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Yuseph Mahmoud Mohamed, 6 th Year, Group 5

INTEGRATED STUDY MASTER'S THESIS

Plaučių karcinoidinis navikas: atvejo ataskaita ir literatūros apžvalga

Lung Carcinoid. Literature Review and Case Report

Supervisor lecturer Rūta Kibarskytė-Gustainė

Head of the department or clinic prof. dr. (HP) Edvardas Danila

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Student's email: yuseph.mohamed@mf.stud.vu.lt

Structure

1. Abstract

Lung carcinoids are truly rare neuroendocrine tumours that present a distinctly clinical challenge in view of their diversity of presentation, slow-growing pattern, and metastasizing potential. The following thesis represents a detailed case study regarding a 74-year-old female with the diagnosis of typical carcinoid tumour in the intermediate bronchus of the right lung. The patient presented to us for a first opinion with massive haemoptysis and dyspnoea which mandated urgent medical intervention. Diagnostic workup with contrast-enhanced CT and bronchoscopy with biopsy confirmed a low-grade neuroendocrine tumour. Lower bilobectomy was performed, and the patient had a successful resection with clear margins. The postoperative recovery was uncomplicated, and follow-up imaging did not show any recurrence. This case represents the necessity for early diagnosis and surgical intervention in the management of pulmonary carcinoid tumours. The case therefore highlights the good prognosis following complete tumour resection.

2. Introduction

Lung carcinoids are rare, low-grade neuroendocrine tumours accounting for less than 5% of all primary lung cancers. They are divided into typical and atypical variants. Typical carcinoids have lower degrees of malignancy and a somewhat better course than their atypical counterparts. However, even in typical carcinoids, considerable clinical symptoms can be present, mostly due to obstruction of the central airways and consequent haemoptysis or recurrent infections. This thesis presents a case study of the clinical evaluation and management of a typical carcinoid tumour. The patient is a 74-year-old woman with significant hypertension and a smoking history who was admitted to the hospital with symptoms of central airway obstruction. The diagnostic approach adopted in this case was comprehensive and has included imaging and histological approaches for confirmation of diagnosis and guiding treatment. Surgical resection remains the cornerstone of treatment for localized carcinoid tumours, and in this case, lower bilobectomy was performed with satisfactory outcomes.

This introduction contains general information about lung carcinoids, including their epidemiology, pathophysiology, and clinical importance. Furthermore, it delineates the aims of the thesis, such as the diagnostic dilemma, therapeutic strategies, and long-term management of a patient with a typical carcinoid tumour.

3. Case description

3.1 Patients' description, chief complaints, and anamnesis

A 74-year-old female patient comes in for complaints of progressive haemoptysis, nonspecific dyspnoea, rhinorrhoea, and vomiting. Days before her admission, she was in poor condition due to sudden haemoptysis, which showed a tendency to increase even more during the following days. In about one week, the patient presented with significant haemoptysis-massive expectoration of blood clots, with losses of up to a glass of blood per day-and calmly sought medical care in the emergency department. She also complained of increasing dyspnoea on exertion.

Life History: The medical anamnesis showed that the patient suffered from several chronic diseases. She had primary hypertension that she was managing for a few decades, controlled with the help of antihypertensive drugs. She also had a history of dyslipidaemia and spinal osteochondrosis, which likely contributed to the overall health status and complexity of her medical management.

She had a significant history of smoking: half a pack per day for over 50 years.

3.1.1 Initial laboratory investigation

The patient was initially evaluated at the district hospital. The history of haemoptysis raised concerns about a possible pulmonary embolism (PE). Before diverting to a tertiary hospital, initial laboratory tests were performed. The results of the abnormal tests are summarized in Table 1.

Parameter	Patient Value	Reference Range
D-dimer	1.1 mg/L	< 0.5 mg/L
Haemoglobin (Hb)	144 → 134 g/L	120–160 g/L (Female)
C-reactive protein	7.89 mg/L	< 5 mg/L

Table. 1: Initial Laboratory Evaluation at District Hospital

The elevated D-dimer level additionally enhanced concerns about pulmonary embolism, a potentially life-threatening condition that needed to be ruled out. The decreasing haemoglobin level's indicated ongoing blood loss, likely due to haemoptysis. A CT angiography scan ruled out pulmonary embolism, revealing material filling the segmental bronchi and atelectasis (collapse) in the right lung.

Due to the severity of the symptoms and the initial findings, the patient was transferred to a specialized Pulmonology and Allergology Centre for further evaluation.

The patient was stabilized with oxygen therapy and antihypertensive medications while the medical team prepared for further diagnostic investigations to confirm the nature of the pulmonary lesion and determine the appropriate course of treatment. These findings further guided the stabilization of the patient, particularly the need for ongoing oxygen treatment blood pressure management, and monitoring of renal and cardiac function. Following stabilization, a comprehensive diagnostic workup was initiated to identify the nature of the pulmonary lesion and determine the appropriate treatment strategy.

3.2 Principal findings of laboratory investigations

Objectively: Temperature-36.4C, Pulse – 75/min, Respiratory rate – 16/min, SpO2 94 % (with 2 l of oxygen), Capillary refill time <2s

Upon the patient's arrival at the tertiary hospital, a comprehensive set of laboratory tests was performed to further assess her condition, particularly in light of her presenting symptoms of haemoptysis and dyspnoea. These tests were crucial for evaluating the extent of her blood loss, detecting any underlying infection or inflammation, assessing cardiac stress, and monitoring renal function. The results are summarized in the tables below (Table 2 and Table 3).

Parameter	Patient value	Reference Range
Haemoglobin (Hb)	134 g/L	120-160 g/L (Female)
White Blood Cell Count (WBC)	7.94 x10^9/L	4.0-11.0 x10^9/L
Neutrophils (NEU)	49.60%	40-70%
Lymphocytes (LYM)	35.50%	20-45%
Monocytes (MON)	12.90%	2-10%
Eosinophils (EOS)	1.50%	1-6%
Basophils (BAS)	0.50%	0-2%
Red Blood Cell Count (RBC)	5.04 x10^12/L	4.2-5.4 x10^12/L
Haematocrit (Hct)	0.427 L/L	0.36-0.46 L/L
Platelet Count (Plt)	251 x10^9/L	150-450 x10^9/L

Table 2: Complete Blood Count (CBC) Results

The patient's haemoglobin level was slightly decreased from 144 g/L to 134 g/L, likely due to ongoing haemoptysis. The normal white blood cell count indicated no acute infection, while the elevated monocyte count suggested a possible stress or inflammatory response, which is common in patients with chronic illness.

Coagulation Profile: To rule out any bleeding disorders and assess the patient's coagulation status, a coagulation profile was conducted, as shown in Table 3.

Parameter	Patient Value	Reference Range

Activated Partial Thromboplastin Time (APTT)	27.2 s	25-35 s
International Normalized Ratio (INR)	0.97	0.8-1.2
Creatine	97 µmol/L	60-110 µmol/L
C-Reactive Protein (CRP)	7.89 mg/L	<5 mg/L
Brain Natriuretic Peptide (BNP)	191.4 ng/L	<100 ng/L
Troponin I	34 ng/L	<0.04 ng/L
Glucose	9.0 mmol/L	4.0-6.0 mmol/L

Table 3: Coagulation Profile Results and other biochemical testing

3.2.1 Initial Chest CT Scan with Contrast

A contrast-enhanced computed tomography (CT) scan of the chest was the initial imaging modality performed for the evaluation of suspected pulmonary malignancy in this patient. The CT scan revealed a large mass within the segmental bronchi of the right lung, causing partial obstruction and resultant atelectasis of the right lower lobe (Figure 1 and 2).

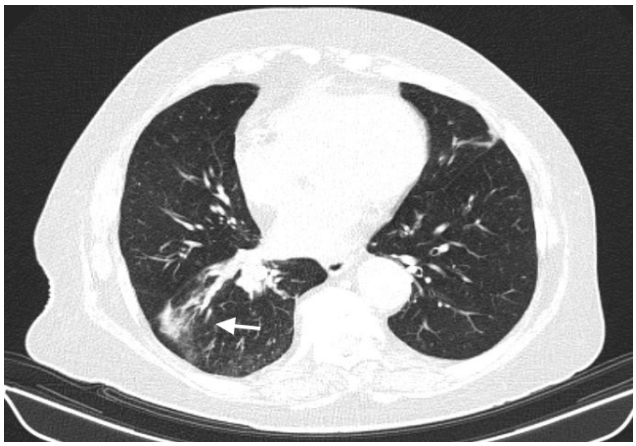

Figure 1: CT partial atelectasis (marked by white arrow)

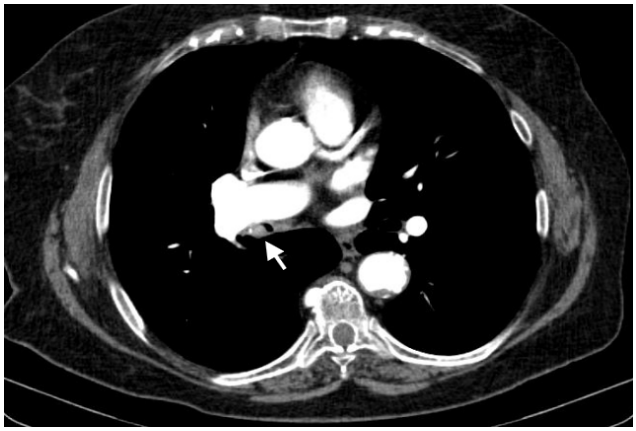

Figure 2: CT right L3 endobronchial growth (marked by white arrow)

In addition to these being secondary findings, the scan also showed bilateral adrenal adenomas, significant aortic atherosclerosis, and renal artery stenosis. Although these findings contribute to valuable information regarding a patient's underline condition, they are more likely incidental and not specifically related to the primary pulmonary pathology. Of most importance in this case, given high D-dimer levels as an initial clinical concern, the CT angiography scan did not demonstrate any occult pulmonary embolus.

These findings at CT were very helpful in guiding further diagnostic evaluation, including the need to perform bronchoscopy guided by biopsy, which is important for confirming the nature of the lesion and planning suitable treatment.

3.2.2 Radiologist Consultation and Imaging Review

Following the initial CT findings, a radiological consultation was undertaken to further characterize the detected mass and evaluate its potential impact on adjacent structures. The review was conducted by a thoracic imaging subspecialist who reviewed the CT images regarding the details of obstruction in the bronchus, extent of atelectasis, and surrounding tissue involvement.
The radiologist confirmed that mass was endobronchial in location within the right lower lobe bronchus, associated with atelectasis and mucus plugging.

3.2.3 Bronchoscopy and Endobronchial Ultrasound (EBUS)

In this patient, bronchoscopy was performed to further investigate the endobronchial mass identified on CT imaging and to procure biopsy samples necessary for confirming the diagnosis.
During the procedure, a friable and highly vascular tumour was visualized in the right intermediate bronchus (Figure 3 and 4). The tumour was actively bleeding, necessitating immediate haemostasis, which was achieved using diluted adrenaline and argon plasma coagulation (APC). Despite the bleeding, biopsy samples were successfully obtained from the lesion.

