) and mediastinal (B) windows shows a medial left lower lobe 2.1 cm nodule (arrows) that abuts and narrows the lobar bronchus. Intraoperatively, bronchial invasion was confirmed.

multifocal deposition of tumorlets along peripheral airways, which may be due to metastatic disease or diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) [5]. Patients with DIPNECH are typically present with symptoms of reactive small airways disease and frequently undergo multiregimen treatment for asthma without improvement [1].

Here, we present a case of a patient with an initial diagnosis of left lower atypical carcinoid and concomitant DIPNECH discovered during workup of chronic cough. Subsequent metastases to the brain and left breast were found after 2 years in remission.

## Case report

The patient is a 51-year-old Caucasian female who presented to the pulmonology service with a chronic cough interfering with daily activities. She was referred to pulmonology after numerous years of multiple unsuccessful treatment trials for reactive small airways disease. Upon further workup, CT chest demonstrated medially located 2.1 cm left lower lobe solitary pulmonary nodule, closely abutting and narrowing left lower lobar bronchus (Figs. 1A and B). Subsequent FDG-PET/CT demonstrated significant hypermetabolic activity of the lesion (Fig. 2). The patient underwent bronchoscopy with biopsy with final tissue diagnosis of a neuroendocrine tumor consistent with well-differentiated carcinoid. Intraoperative histopathologic assessment reported staging as pT3N1, with evidence of invasion of the left lower lobar bronchus, the adjacent left inferior pulmonary vein, and a lymph node just medial to the bronchus. Some residual neoplastic tissue was found at the surgical stump, necessitating long-term monthly Sandostatin injections following left lower lobectomy and partial mediastinal lymph node dissection.

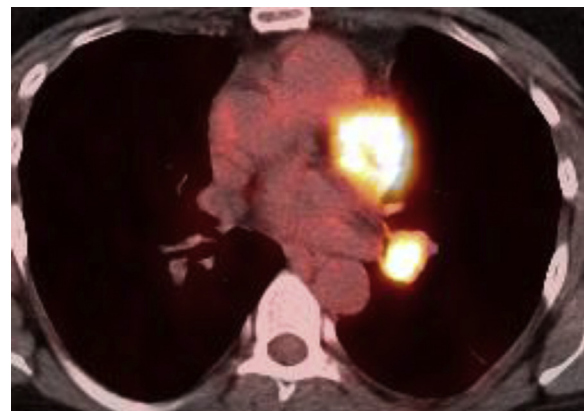
Two years later, a routine screening mammogram revealed a new 7-mm indistinct mass (Figs. 3A and B) in the left breast. Subsequent workup with diagnostic mammography and breast ultrasound (Figs. 4A and B and Figs. 5A and B) confirmed the lesion as highly suspicious. Intraoperative histopathologic analysis and special immunostains of the lesion (Figs. 6–9) revealed a neuroendocrine cell origin with positive stains for synaptophysin and chromogranin (markers of

neuroendocrine differentiation) and negative for GATA3 immunostain (marker of primary breast malignancy) [1]. During further metastatic workup, contrasted MRI of the brain demonstrated several focal lesions with biopsy results of neuroendocrine cell metastases as well (Figs. 10A and B).

The patient had since completed whole-brain radiation therapy for metastatic carcinoid tumor to the brain. She then initiated everolimus every other day for her persistent cough. A slowly growing small nodule was noted in the left upper lobe on follow-up CT chest representing either progression of metastatic tumorlets or worsening concomitant DIPNECH (Fig. 11).

## Discussion

Atypical carcinoids are categorized as intermediate-grade malignancies, with the designation as atypical carcinoid being based on moderate cytological atypia, necrosis, mitotic



**Fig. 2** – FDG-PET/CT shows significant hypermetabolic activity of left lower lobe nodule with a maximum SUV of 8.0. Notice the close relationship to the left inferior pulmonary vein that was found to be invaded in intraoperative examination. FDG-PET/CT, fluorodeoxyglucose positron emission tomography/computed tomography; SUV, standardized uptake value.

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