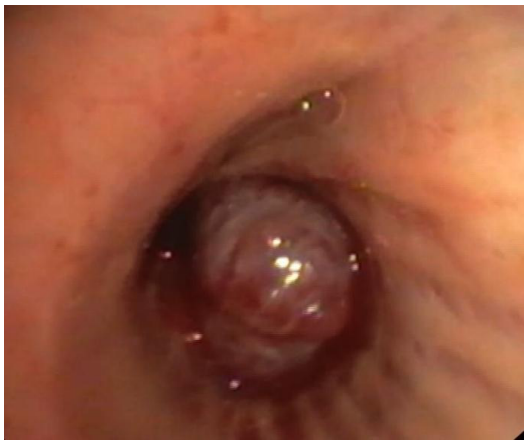

Figure 3: Endobronchial view

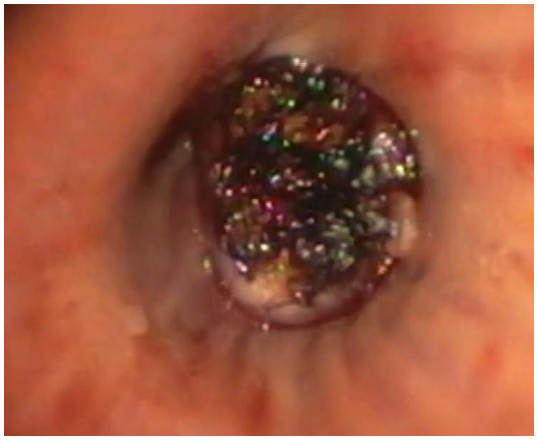

Figure 4: Bronchoscopy view after biopsy and haemostasis using APC

3.3 Histological analysis and pathological findings

Endobronchial Biopsy and Initial Histological Evaluation:

The biopsy material showed that the tumour was a typical carcinoid with its cells arranged in nests and trabecular pattern. The cells within the tumour showed moderate eosinophilic cytoplasm and small centrally located nuclei, characteristic of carcinoid morphology. IHC confirmed the neuroendocrine nature of the tumour. The cells were strongly positive for PanCK, Synaptophysin, and Chromogranin A, and the Ki67 proliferation index was low at 1%, characteristic of indolent typical group carcinoid tumours

3.4 SPECT: Functional Imaging and Tumour Characterization

Single-Photon Emission Computed Tomography (SPECT) combined with CT was employed to assess the functional characteristics of the pulmonary lesion, particularly to determine the presence of somatostatin receptors.
The SPECT/CT scan revealed no pathological uptake of the radio indicator, indicating the absence of somatostatin receptor expression in the tumour. Despite this lack of receptor expression, the mass in the right lower lobe was consistent with previous imaging findings, confirming the presence of a centrally located lesion with characteristics typical of a carcinoid tumour.

3.5 Management, Treatment, and Interventions

3.5.1 Initial Stabilization and Symptom Management

Upon presentation with significant haemoptysis and dyspnoea, the initial management focused on stabilizing the patient's condition and controlling symptoms. The patient was provided with oxygen therapy to address hypoxemia and ensure adequate oxygenation. In addition, antihypertensive medications were administered to manage her blood pressure, which is critical in preventing further complications, particularly given her history of primary hypertension.

Haemoptysis Management:

Supportive care included oxygen therapy, close monitoring of vitals, and bronchoscopy for both diagnosis and intervention. During the procedure, active bleeding from the vascular endobronchial tumour was managed using diluted adrenaline and argon plasma coagulation (APC), effectively achieving haemostasis.

Surgery and Postoperative Care:

The patient underwent a right-sided bilobectomy to excise the typical carcinoid tumour located in the right intermediate bronchus, which involved removal of the middle and lower lobes. Postoperatively, she was monitored in the ICU for 24 hours. Pain control was achieved using epidural analgesia and intravenous medications. Respiratory physiotherapy, including deep-breathing exercises, was initiated to prevent atelectasis and support recovery. Her postoperative course was uneventful, with no complications.

3.6 Outcome

After the initial postoperative recovery, the patient was enrolled in a structured rehabilitation program. Given the favourable prognosis following the complete resection of the typical carcinoid tumour, the long-term management plan emphasized regular follow-up visits to monitor for recurrence and to assess pulmonary function. The patient was advised to adhere to her antihypertensive regimen and to maintain a healthy lifestyle to support her recovery and overall health.
A follow-up CT performed several months later showed no evidence of recurrence. Regular imaging and pulmonary function monitoring was planned.

4. Literature Review

4.1 Classification of Pulmonary Carcinoid Tumours

Pulmonary carcinoid tumours are rare, well-differentiated neuroendocrine neoplasms (NETs) of the lung, representing approximately 1–2% of all primary lung malignancies and about 25% of all bronchial NETs [1]. They originate from Enterochromaffin cells, a type of neuroendocrine cell located within the bronchial epithelium. The World Health Organization (WHO) 2021 classification of thoracic tumours divides pulmonary neuroendocrine tumours into four main categories based on morphological differentiation, mitotic activity, and presence of necrosis [2,3]:

Type	Grade & Differentiation	Mitoses	Necrosis	Ki-67 Index	Metastatic Potential	Prognosis
Typical Carcinoid (TC)	Low-grade, well-differentiated	<2 per 2 mm²	Absent	<2%	Low (~10–15% risk of lymph node involvement)	Favourable; 5-year survival ~85–95%
Atypical Carcinoid (AC)	Intermediate grade	2–10 per 2 mm²	Focal	5–20%	Moderate (~30–50% risk of nodal spread)	5-year survival ~50–70%
Large-cell Neuroendocrine Carcinoma (LCNEC)	High-grade, aggressive growth	>10 per 2 mm²	Extensive	40–80%	High; frequent distant metastases	Poor; 5-year survival 20–40%
Small-cell Lung Carcinoma (SCLC)	Very high-grade, poorly differentiated	>10 per 2 mm²	Extensive	>80%	Extremely high; most present with	Very poor; 5-year survival <10%

Type	Grade & Differentiation	Mitoses	Necrosis	Ki-67 Index	Metastatic Potential	Prognosis
	neuroendocrine carcinoma				distant metastases	

Table 4: Neuroendocrine tumour classification

4.2 Epidemiology

Pulmonary carcinoids are rare tumours, with less than 5 cases annually per million individuals [4]. Historically, they have been underdiagnosed since they grow slowly and present with atypical and unspecific symptoms, simulating benign lung disease. The incidence, though, seems to be rising steadily because of advances in imaging and bronchoscopy and with heightened awareness [5].

Typical carcinoids represent about 85–90% of pulmonary carcinoids and atypical carcinoids account for the remaining 10–15% [6]. The tumours mostly present at a younger median age (40–60 years) than other lung cancers, and there is little gender predominance. Though a slight female predominance is cited by some studies in typical carcinoids [7].

Smoking has been identified as an important risk factor for atypical carcinoids and high-grade neuroendocrine tumours, whereas there is no definite association between smoking and typical carcinoids [8]. There are other systemic diseases that may be associated with pulmonary carcinoids. For example, familial disorders like Multiple Endocrine Neoplasia type 1 (MEN1) predisposes to pulmonary carcinoids, especially in younger patients [9].

The majority of carcinoid tumours are spontaneous, though rising incidence implies there may be environmental or genetic causes still to be determined. Due to rarity and slow growth, they are often picked up at an early stage incidentally, as when imaging is done for other reasons.

4.3 Pathophysiology of Lung Carcinoids

Pulmonary NETs are a specialized group of lung cancer from the bronchopulmonary epithelial neuroendocrine cells. The cells involved in this case are the Enterochromaffin cells and are major in airway function regulation through the secretion of neuropeptides and amines, control of local immune responses, airway tone, and epithelial homeostasis.

Neuroendocrine tumours in the lung include slow-growing low-grade tumours (classic carcinoids) to highly aggressive tumours (small cell lung cancer, SCLC). Despite the pulmonary NET's 1-2% representation among all primary lung tumours, they are noteworthy because they are heterogeneous in terms of behaviour, in patterns, and in responses to treatments [7].

Lung carcinoids, the focus of this thesis, are also categorized into typical and atypical carcinoids, and the atypical are separated from the typical by the difference in the histopathologic features, the cell-proliferation rate, and the clinical course. Typical carcinoid tumours, in contrast to the high-grade varieties, are slow-growing, well-differentiated, and minimally metastatic, and are also prone to causing significant morbidity by local airway obstruction and endocrinologic secretion in some.

Pulmonary typical carcinoids, despite being the least aggressive among lung NETs, still pose diagnostic and therapeutic challenges due to their central airway location and potential for causing airway obstruction, recurrent infections, and, in some cases, hormone-mediated symptoms.

4.3.1 Cellular and Molecular Mechanisms

At the molecular level, well-differentiated carcinoid tumours differ genetically from poorly differentiated neuroendocrine carcinomas. Typical and atypical carcinoids have fewer chromosomal aberrations and genetic mutations than small-cell lung cancer and large-cell neuroendocrine carcinoma. One of the main molecular changes in pulmonary carcinoids is inactivation of MEN1 gene, encoding a tumour suppressor menin protein. Loss of heterozygosity (LOH) of chromosome 11q13, situating the MEN1 locus, has occurred in as many as 50% of typical and atypical carcinoids, especially in familial cases and individuals with multiple endocrine neoplasia type 1 (MEN1) [1,2].

Further studies have revealed defects in the PI3K/AKT/mTOR signalling system, which regulates cell growth and survival. The activation of this system drives tumour growth and is linked to neuroendocrine cell hyperplasia and resistance to apoptosis [3]. The clinical significance of this system is supported by treatment using Everolimus, an mTOR blocker, in advanced carcinoids.

In contrast to high-grade neuroendocrine neoplasms, pulmonary carcinoids do not commonly show TP53 and RB1 mutations, hallmarks of SMALL-CELL LUNG CARCINOMA. The largely intact genome of carcinoids mirrors their indolent biology and low mitotic index, separating them from their aggressive counterparts [4].

Specific changes in cellular and molecular mechanisms are described below in more detail.

MEN1 mutations and chromatin remodelling

A crucial genetic mutation in pulmonary carcinoid tumours is the loss-of-function inactivation of the MEN1 gene encoding menin, a tumour suppressor. Menin controls chromatin structure, transcription, and neuroendocrine differentiation. MEN1 mutations can be identified in about 30–50% of pulmonary carcinoids, more commonly in atypical than typical types [1]. Resulting loss of function causes epigenetic deregulation, enhancing neuroendocrine marker over-expression (e.g., Chromogranin A, Synaptophysin) and clonal growth of poorly differentiated cells.

Loss of heterozygosity (LOH) at chromosome 11q13, site of MEN1, is frequent in these tumours [2]. Other aberrations include losses of 5q and 10q and, in atypical carcinoids, gains of 17q and losses of 3p, which may be responsible for their aggressive clinical behaviour.

PI3K/AKT/mTOR Signalling Pathway

The PI3K/AKT/mTOR signalling cascade is often hyperactivated in pulmonary carcinoids and controls survival, growth, and metabolism of cells. mTORC1 hyperactivation induces tumour growth and protein synthesis, whereas upstream changes (such as mutations in PI3K or activation of IGF-1 receptors) cause persistent AKT activity and resistance to apoptosis [3]. This also drives phosphorylation of ribosomal S6 kinase (S6K1) and neuroendocrine differentiation.

Clinically, this pathway supports the treatment application of Everolimus, an mTOR inhibitor revealed in the RADIANT-4 trial to extend progression-free survival in advanced pulmonary carcinoids [4].

Notch signalling and neuroendocrine differentiation

The Notch signalling system is critical in cell differentiation and growth control. Downregulation of Notch1 is characteristic of pulmonary carcinoids and leads to increased neuroendocrine properties, decreased maturation, and survival of tumour cells [5].

Preclinical research has shown that re-activation of the Notch signalling cascade, specifically using gamma-secretase inhibitors (GSIs), can inhibit tumour growth by re-establishing differentiation and inducing cell cycle arrest. Though still unexplored therapeutically, modulation of Notch continues to represent an intriguing therapeutic target in carcinoid biology.

MEN1 Mutation and Syndromic Carcinoids

In familial syndromes such as Multiple Endocrine Neoplasia type 1 (MEN1), patients develop pulmonary carcinoids as part of a broader endocrine tumour spectrum. MEN1 mutations result in a loss of the tumour suppressor protein menin, leading to chromatin remodelling dysfunction. Pulmonary carcinoids in MEN1 patients are often multiple, bilateral, and tend to occur at a younger age.

Current research is investigating HDAC inhibitors and epigenetic therapies targeting these chromatin abnormalities. Identification of MEN1 mutations in sporadic cases also suggests that genetic screening may be warranted in young patients or those with multiple endocrine neoplasia.

4.3.2 Histopathology and Tumour Microenvironment

The histopathology of a typical carcinoid is characterized by well-differentiated cellular structure, minimal mitotic activity (<2 mitoses/2 mm^2 of tissue), and no necrosis. Thus, they are distinguishable from atypical carcinoid tumours and from higher-grade neuroendocrine carcinomas such as small-cell lung cancer and large-cell neuroendocrine carcinoma.

Histologically, typical carcinoids exhibit trabecular, insular, or organoid patterns of growth with oval to rounded nuclei and finely dispersed chromatin ("salt-and-pepper" appearance) and moderately eosinophilic cytoplasm. In sharp distinction to atypical carcinoids with focal necrosis and greater mitotic activity (2-10 mitoses/2 mm^2), typical carcinoids exhibit minimal cytologic atypia that underlies their indolent behaviour and reduced metastatic potential.

Immunohistochemical staining is critical in diagnosing and distinguishing pulmonary carcinoids from other lung tumours. Typical carcinoids are positive for high expression of neuroendocrine markers like chromogranin A, synaptophysin, and CD56. TTF-1 expression is variable and can be used to differentiate pulmonary carcinoids from gastrointestinal neuroendocrine tumours [4,6]. Small Cell Lung Cancer) and Large Cell Neuroendocrine Carcinoma are typically positive for having a high Ki-67 proliferation index (>50%), overexpression of p53, and RB1 mutations that are not present in typical carcinoids.

Neuroendocrine Tumour Microenvironment

The tumour microenvironment of pulmonary carcinoids plays a crucial role in tumour growth, immune evasion, and response to treatment. Unlike high-grade neuroendocrine tumours, which exhibit high cellular proliferation and stromal desmoplasia, typical carcinoids maintain a relatively quiescent microenvironment with limited angiogenesis and immune cell infiltration [17].

Role of Stromal and Immune Components

Pulmonary carcinoid tumours are sustained by a stromal bed of fibrovascular tissue with a structural function and a function in oxygen and nutrient exchange. Pericytes and stromal fibroblasts are essential for tumour cell survival but do not have the extensive desmoplastic response found in small cell lung carcinoma and LARGE CELL NEUROENDCOCRINE CARCINOMA. The extracellular matrix in carcinoid tumours consists of collagen IV and laminin that are responsible for promoting adhesion and neuroendocrine differentiation.

Infiltration by immune cells is minimal in typical carcinoids compared to aggressive lung cancer and is a contributor to inadequate immune-mediated tumour control. Tumour-associated macrophages and regulatory T-cells have been observed in small numbers in studies and suggest that pulmonary carcinoids are immunologically weak compared to aggressive lung cancer [7]. Such an immunologically "cold" tumour environment is one of the reasons immune checkpoint inhibitors are not very effective in pulmonary carcinoids.

Angiogenesis and Vascularization

Unlike high-grade neuroendocrine carcinomas, which exhibit extensive neovascularization and high vascular endothelial growth factor (VEGF) expression, typical carcinoids have moderate microvascular density. However, due to their bronchial location, these tumours are highly vascularized and prone to tumour-associated haemorrhage, which contributes to the presentation of haemoptysis in affected patients. Given their vascularity, targeting VEGF-mediated pathways with anti-angiogenic therapies (e.g., bevacizumab) is being explored as a potential treatment for advanced disease. The comparison of pulmonary NETs histopathology is displayed in Table 5.

Feature	Typical Carcinoid	Atypical Carcinoid	LCNEC / SCLC
Mitoses (/2 mm²)	<2	2–10	>10
Necrosis	Absent	Focal	Extensive
Ki-67 Index (%)	<2	2–20	>50
Chromogranin A	Strongly Positive	Positive	Focal / weak
Synaptophysin	Strongly Positive	Positive	Positive
CD56	Positive	Positive	Positive
TTF-1	Variable	Often Positive	Positive (SCLC)
Prognosis	Excellent (90% 5-yr)	Intermediate (50–70%)	Poor (<20% 5-yr)

Table 5: Comparative Histopathology

4.3.3 Tumour Growth and Functional Activity

Pulmonary carcinoid tumours grow slowly and remain localized and, in many cases, will remain within and limited to the bronchial wall for many years. Tumour grade and location both influence growth. The typical carcinoids tend to grow intraluminal. However, atypical carcinoids tend to have increased parenchymal invasion and nodal spread [16].

Some pulmonary carcinoids are functionally active and have the ability to secrete peptides and neuroendocrine markers such as serotonin, chromogranin A, and neuron-specific enolase (NSE). The secretory tumours may cause carcinoid syndrome. Carcinoid syndrome affects between 2–5% of pulmonary carcinoid patients, predominantly those with advanced disease [2,17].

Tumour growth and local growth

Most pulmonary carcinoids develop in the central airways—the trachea, main bronchi, or segmental bronchi. The tumours grow as polypoid intraluminal masses, and depending on the level of airway obstruction, they cause obstructive symptoms. Wheezing or shortness of breath can be caused by partial obstruction, often misdiagnosed as asthma or chronic bronchitis, whereas complete obstruction results in post-obstructive pneumonia, atelectasis, and plugging of mucus.

Haemoptysis can result, especially in lesions with vascular invasion or mucosal ulceration, necessitating earlier clinical assessment. Radiologically, they present as well-circumscribed, contrast-enhancing masses on computed tomography, usually with evidence of airway narrowing, distal collapse, or hyperinflation—features also noted in this patient's imaging.

Hormonal Secretion and Functional Activity

Approximately 10–15% of pulmonary carcinoids can be typed as functionally active, as they produce hormones or peptides leading to endocrine syndromes of systemic origin. The best known of these is carcinoid syndrome due to excess secretion of serotonin and presenting as flushing, diarrhoea, bronchospasm, and valvular heart disease on the right side. Although uncommon in lung carcinoids (it occurs in 1–3% of patients), it needs to be considered when there is metastatic disease. Measurement of urinary 5-HIAA continues to be the standard biochemical test of serotonin excess [12,13]. Another significant presentation is ectopic ACTH production, leading to Cushing’s syndrome. This is seen in 1–5% of cases, mostly in atypical carcinoids. The patients can present with central obesity, hypertension, weakness of the muscles, and hyperglycaemia. The diagnosis relies on increased ACTH and cortisol, as evidenced by dexamethasone suppression testing.

Infrequently, pulmonary carcinoids can secrete histamine, bradykinin, or other vasoactive agents and present with episodic hypotension and flushing and wheezing. Such presentations can be mistaken for asthma or an allergic reaction and can be treated by somatostatin analogues like octreotide, which block hormone secretion.

4.3.4 Tumour Microenvironment and Immune Evasion

Pulmonary carcinoids, while generally considered indolent, exhibit complex interactions with their tumour microenvironment. This includes stromal fibroblasts, endothelial cells, pericytes, and infiltrating immune cells such as T lymphocytes and tumour-associated macrophages (TAMs). Unlike high-grade neuroendocrine carcinomas, typical carcinoids often have a "quiet" immune landscape, with lower mutational burden and immune checkpoint expression. However, recent studies suggest that in atypical carcinoids, particularly those with higher Ki-67 indices, there may be increased PD-L1 expression and immune evasion mechanisms.

TAMs, which often polarize into an M2 phenotype in carcinoid tumours, have been shown to promote angiogenesis and suppress effective cytotoxic T-cell responses. This environment supports local tumour growth and resistance to therapy. The interplay between angiogenic factors like VEGF and immune suppression is of particular interest as a potential target for future combination therapies (e.g., anti-VEGF + immunotherapy).

4.3.5 Tumour Progression and Metastasis

Although typical carcinoid tumours are slow-growing and have low metastatic potential, they can still spread via direct invasion, lymphatic dissemination, and hematogenous routes. The risk of metastatic spread depends on tumour size, lymphovascular invasion (LVI), and perineural infiltration. While SMALL-CELL LUNG CARCINOMA and LARGE Cell NEUROENDCOCRINE CARCINOMA exhibit aggressive, early metastasis, typical carcinoids remain localized for prolonged periods before dissemination occurs [6,7].

Local Invasion and Peribronchial Spread

Typical carcinoids tend to remain confined to the bronchial lumen, where they exhibit endobronchial growth and peribronchial extension. This may lead to:

- Bronchial wall invasion, resulting in chronic airway obstruction.
- Peribronchial fibrosis, causing irreversible airway narrowing.
- Mucus plugging and post-obstructive pneumonia, a common complication in centrally located tumours.

Histological studies have shown that perineural invasion (PNI) and lymphovascular invasion (LVI) are rare in typical carcinoids but more common in atypical carcinoids, correlating with a higher risk of nodal spread. The absence of destructive invasion into surrounding lung parenchyma is a key differentiating feature between typical carcinoids and aggressive lung cancers.

Lymphatic Spread and Nodal Involvement

Lymphatic dissemination occurs in 10-15% of typical carcinoid cases, with nodal involvement typically limited to hilar and mediastinal lymph nodes. In contrast, atypical carcinoids exhibit higher rates of nodal metastases (30-50%), with a greater propensity for spread beyond regional lymph nodes. Sentinel lymph node mapping has been explored as a potential tool for predicting metastatic spread in pulmonary carcinoids.

Common sites of lymphatic involvement in typical carcinoids:

- Hilar lymph nodes (N1)
- Mediastinal lymph nodes (N2)
- Peribronchial lymph nodes

The presence of nodal metastases significantly impacts prognosis, reducing 5-year survival rates from 95% (N0) to ~70% (N1-2). Reinforcing the importance of systematic lymph node dissection during surgical resection.

Distant Metastases and Hematogenous Spread

Distant metastases are uncommon in typical carcinoids (<5%) but can occur in advanced cases. When present, metastatic spread typically follows a hematogenous route, involving:

- Liver (most common site)
- Bone (osteoblastic metastases)
- Adrenal glands
- Brain (rare but possible in atypical carcinoids)

Atypical carcinoids exhibit a significantly higher metastatic potential (~30%), often presenting with multiple organ involvement at diagnosis. Studies suggest that higher Ki-67 indices (>5%) and larger tumour sizes (>3 cm) correlate with increased metastatic risk.

Prognostic Factors and Survival Outcomes Depending on Tumour Spread

The prognosis of pulmonary carcinoids depends on tumour stage, size, and lymph node involvement. In typical carcinoids:

- 5-year survival (localized, N0): 85-95%
- 5-year survival (nodal involvement, N1-2): 50-70%
- 5-year survival (distant metastases, M1): <40%

Factors associated with poor prognosis include tumour size >3 cm, LVI positivity, nodal involvement (N1/N2), and elevated Ki-67 index (>2%).

4.4 Clinical Presentation

The clinical presentation of pulmonary carcinoid tumours varies depending on tumour location, size, hormone secretion, and grade. Due to their slow-growing and indolent nature, many cases remain asymptomatic for prolonged periods and are often discovered incidentally during imaging for unrelated reasons. However, symptomatic cases frequently arise due to mechanical obstruction of the airways, particularly in tumours originating in the central bronchial tree, which accounts for the majority of typical carcinoids.

Respiratory Symptoms Due to Obstruction

The most common symptoms result from endobronchial growth, which can partially or completely obstruct airflow. Patients often present with a persistent non-productive cough, exertional dyspnoea, wheezing, or recurrent pneumonia. These symptoms are frequently misdiagnosed as asthma or bronchitis, especially in younger patients without a smoking history. Complete airway obstruction may cause lobar collapse or post-obstructive infections, leading to fever, haemoptysis, or localized chest pain [5]. In this patient, such symptoms prompted further imaging and led to detection of the mass in the right intermediate bronchus.

Haemoptysis, ranging from blood-streaked sputum to frank bleeding, occurs in up to 50% of symptomatic patients, often due to the tumour's high vascularity and friable surface [3,4,5]. Occasionally, tumours with mucosal ulceration may present with spontaneous bleeding, sometimes requiring emergency intervention. Other manifestations may include wheezing localized to one lung, which is a particularly important clue in young non-smokers and should prompt evaluation for an endobronchial lesion.

Endocrine and Paraneoplastic Manifestations

Although most pulmonary carcinoids are non-functional, a minority may present with endocrine syndromes, including carcinoid syndrome or Cushing's syndrome, as detailed in Section 4.3.2. As mentioned, functional tumours may present with flushing, diarrhoea, bronchospasm, or signs of hypercortisolism, depending on the specific hormone produced. These symptoms may precede respiratory complaints and can be easily misattributed to other systemic conditions if the diagnosis is not considered.

In very rare cases, patients may also exhibit neurological symptoms, such as confusion or altered mental status, due to paraneoplastic limbic encephalitis, although this is exceedingly rare and typically associated with more aggressive variants like atypical carcinoids or large-cell neuroendocrine carcinoma.

Physical Examination and Clinical Findings

On examination, most patients have non-specific signs. Decreased breath sounds, localized wheezing, or crackles may be noted in cases of partial or complete bronchial obstruction. Clubbing and features of right-sided heart failure may occur in advanced carcinoid syndrome. However, many patients appear well, and physical examination findings may be subtle or absent, reinforcing the need for a high index of suspicion in recurrent or unexplained respiratory symptoms.

4.5 Diagnosis of Lung Carcinoids

The Accurate diagnosis of the pulmonary carcinoid tumours is important in order to determine the proper treatment and prognosis. The tumours represent 1–2% of all lung cancers and, in the majority, occur as central airway masses with symptoms such as cough, haemoptysis, wheezing, or recurrent infections. However, many of the patients are asymptomatic, and diagnosis is therefore postponed until incidental imaging detection [8].

The diagnosis of lung carcinoids requires multimodal evaluation due to their overlap in clinical and radiologic presentation with other lung neoplasia and benign conditions. Imaging studies such as computed tomography (CT) and magnetic resonance imaging (MRI) help in early tumour detection, while functional imaging (PET/SPECT scans) is useful in assessing metabolic activity and somatostatin receptor expression [16]. Histopathologic and molecular examination, however, is definitive in the diagnosis of typical carcinoids from atypical carcinoids and high-grade neuroendocrine carcinomas. The variable presentation in lung carcinoids is one of the difficulties in their diagnosis, with numerous cases being initially misdiagnosed as a different lung tumour (e.g., adenocarcinoma, small-cell lung cancer) or even non-neoplastic respiratory conditions like asthma or chronic bronchitis. Fine-needle aspiration biopsies also do not always provide sufficient material for tumour grading, and larger biopsies by bronchoscopy or surgical resection become necessary for proper classification [7].

This section will describe the imaging studies, histopathology and molecular testing of the pulmonary carcinoids, followed by a general overview of the typical diagnostic pitfalls and differentials.

4.5.1 Imaging Techniques for Lung Carcinoids

Imaging plays a paramount role in the diagnosis of lung carcinoid tumours since it is utilized for localizing the lesion, defining the location, assessing the involvement of the airway, and determining metastatic spread. Because the typical carcinoids exhibit indolent behaviour and a tendency for

obstructive, but not aggressive, invasion, imaging is a primary means in early detection and classification.

Compared with other lung cancers such as non-small-cell lung cancer (NSCLC) or small-cell lung cancer (SCLC), which typically manifest as spiculated or ill-defined masses, pulmonary carcinoids are typically round, well-circumscribed, and highly enhanced masses secondary to their vascularity [8]. More aggressive radiologic features such as ill-defined borders, necrosis, and increased likelihood of lymph node involvement, however, characterize atypical carcinoids.
The choice among imaging modalities is determined by clinical presentation, tumour location, and differential diagnosis. The following section addresses the role of chest X-ray, computed tomography (CT), magnetic resonance imaging (MRI), and functional imaging (PET/SPECT scans) in detecting and characterizing pulmonary carcinoid tumours.

4.5.1.1 Chest Radiography (X-ray): The Initial Screening Tool

Although chest X-ray is commonly the first imaging modality employed in patients with respiratory symptoms, it has limited diagnostic utility in detecting pulmonary carcinoids. Central carcinoids, which account for approximately 60–70% of cases, may appear as hilar or perihilar masses with well-defined margins, whereas peripheral carcinoids may manifest as round nodules within the lung parenchyma. Radiographs may also reveal secondary signs such as post-obstructive pneumonia, atelectasis, or bronchiectasis, especially in larger tumours. Calcifications, seen in roughly 30% of cases, can appear as punctate or "popcorn-like" densities, offering a subtle clue to the diagnosis.

However, chest X-ray has several limitations. Small carcinoids (<2 cm), particularly those in peripheral lung fields, are often missed, and the modality cannot differentiate carcinoids from other pulmonary lesions, such as non-small-cell lung carcinoma or hamartomas. Furthermore, chest X-rays cannot evaluate airway involvement, lymphadenopathy, or distant metastases, thus necessitating further assessment with contrast-enhanced CT [5,8].

4.5.1.2 Computed Tomography (CT): The Gold Standard

Computed tomography (CT) is the primary and most informative imaging modality used in the diagnosis and management of pulmonary carcinoid tumours. It offers superior anatomical resolution, enables accurate tumour size measurement, and provides essential information on airway involvement, vascularity, and metastatic spread. In contrast to chest X-ray, which often fails to detect small or centrally located lesions, CT is significantly more sensitive in visualizing both typical and atypical carcinoids, particularly when optimized protocols are used [5,8].

CT Protocols and Imaging Techniques

The accuracy of CT imaging depends heavily on the scanning technique. A non-contrast CT is often used initially to assess for airway obstruction, atelectasis, and calcifications—the latter being present in approximately 30% of typical carcinoids, often in a punctate or "popcorn-like" configuration.

Contrast-enhanced CT is indispensable for evaluating tumour vascularity and differentiating carcinoids from other lung malignancies. Carcinoids, especially typical types, demonstrate intense arterial enhancement due to their hypervascularity, with attenuation values typically exceeding 100–150 Hounsfield Units during the arterial phase (30 seconds post-contrast injection). The venous phase (60–90 seconds) helps assess contrast washout and delayed enhancement, further aiding in distinguishing carcinoids from adenocarcinomas or squamous cell carcinomas.

High-resolution, thin-slice CT (≤1 mm) with multiplanar reconstruction and 3D volume rendering is particularly valuable for detecting small, centrally located tumours, and for assessing the relationship of the lesion to the airway, vessel, and adjacent structures. In surgical candidates, virtual bronchoscopy or CT bronchography may be employed to simulate airway navigation and assist in planning for bronchoscopic or surgical resection.

Advanced protocols such as Dynamic Contrast-Enhanced CT and perfusion imaging offer further insight into tumour vascularity and perfusion characteristics. Typical carcinoids demonstrate rapid enhancement and prolonged contrast retention, patterns that differ markedly from other lung tumours and may correlate with tumour aggressiveness [3,5].

Typical vs. Atypical Carcinoids on CT

CT findings can sometimes give insight into differentiating between classic and atypical carcinoids but always ultimately rely on definitive histopathology.

Typical carcinoids are most frequently found in the central bronchi in the form of well-defined, smooth, oval or rounded masses. They are normally strongly enhanced with contrast and tend to have superimposed central calcification. Airway compromise may be seen in the form of post-obstructive pneumonia, mucus plugging, or atelectasis; however, lymphadenopathy is unusual (10-15%).

The CT characteristics of typical and atypical carcinoids are summarized in Table 6 below.

In contrast to well-differentiated carcinoids, atypical carcinoids occur in a more peripheral location in the segmental bronchi. They have irregular or lobulated margins, less homogeneous or heterogeneous enhancement, and can show necrosis or cavitation, characteristics that are unfavourable to their well-differentiated counterparts. Lymph node metastasis is much more prevalent in atypical carcinoids (30–50%) and warrants additional investigation via modalities like EBUS-TBNA or mediastinoscopy.

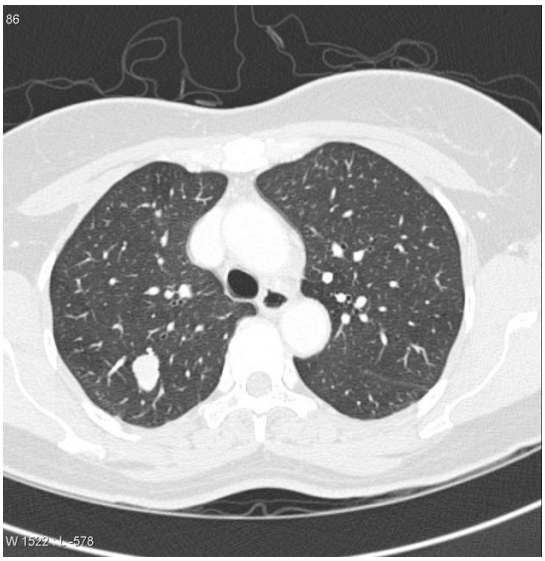

Figure 5: Axial lung window computed tomography (CT) image demonstrating an atypical peripheral carcinoid tumour. [20]

Differentiation from Other Pulmonary Lesions

CT has a key role in both the detection and localization of pulmonary carcinoids as well as in differentiating them from other lung tumours:

- Squamous cell carcinoma (SCC): Tends to cavitate, invade contiguous structures, and have irregular margins.
- Adenocarcinoma: Typically peripheral in location, with ground glass opacities, spiculated
- Small-cell lung cancer: Usually central and bulky, with widespread mediastinal lymphadenopathy and invasive local extension.
- Pulmonary hamartomas: Have fat and coarse calcification, such as the characteristic "popcorn" pattern, but are not enhancing or vascular like carcinoids.

CT in Tumour Staging and Surgical Planning

CT is critical in staging lung carcinoids. It enables measurement of tumour dimension, bronchial invasion, and mediastinal node status, and all these influence bronchoscopic management decisions, surgical excision, and the degree of lymphadenectomy necessary. Distant metastases to liver, bones, and brain are seen in CT in advanced tumours although these are rare in classic carcinoids.

For preoperative planning, CT bronchography helps define the proximal and distal extent of airway obstruction, ensuring that adequate surgical margins are obtained and guiding the decision between lobectomy and sleeve resection [5,8].

Limitations of CT and Role of Functional Imaging

Despite its strengths, CT provides only anatomical information and cannot assess tumour biology, including somatostatin receptor expression, which is essential for both diagnosis and therapeutic planning in neuroendocrine tumours. Functional imaging modalities like Gallium-68 DOTATATE PET/CT or SPECT/CT with 111In-pentetreotide are needed to evaluate SSTR status, which predicts responsiveness to somatostatin analogues or Peptide Receptor Radionuclide Therapy.

While CT remains the first line imaging modality, combining it with functional imaging enables a comprehensive diagnostic workup, aligning anatomical findings with molecular activity**,** and guiding long-term management.

CT Characteristics of Typical vs. Atypical Carcinoids:

Feature	Typical Carcinoid (TC)	Atypical Carcinoid (AC)
Location	Central (main bronchi)	Peripheral (segmental bronchi)
Margins	Well-defined, smooth	Irregular, spiculated
Enhancement	Intense contrast enhancement (high vascularity)	Moderate enhancement
Necrosis/Cavitations	Absent	Common
Calcifications	Punctate or diffuse	Rare
Lymph Node Metastasis	Rare (~10–15%)	Common (~30–50%)

Table 6: CT characteristics of lung carcinoids

4.5.1.3 Magnetic Resonance Imaging (MRI)

MRI is not routinely used in the diagnosis of pulmonary carcinoids but can be beneficial in specific situations, such as:

- Evaluating vascular invasion near the mediastinum,
- Assessing cardiac or paravertebral extension,
- Or as an alternative to CT in patients with contraindications to iodinated contrast agents.

MRI offers superior soft tissue contrast and is particularly useful for detecting liver or brain metastases in advanced disease. Pulmonary carcinoids generally appear iso- to hypointense on T1-weighted images and hyperintense on T2-weighted images, with enhancement post-contrast, similar to their CT profile [5].

4.5.1.4 Functional Imaging in Pulmonary Carcinoid Diagnosis

Although CT and MRI supply critical anatomic information, functional imaging is important to evaluate pulmonary carcinoids by detecting tumour metabolism and somatostatin receptor (SSTR) expression. Such characteristics are most important in neuroendocrine tumours (NETs), in which receptor status will influence diagnosis and therapy planning [16].

18F-fluorodeoxyglucose (FDG) PET/CT is extensively employed in lung cancer but has low sensitivity in well-differentiated carcinoids because such tumours are low in glycolysis and in their Ki-67 proliferation index of less than 2%. Therefore, FDG-PET tends to underestimate extent in well-differentiated carcinoids with a high rate of false negatives [14]. On the other hand, atypical carcinoids, because of their higher mitotic activity, tend to have variable uptake on FDG, and small. Cell lung carcinoma and LARGE CELL NEUROENDCOCRINE CARCINOMA are typically highly FDG-avid and representative of aggressive biology.

In addition to its limitations, however, FDG-PET has utility in atypical carcinoids, in suspected high-grade transformation cases, and in assessing metastatic spread when disease is heterogeneous in receptor expression or biology.

The gold standard for functional imaging in carcinoids is Gallium-68 DOTA-TATE PET/CT. A somatostatin receptor imaging technique with specificity for SSTR2 and SSTR5, generally overexpressed in carcinoids. While FDG-PET measures glucose metabolism, in contrast, Gallium-68 DOTA-TATE PET/CT reflects a direct measure of receptor expression and allows for better localization of tumours, staging, and planning of therapy.

Gallium-68 DOTA-TATE PET/CT is beneficial in several ways. It is more sensitive than FDG-PET. Has an ability to detect low-metabolic and very small tumours. Has greater contrast and resolution and is useful for identifying occult metastases. It is also useful in assessing eligibility for peptide receptor radionuclide therapy (PRRT) with Lutetium-177 DOTA-TATE. This functional imaging modality is useful in differentiating between typical carcinoids (these are typically SSTR-positive) and small cell lung carcinoma or non-small cell lung carcinoma tumours (those without somatostatin receptor expression and thus unsuitable for PRRT) [13].

While Gallium-68 DOTA-TATE PET/CT has largely succeeded in replacing older imaging techniques, SPECT/CT with 111In-pentetreotide (Octreoscan) is still used in some facilities in areas in which PET imaging is unavailable. SPECT will detect SSTR-positive lesions but is less sensitive and has lower spatial resolution than PET and is less precise in detecting small or early-stage carcinoids [7]. SPECT/CT was conducted in this patient and was negative for pathological uptake, consistent with low SSTR expression and supporting a diagnosis of a non-functional typical carcinoid tumour.

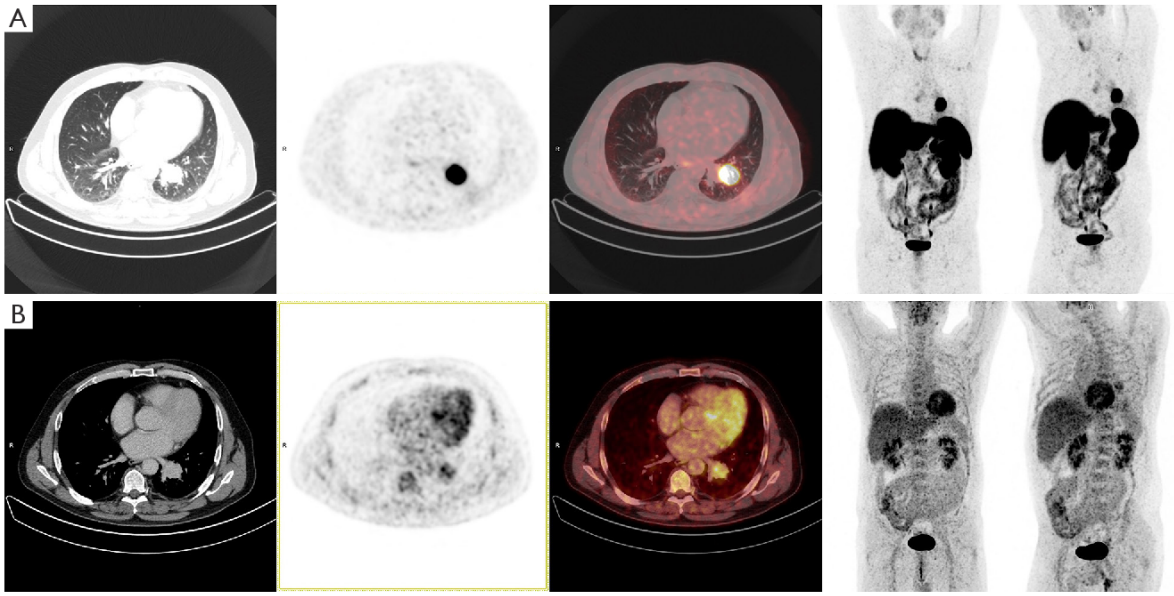

Figure 6: Preoperative PET/CT imaging. (A) Gallium-68-Edotreotide [68Ga]-DOTATOC PET/CT. (B) [18F]-FDG-PET/CT. To improve visualization of the FDG uptake of the carcinoid located dorsally of the heart, maximum intensity projections (MIP) are shown in anterior and left anterior oblique views. PET/CT, positron emission tomography-computed tomography; [68Ga]-DOTATOC, Gallium-68Edotreotide; [18F]-FDG, fluorine-18-fluorodeoxyglucos [21]

A comparison of functional imaging modalities for pulmonary NETs is presented in Table 7.

Modality	Mechanism	Best for Detecting	Limitations
FDG-PET/CT	Measures glucose metabolism	Atypical carcinoids, SCLC, LCNEC	Poor sensitivity for typical carcinoids
Gallium-68 DOTA-TATE PET/CT	Detects somatostatin receptor expression	Typical and atypical carcinoids, PRRT candidate selection	Limited availability in some centres
SPECT/CT (Octreoscan)	Uses Indium-111 Octreotide for receptor imaging	Neuroendocrine tumours in PET-inaccessible centres	Lower sensitivity than PET, poorer spatial resolution

Table 7: Comparison of Functional Imaging Modalities in Lung Carcinoids

4.5.2 Biopsy Techniques, Histopathology and Molecular Testing

While imaging modalities are essential for detecting and characterizing lung carcinoid tumours, a definitive diagnosis and histological grading require histopathological examination of tumour tissue. The distinction between typical and atypical carcinoids depends on mitotic activity, necrosis, and immunohistochemical profile, none of which can be assessed radiologically. Because many pulmonary carcinoids are centrally located, they are accessible via bronchoscopy. However, in peripheral lesions or when bronchoscopic access is insufficient, CT-guided transthoracic biopsy or surgical excision becomes necessary.

A major challenge in carcinoid biopsy is sampling error. Atypical carcinoids are defined by focal necrosis and higher mitotic counts, which may not be present in limited biopsy samples. Thus, when biopsy material is inconclusive, surgical excision may be required for definitive classification.

Bronchoscopic Techniques

I. Flexible Fiberoptic Bronchoscopy (FOB)

Flexible bronchoscopy is also used most frequently to obtain tissue samples of centrally located carcinoids. It permits direct visualization and tissue biopsy of endobronchial tumours, which are best seen as polypoid, reddish, and well-defined lesions. The tumours are generally very vascular, and this increases the danger of bleeding during biopsy. Submucosal extension of tumours also limits how deep a biopsy can go with a forceps biopsy and may decrease diagnostic yield.

II. Rigid bronchoscopy

Rigid bronchoscopy yields superior access to tissue in tumours located in the centre of the lungs when larger samples of tissue are necessary to check for mitotic activity and necrosis. It also provides superior control of haemorrhage in highly vascular carcinoids and allows for therapeutic interventions such as argon plasma coagulation and laser therapy. It is more invasive and requires general anaesthesia, however, and so may be impossible to use in all patients.

III. Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration (EBUS-TBNA)

EBUS-TBNA is most useful in staging, specifically in evaluating mediastinal or hilar nodal involvement. While it is very sensitive in sampling lymph nodes, in primary carcinoids it is of limited diagnostic value owing to the small volume of tissue yielded with fine-needle aspiration that is frequently too little to evaluate mitotic rate or necrosis.

Even though EBUS-TBNA is highly sensitive in staging, it is less sensitive in diagnosing primary tumours, particularly when very little material from the fine-needle aspirate (FNA) is recovered. Since lung carcinoids require histologic examination of the mitotic rate, very little FNA material would be inadequate for grading. EBUS is, therefore, generally supplementary to other biopsy techniques but not a first-line diagnostic tool [4].

CT-Guided Transthoracic Needle Biopsy (TTNB)

For peripherally located carcinoids that are not reachable by bronchoscopy**,** CT-guided transthoracic biopsy is a viable alternative. This technique offers precise localization and larger tissue samples than fine-needle aspiration. However, there are risks of pneumothorax, particularly in subpleural lesions, and bleeding, especially given the hypervascularity of carcinoid tumours. Despite these risks, TTNB remains a critical tool in cases where bronchoscopy is contraindicated or uninformative

Histopathological Evaluation

Histopathological examination remains the gold standard for diagnosing pulmonary carcinoids. These tumours arise from Enterochromaffin cells of the bronchial epithelium and are classified by the 2021 WHO guidelines into:

- Typical carcinoid (TC): Low-grade neuroendocrine tumour
- Atypical carcinoid (AC): Intermediate-grade tumour
- Large-cell neuroendocrine carcinoma (LCNEC): High-grade carcinoma

- Small-cell lung carcinoma (SCLC): High-grade carcinoma

The distinction between TCs and ACs is based on:

- Mitotic rate: <2 mitoses/2 mm² for TCs, 2–10 mitoses/2 mm² for ACs
- Necrosis: Absent in TCs; focal necrosis present in ACs

Microscopically, both TCs and ACs show organoid, trabecular, or rosette-like growth patterns, with salt-and-pepper chromatin and moderate eosinophilic cytoplasm. Atypical carcinoids exhibit greater nuclear pleomorphism, prominent nucleoli, and higher mitotic counts, correlating with a poorer prognosis and higher metastatic potential

Immunohistochemical Markers

Immunohistochemistry (IHC) plays a pivotal role in confirming neuroendocrine differentiation**,** distinguishing pulmonary from extrapulmonary carcinoids**,** and supporting histological grading

Key markers include:

- Chromogranin A (CgA) and Synaptophysin**:** Highly specific and sensitive for neuroendocrine origin
- CD56**:** Expressed in most NETs but less specific
- TTF-1: Often positive in pulmonary NETs, helps differentiate from GI carcinoids
- Ki-67 index: <2% in TCs, 2–20% in ACs, >50% in LARGE CEKK NEUROENDCOCRINE CARCINOMA and SMALL CELL LUNG CARCINOMA

Ki-67 is especially important for grading and prognostication, and though not required for WHO classification, it is commonly used in clinical practice to inform management.

4.6 Treatment Modalities

The management of carcinoids is determined by several factors including tumour type (typical vs. atypical carcinoid), tumour size, lymph node involvement, functional status, and patient comorbid conditions. When contrasted with the aggressive neuroendocrine tumours small-cell lung cancer and large-cell neuroendocrine carcinoma, the carcinoids grow slowly with an indolent course and the mode of treatment in most cases is surgical resection.

Aside from surgery, some cases can be managed with medical therapies like somatostatin analogues (SSAs), mTOR inhibitors, and peptide receptor radionuclide therapies. Chemotherapy and radiotherapy are only occasionally helpful in common carcinoids but can be employed in unresectable or metastatic atypical carcinoids. Long-term follow-up measures should also be undertaken to screen for recurrence and metastatic disease.

This section deals with the surgical approaches, medical therapies, radiotherapy, chemotherapy, and follow-up treatments for the management of pulmonary carcinoids.

4.6.1 Surgical Treatment: The First-Line Therapy

The only curative therapy for pulmonary carcinoids is surgical resection, particularly for localized disease. Due to their slow growth and minimal metastatic potential, complete resection provides excellent long-term survival with 5-year survival rates of greater than 90% for typical carcinoids.

The National Comprehensive Cancer Network and the European Society for Medical Oncology guidelines recommend complete surgical resection with systematic lymph node dissection for all resectable pulmonary carcinoids.

Types of Surgical Resection

Lobectomy: The Definitive Surgical Procedure

Lobectomy with systematic dissection of the lymph nodes is the preferred procedure for localized carcinoids, particularly when:

- The tumour measures at least 2 cm.
- There is suspected or confirmed lymph node involvement.
- There is parenchymal invasion below the bronchus.

Lobectomy ensures complete tumour removal with clear margins, significantly reducing the risk of local recurrence. A study by Filosso et al. (2013) analysing over 2,500 pulmonary carcinoid cases showed that lobectomy reduces recurrence rates compared to sub lobar resections.

Sleeve Resection: A Substitute for Lobectomy

For centrally located carcinoids, particularly those involving a mainstem bronchus, a sleeve resection (segmental bronchial resection with reanastomosis) is preferred over lobectomy to preserve lung function. This approach has been shown to provide oncologic outcomes comparable to lobectomy, with the advantage of maintaining more pulmonary parenchyma [18].

Limited Resections: (Segmentectomy, Wedge resection)

For small, peripheral carcinoid tumours (<2 cm) without lymph node involvement, a wedge resection or segmentectomy may be performed. However, studies indicate that limited resections are associated with higher local recurrence rates compared to lobectomy [18,19].

Lymph Node Dissection in Pulmonary Carcinoids

While lymph node involvement is rare in typical carcinoids (~10-15%), atypical carcinoids demonstrate higher rates of nodal metastasis (~30-50%).

Systematic mediastinal lymph node dissection is recommended during surgery to assess nodal spread and guide adjuvant therapy. Failure to remove involved nodes increases recurrence risk and may impact survival outcomes [19].

4.6.2 Medical Management of Pulmonary Carcinoids

Treatment of pulmonary carcinoids is generally reserved for unresectable, metastatic, or progressive cases. And those patients with comorbidities that preclude surgical treatment. Since surgery is the only curative approach, systemic therapies are primarily palliative and intended to control tumour progression and alleviate symptoms.

Somatostatin Analogs (SSAs)

SSAs, including octreotide and lanreotide, are the first-line medical therapy for both functioning and non-functioning pulmonary carcinoids. These drugs bind to somatostatin receptors (SSTR2 and SSTR5) expressed on tumour cells, inhibiting hormone secretion and suppressing tumour growth. Their role is especially crucial in functionally active carcinoids, where they alleviate symptoms of carcinoid syndrome, including flushing, diarrhoea, and bronchospasm.

The PROMID trial demonstrated that octreotide Long-Acting Release LAR significantly prolonged progression-free survival (PFS) in patients with metastatic midgut NETs, and the CLARINET trial showed that lanreotide reduced the risk of disease progression by 53% in well-differentiated, non-functioning NETs, including pulmonary carcinoids [1,2]. SSAs are also used in patients with advanced inoperable disease for tumour stabilization.

Standard dosing includes octreotide LAR 30 mg intramuscularly every four weeks or lanreotide 120 mg subcutaneously every four weeks. Short-acting octreotide may be used for carcinoid crisis. Or as a bridging therapy prior to initiating long-acting formulations.

Common adverse effects include gastrointestinal disturbances (e.g., abdominal pain, nausea, bloating), gallstone formation due to reduced gallbladder motility, and mild glucose intolerance or hyperglycaemia. Despite these, SSAs remain safe and effective as first-line agents [1].

Peptide Receptor Radionuclide Therapy (PRRT)

PRRT is an advanced systemic therapy that uses radiolabelled somatostatin analogues—most commonly Lutetium-177 DOTA-TATE—to deliver targeted radiation to SSTR-positive tumour cells. This therapy is particularly effective in progressive, metastatic pulmonary carcinoids with confirmed SSTR expression on Gallium-68 DOTA-TATE PET/CT.

The NETTER-1 trials demonstrated that Lutetium-177 DOTA-TATE significantly improved both PFS and overall survival in patients with advanced NETs [3]. Although the trial focused on midgut tumours, retrospective studies have confirmed PRRT's efficacy in pulmonary carcinoids, with response rates around 30% and durable disease control in a subset of patients.

PRRT is typically administered as 200 mSv per cycle every eight weeks, for a total of four cycles. Renal function must be monitored closely due to the risk of nephrotoxicity, and patients are often co-administered amino acid infusions for kidney protection.

Adverse effects include mild bone marrow suppression, transient fatigue, nausea, and rare but important renal toxicity, necessitating periodic haematological and renal monitoring during and after treatment [13].

mTOR Inhibitors (Everolimus)

Everolimus is a targeted oral agent that inhibits the PI3K/AKT/mTOR signalling pathway, a critical regulator of cell growth and angiogenesis. This pathway is frequently upregulated in neuroendocrine tumours, including lung carcinoids.

The RADIANT-4 trial showed that everolimus (10 mg orally once daily) significantly improved progression-free survival in patients with advanced non-functioning NETs of the lung and gastrointestinal tract [13,14]. It is particularly beneficial in progressive atypical carcinoids or when SSAs and PRRT are not viable options.

However, its use may be limited by adverse effects, including oral ulcers (stomatitis), hyperglycaemia, hyperlipidaemia, and rare cases of non-infectious interstitial pneumonitis, which require dose reduction or discontinuation in some patients [14].

Chemotherapy

Chemotherapy is not effective for typical carcinoids and is only used in highly aggressive, metastatic atypical carcinoids. Chemotherapy is generally reserved for rapidly progressing atypical carcinoids, or in cases where tumours have undergone high-grade transformation into large-cell or small-cell neuroendocrine carcinomas. It is not effective for well-differentiated typical carcinoids due to their slow growth rate and low proliferation index**.**

4.6.3 Endobronchial Treatments for Small or Inoperable Tumours

For centrally located intraluminal carcinoids causing airway obstruction, endobronchial resection via rigid bronchoscopy may be used for both diagnosis and palliation. Techniques such as argon plasma coagulation (APC)**,** laser photo resection, and cryotherapy can be applied to relieve obstruction or control bleeding.

Endobronchial treatment may be curative in a select group of patients with purely intraluminal typical carcinoids, no nodal involvement, and clear margins confirmed on follow-up imaging and bronchoscopy. However, it is generally reserved for:

- Patients who are not surgical candidates**,** or
- Bridging therapy before definitive surgery.

Long-term surveillance is required after endobronchial therapy due to the risk of recurrence (Rindi et al., 2014).

4.7 Prognosis and Follow-up

Rationale for Long-Term Monitoring

Following treatment, long-term surveillance of pulmonary carcinoids is essential due to the risk of recurrence, late metastasis**,** and hormone-related complications**.** Although typical carcinoids have a

low metastatic potential and an indolent course, atypical carcinoids present a significantly higher recurrence risk and demand a more intensive follow-up strategy. Current surveillance guidelines are informed by major bodies such as the European Society for Medical Oncology (ESMO), European Neuroendocrine Tumour Society (ENETS), and the National Comprehensive Cancer Network (NCCN).

Risk-Stratified Surveillance Strategies

The intensity of surveillance is primarily dictated by tumour biology. In typical carcinoids, NCCN guidelines recommend contrast-enhanced CT (CECT) every 6 to 12 months for five years, followed by imaging every two years. For atypical carcinoids, which have higher rates of nodal involvement and distant spread, CT or MRI is advised every 3 to 6 months for the first two years, then annually for at least five years

In patients with unresectable or metastatic tumours, the frequency and modality of imaging should be adapted based on tumour burden and response to systemic therapy.

Role of Imaging in Recurrence Detection

Cross-sectional imaging, primarily CECT, is the cornerstone of post-treatment surveillance. It is highly effective for detecting local recurrence, mediastinal lymph node involvement, and pulmonary metastases. MRI is reserved for long-term follow-up or when brain metastases are suspected. Gallium-68 DOTA-TATE PET/CT has emerged as the most sensitive tool for identifying recurrent or metastatic disease, especially in patients with somatostatin receptor-expressing tumours, and is preferred over FDG-PET/CT in typical carcinoids.

Functional imaging is especially important in cases of biochemical marker elevation or when conventional imaging fails to detect residual disease.

Biochemical Monitoring

Biochemical markers can provide early warning signs of tumour progression, particularly in functional carcinoids. Chromogranin A (CgA) is elevated in up to 80% of NETs, though its specificity is limited by factors such as proton pump inhibitor use, renal dysfunction, or chronic inflammation. Urinary 5-Hydroxyindoleacetic Acid (5-HIAA) is highly sensitive for serotonin-secreting carcinoids and should be measured serially to monitor disease activity. Rising marker levels should prompt functional imaging to detect subclinical recurrence.

Patterns of Recurrence and Sites of Metastasis

Recurrence patterns vary significantly by tumour type. Typical carcinoids recur in 5–10% of patients, whereas atypical carcinoids have a recurrence rate of 15–30%, especially in cases with nodal involvement. Local recurrence is more common after limited resections, such as wedge resection or segmentectomy, than after lobectomy, which is therefore preferred for long-term disease control.

Distant metastases most commonly affect the liver and bones, with bone involvement reported in 10–20% of advanced cases. Central nervous system (CNS) metastases are rare but should be excluded in patients presenting with neurological symptoms. Recommended investigations include bone scintigraphy or MRI for suspected skeletal disease and brain MRI for neurologic assessment

Survivorship and Quality of Life Considerations

Given the chronic course of carcinoid tumours and the potential for late recurrence**,** survivorship care must extend beyond imaging and lab follow-up. Patients who have undergone lung resection**,** especially lobectomy, should receive annual pulmonary function tests (PFTs) to assess respiratory function. For those with functionally active tumours**,** periodic endocrine evaluations are needed to detect late hormonal syndromes**.** Additionally**,** psychosocial evaluation and support should be incorporated into follow-up care, particularly for patients coping with chronic disease, systemic therapy, or metastatic burden

Tumor Type	Imaging Frequency	Duration	Biomarker Monitoring
Typical Carcinoid	CT every 6–12 months → Biennial	Minimum 5–10 years	CgA (if functional), annual PFT
Atypical Carcinoid	CT/MRI every 3–6 months → Annual	Minimum 10 years	CgA, 5-HIAA, Ki-67 if available
Unresectable	Tailored based on response	Lifelong	Ga-68 PET if markers rise

Table 8: Surveillance Table

4.7.1 Postoperative Rehabilitation and Supportive Care

Rehabilitation is an important, though frequently underappreciated, aspect of the treatment process of patients who undergo surgical removal of pulmonary carcinoids. After lobectomy or bilobectomy, patients have potential alterations in pulmonary function, fatigue, mobility problems, and emotional distress. A formalized recovery plan seeks to restore breath capacity, avoid complications, and maximize total recovery.

Pulmonary Rehabilitation

Patients after lung tumour resection are particularly vulnerable to having decreased forced expiratory volume in 1 second (FEV_1) and vital capacity. Pulmonary rehabilitation should be initiated early in the recovery state and encompasses:

- Incentive spirometry to enhance lung expansion and prevent atelectasis.
- Deep breathing and coughing exercises to mobilize secretions.
- Supervised physical therapy aimed at enhancing diaphragmatic function and minimizing the risk of postoperative pneumonia.

As stated by the American Thoracic Society (ATS) and the European Respiratory Society (ERS), early rehabilitation decreases hospital length of stay and postoperative pulmonary complications [12].

Physical Activity and Mobilization

Early mobilizing, usually within 24 hours of surgery, correlates with improved function. Walking programs or individualized physical therapy minimize the risk of venous thromboembolism (VTE)

and enhance cardiopulmonary tolerance. The interventions are most crucial in elderly or comorbid patients like the index patient, who presented with associated hypertension and osteochondrosis.

Nutritional and Psychological Support

Nutritional counselling should be provided, particularly in the patient experiencing loss of appetite, weight loss, or gastrointestinal side effects from treatment with somatostatin analogues. Concurrently, psychological counselling is crucial, especially in the patient who is likely to encounter anxiety related to recurrence or long-term health status. Counselling and support groups may enhance quality of life, compliance with treatment, and strategies to deal with it.

Smoking cessation and modification of respiratory risk

Since most pulmonary carcinoids, including the index patient, have tobacco exposure histories, smoking cessation programs should be arranged. Smoking cessation decreases recurrence rates, improves healing after surgery, and enhances pulmonary function overall. Options that are available as support may be pharmacological (e.g., varenicline, patches) and/or behaviour therapy.

Long-Term Surveillance Integration Rehabilitation should be coordinated with the long-term follow-up plan. This involves educating the patient regarding the importance of follow-up imaging, surveillance of recurrence signs, and comorbidity control. An interdisciplinary approach that brings together pulmonologists, thoracic surgeons, physiotherapists, dietitians, and psychologists optimizes continuity and care quality.

5. Discussion

5.1 Comparison of Clinical case data and Literature

5.1.1 Clinical Presentation and Radiological Features

The patient first presented with progressive haemoptysis, fatigue, and mild dyspnoea—classic symptoms of central airway obstruction. On arrival her respiratory failure was not pronounced and easily compensated with oxygen therapy by nasal cannula. Auscultation revealed vesicular breathing with scattered crackles above the right lung area. In addition, she was haemodynamically stable, prone to hypertension.

This clinical presentation is highly consistent with central pulmonary carcinoids, which most commonly present due to bronchial obstruction. Haemoptysis is one of the most frequent initial symptoms in typical carcinoids and has been reported in 30–40% of cases, often due to the tumour's endobronchial location and rich vascularity [4,16]. Dyspnoea and recurrent respiratory symptoms typically stem from partial airway obstruction, mucus plugging, and postobstructive atelectasis. In a cohort study by Skuladottir et al. (2002), over 60% of centrally located bronchial carcinoids presented with some form of respiratory obstruction, with hemoptysis in ~35%, and recurrent pneumonias in ~20%. This patient's clinical picture mirrored these findings, with bronchoscopic evidence of a friable, bleeding tumour and CT signs of post-obstructive pneumonia and collapse of the right lower lobe.

Based on the presenting hemoptysis and dyspnea, pulmonary embolism (PE) was one of the initial differential diagnoses entertained, especially with her raised D-dimer levels. Contrast-enhanced CT

scans, however, excluded PE, which did not demonstrate pulmonary artery filling defects. The same scan, however, identified a hyper vascular endobronchial tumour with right lower lobe collapse and mucus plugging features not typical for embolic obstruction. Moreover, lack of aggressive pleuritic chest pain, tachycardia, and abrupt onset of hypoxia made PE less probable. This investigation thus redirected attention to a central obstructive lesion, as was later confirmed with a typical carcinoid tumour.

Radiological Findings and Imaging Interpretation

Radiological studies further supported the clinical suspicion. Contrast CT scan of the thorax, revealed a sharply demarcated, enhancing lesion of size 2.4 ×2.1 cm in the right intermediate bronchus. The lesion was hyper vascular and resulted in distal collapse of the right lower lobe with resultant mucus impaction, consistent with post-obstructive atelectasis. These findings are characteristic of central carcinoids, which are known to occur in the major bronchi and present with focal airway involvement instead of early systemic spread.

According to established imaging criteria, typical carcinoids generally present as central, well-circumscribed lesions that demonstrate intense arterial contrast enhancement due to their high vascularity and low-grade nature [7]. This patient's CT findings were consistent with this description, especially the vivid contrast uptake and the lack of necrosis or cavitation, which would be more typical of atypical carcinoids or NNON SMALL CELL LUNG CARCINOMA.

Such imaging features were strongly suggestive of a central carcinoid tumour based on the lesion's vascular enhancement, mucus impaction, and lobar collapse. Yet radiologically, at that point, the differential diagnosis was still wide-ranging. Centrally located endobronchial masses also comprise benign processes like hamartomas, which are usually fat or calcified, inflammatory polyps that occur after infection, and foreign body aspiration, especially in older patients or those at risk of aspiration. Malignant simulations like squamous cell carcinoma, mucoepidermoid carcinoma, or metastasis to the bronchial wall also needed to be ruled out. Lack of necrosis, irregular margins, and CT evidence of lymphadenopathy decreased the suspicion for a high-grade malignancy. Eventually, bronchoscopy and histological confirmation were needed to narrow the diagnosis and dictate suitable surgical intervention.

Functional Imaging Correlation

Although Gallium-68 DOTA-TATE PET/CT is the gold standard for imaging of the somatostatin receptors in neuroendocrine neoplasms, in this scenario, SPECT with Octreotide was utilized because of availability. The scan did not show evidence of expressed somatostatin receptors, as with SSTR-negative typical carcinoids. Most typical carcinoids are SSTR2-positive, but a subgroup—such as in this example—can fail to be demonstrated with somatostatin receptor scanning, and this renders evaluation of eligibility for PRRT more challenging.

This is consistent with published literature that reports that around 20–30% of typical carcinoids will demonstrate reduced or absent uptake on Octreoscan SPECT, particularly if the tumour is small or has low receptor density [3,8].

Diagnostic Implications

The co-occurring findings of centrally located, hyper vascular, endobronchial mass with accompanying post-obstructive alterations, positive visualization by bronchoscopy, and SSTR-negative functional scanning highly attested to the diagnosis of non-functional, classic pulmonary carcinoid. These characteristics ruled out such higher-grade neuroendocrine neoplasms as large cell neuroendocrine carcinoma and small cell lung carcinoma, characterized by aggressive behaviour, marked dedifferentiation, necrosis, and increased 18F-fluorodeoxyglucose activity

5.1.2 Histopathology and Tumour Biology

Histopathology is still the gold standard in the diagnosis and classification of pulmonary carcinoids. Here, both the preoperative endobronchial biopsy and the postoperative resection established the diagnosis of the patient with a typical carcinoid tumour. The patient's findings are in accord with the recognized histological and immunohistochemical characteristics delineated by the World Health Organization (WHO) classification of thoracic tumours in the year 2021 and the guidelines of the European Neuroendocrine Tumour Society (ENETS).

Morphological characteristics

The patient's biopsy from the endobronchial tissue, taken during bronchoscopy, consisted of uniform cells in nests and trabeculae with moderate eosinophilic cytoplasm and round-oval nuclei. Notably, there was no necrosis observed, and mitosis was very low, both of which are characteristic of classical carcinoid tumours (WHO 2021).

This morphology was also supported by the histology after surgery, where the tumour was noted as pT1a, pN0, LVI0. Representing a well-differentiated neuroendocrine tumour with no lymphovascular invasion or nodal metastasis. This is in keeping with regular carcinoids, unlike atypical carcinoids that frequently express focal necrosis and 2–10 mitoses per 2 mm² (WHO, 2021)

Immunohistochemical Profile

The patient's tumour exhibited strong immunoreactivity for Chromogranin A, Synaptophysin, and TTF-1, with positive Pan-Cytokeratin (PanCK) staining. The Ki-67 proliferation index was reported as 1%, a crucial finding confirming the diagnosis of a typical carcinoid tumour, as this lies well below the <3% threshold defined by ENETS and WHO for low-grade neuroendocrine tumours [14].

Chromogranin A and Synaptophysin positivity supports neuroendocrine differentiation, common to all NETs. Ki-67 index serves as a prognostic marker: lower values (<3%) correlate with indolent behaviour. TTF-1 positivity is frequently seen in pulmonary NETs and helps distinguish primary lung carcinoids from metastatic GI neuroendocrine tumours.

These findings match data from recent literature, which states that typical carcinoids nearly always express neuroendocrine markers (Chromogranin A and Synaptophysin), have low proliferation indices, and are often positive for TTF-1, especially in centrally located bronchial lesions.

The main histopathology and immunohistochemical features of the case vs literature are presented in Table 9 below.

Feature	Patient Data	Typical Carcinoid (Literature)
Tumour Type	Typical carcinoid (pT1a, pN0)	Well-differentiated NET, low mitotic rate
Ki-67 Index	1%	<3% (typical), 3–20% (atypical)
Necrosis	Absent	Absent in typical, present in atypical
Mitotic Figures	Rare (<2 per 2 mm²)	<2 per 2 mm² for typical
Chromogranin A	Positive	Positive in >90% of typical carcinoids
Synaptophysin	Positive	Strongly positive in typical carcinoids
TTF-1	Positive	Variable, often positive in pulmonary NETs
Lymph Node Involvement	None	<15% in typical carcinoids
Lymphovascular Invasion (LVI)	Absent	Rare in typical carcinoids

Table 9: Patient data vs. Literature

Clinical Implications

The patient's histological pattern is consistent with that in the literature and confirms the recommendation for curative resection without adjuvant therapy. Lack of adverse prognostic factors like high Ki-67, necrosis, lymphovascular invasion, or nodal involvement puts the patient in the favourable category with a greater than 90% 5-year survival chance [5].

In addition, this case reiterates the value of extensive histopathology and immunohistochemistry in determining treatment planning in pulmonary carcinoids. Not only is tissue diagnosis definitive in establishing the tumour subtype, but it also has significant prognostic, surveillance interval, and treatment decision implications in the event of recurrence.

5.1.3 Laboratory and Biochemical Findings

The laboratory and biochemical results observed during this patient's initial and subsequent hospital admissions where mostly normal, but some provided valuable insights into both the systemic effects of the tumour and underlying comorbidities that may have influenced presentation, diagnostic interpretation, and overall clinical management.

The patient's presenting complete blood count (CBC) revealed haemoglobin reduction from 144 g/L to 134 g/L in several days. While haemoglobin was still in acceptable range, the relative decrease suggested active bleeding, due to hemoptysis, the patient's presenting symptom. Hemoptysis has been described in the literature in central carcinoid tumours due to tumour vascularity and erosion into the bronchial walls. Especially if the tumour is endobronchial in nature.

The patient's CRP was mildly increased, consistent with low-grade inflammatory process, possibly indicative of post-obstructive changes or local inflammation in the region of the tumour. Although

carcinoids are not known to cause systemic inflammation, secondary reactions like obstructive pneumonia or localized irritation in the bronchi may be associated with mild CRP elevation.

Other tests like coagulation studies helped to rule out coagulopathy or anticoagulation drug use contributing to the hemoptysis. This is important when considering possible differential diagnoses

Looking at the other biochemical markers, there was no suggestion of carcinoid syndrome or liver metastases, This is consistent with the classic presentation of well-differentiated carcinoids that are non-secretory

The patient's lab data generally reflected localized disease with systemic stability. According to the ENETS consensus, no specific lab test is diagnostic for typical carcinoids, although general health markers and tumour markers like Chromogranin A and 5-HIAA are sometimes used for monitoring or evaluating secretory activity (ENETS Guidelines, 2017). In this case, no functional markers were elevated, corroborating the classification of the tumour as non-functional.

5.2 Clinical Challenges

The diagnosis and management of pulmonary carcinoid tumours often present significant clinical challenges, primarily due to the tumour's rarity, variable presentation, and overlap with more common respiratory conditions. In this specific case, several critical challenges were encountered throughout the course of her illness. These reflect common pitfalls described in the literature and illustrate how real-world constraints can affect the ideal diagnostic pathway.

Diagnostic Delay and Misleading Initial Presentation

One of the foremost challenges in this case was the delayed diagnosis, stemming from the non-specific symptoms of hemoptysis and dyspnea on exertion. These are common in a range of respiratory diseases, including bronchitis, pneumonia, or pulmonary embolism. Indeed, her elevated D-dimer on initial presentation raised the suspicion of pulmonary embolism, leading to a CT angiogram — which, although ultimately useful, is not the usual first-choice investigation for a tumour. This delay is consistent with data from literature suggesting that pulmonary carcinoids are often misdiagnosed or overlooked, with one retrospective study reporting that diagnostic delays exceed 6 months in over 30% of cases [19]. The patient's long smoking history may also have biased clinicians toward more common smoking-related diseases like COPD or chronic bronchitis.

Subtle Imaging Clues

On initial CT, the existence of bronchial obstruction with distal atelectasis and plugging of mucus was more indicative of mucous impaction or infection than neoplasia. The mass became only better outlined with radiologist re-evaluation. This is consistent with the recognized radiological nonspecificity of classic carcinoids, and these tend to look like small, sharply defined enhancing masses that are likely to be confused with benign nodules or inflammatory lesions [12,20].

Underdiagnosis and Diagnostic Challenges

Pulmonary carcinoid tumours are often underdiagnosed because they are clinically and radiographically non-specific. Early signs and symptoms, including cough, hemoptysis, or slight dyspnea, are attributed to common complaints like asthma, chronic bronchitis, or pneumonia. A principal barrier to diagnosis is the lack of sensitivity of routine chest radiography. Chest X-rays are often normal or find subtle details that are easily missed — segmental atelectasis, poorly defined opacities, or peribronchial thickening — which cause delayed further investigation with advanced imaging such as contrast-enhanced CT or bronchoscopy, required for characterizing the lesion. Reports like Gaur et al. (2013) and Travis et al. (2021) comment that carcinoids, especially those that are centrally located, cannot be seen on chest X-rays and only detected with high-resolution imaging. Up to 30% of bronchial carcinoids were missed on initial radiographs or yielded no diagnosis according to a review. Raising clinical suspicion and early CT scanning with persistent unexplained clinical symptoms are thus crucial to avoid delay in diagnosis.

Surgical Complexity and Risk Stratification

The choice to adopt a lower bilobectomy instead of one that is more conservative highlights another dilemma — balancing pulmonary preservation against oncologic control. Although carcinoid tumours usually call for lung-sparing resections (e.g., sleeve lobectomy), in this patient the tumour's site in the right intermediate bronchus made removal of two lobes necessary.

The literature favours the individualized approach since standard anatomical resections (and not wedge resections) offer greater long-term control of central tumours but at the expense of increased respiratory compromise [19].

Multidisciplinary Coordination

Another frequently overlooked challenge in managing pulmonary carcinoids is the need for multidisciplinary coordination between pulmonology, thoracic surgery, radiology and pathology. In this patient's case, staging required coordination of CT, SPECT imaging, and histopathology — with delays in scheduling potentially prolonging diagnosis.

While peptide receptor radionuclide therapy (PRRT), is generally reserved for metastatic or unresectable disease, somatostatin receptor imaging (SRI) is still a valuable component of the staging and diagnosis of lung carcinoids. In this patient, no meaningful somatostatin receptor expression was found with the SPECT/CT, effectively eliminating PRRT as a potential future therapy should systemic progression be seen. Although that did not directly influence her management, it reflects a larger concern—only a small subset of well-differentiated carcinoids has enough somatostatin receptor expression to be candidates for PRRT, which restricts long-term treatment options should the disease recur. This is a point for where functional imaging earlier during the carcinoid tumour workup, even when there is potential for resection, is necessary to plan for comprehensive long-term management. even if clinically indicated.

5.3 Implications for Clinical Practice

This case illustrates the essential importance of early diagnostic diligence in the evaluation of elderly patients who present with hemoptysis, especially those with a history of smoking. The patient presented with chronic hemoptysis and dyspnea. Although the elevated D-dimer initially raised suspicion for pulmonary embolism, CT imaging ruled this out, instead revealing bronchial obstruction and atelectasis—prompting further investigation. While endobronchial carcinoid tumours are rare, they must not be overlooked, especially in patients with unexplained hemoptysis, even in the absence of definitive radiologic findings. As emphasized by both the ENETS and BTS guidelines [3,4,12],

early consideration of such rare but significant pathologies is critical to avoid delays in diagnosis and management.

Multimodal imaging, such as contrast-enhanced CT and SPECT, was important in defining tumour characteristics. While CT established the site, size, and secondary atelectasis due to bronchial occlusion, SPECT scanning demonstrated the absence of somatostatin receptor expression. This is consistent with published behaviour of non-functional typical carcinoids and facilitated the exclusion of PRRT as a treatment choice. Endobronchial intraoperative bronchoscopy revealed one very vascular and friable endobronchial lesion, where haemostatic control with adrenaline and APC was required prior to biopsy—a procedure consistent with literature regarding bleeding during carcinoid handling during bronchoscopy (BTS, 2013). Subsequent histological diagnosis of a low Ki-67 indexes and non-lymphatic invasion directed the surgical intervention toward curative resection.

Postoperative care likewise demonstrated guideline-directed care. Notwithstanding mild preoperative respiratory acidosis and elevated preoperative pCO_2 (73.1 mmHg), the patient's physiological reserve was enough to ensure successful lower bilobectomy. Lack of lymph node involvement and minimal tumour size (pT1aN0) offered excellent prognostication with literature evidence of >90% 5-year survival in such cases [8,9]. Her six-month follow-up CT revealed no recurrence. This supports the importance of rigorous long-term surveillance, especially in classic carcinoids in whom late recurrence, though uncommon, is possible. The case highlights the crucial roles of integrated imaging, prudent procedural planning, and tailored surgical decision-making in treating bronchial carcinoids in guaranteeing persistent remission and in controlling potential late consequences.

6. Prognosis and Long-Term Outcomes

The carcinoid pulmonary tumours are, in general, associated with good outcomes, especially the typical subtype with low mitotic count (<2 per 2 mm^2), no necrosis, and less than 2% Ki-67 proliferation index [8,14]. In the current patient, histopathology after surgery revealed a typical carcinoid tumour that is of the pT1aN0LVI0 category with no lymph node extension or lymph vascular invasion in keeping with early disease and good biologic behaviour.

These are consistent with prognostic models by the World Health Organization (WHO) 2021 classification and the European Neuroendocrine Tumour Society (ENETS), both indicating excellent long-term survival in patients with totally resected typical carcinoids. Five-year survival in localized typical carcinoids is greater than 90%, and the disease-specific survival is near 100% if surgical margins are negative [9].

SPECT/CT functional imaging with radiolabelled somatostatin analogues did not show pathological uptake in this patient, in keeping with the diagnosis of non-functional carcinoid. Non-functional pulmonary carcinoids are less likely to cause systemic paraneoplastic syndromes like carcinoid syndrome and have a better prognosis than hormonally active tumours [7]. This supports the indolent behaviour of the tumour in this patient.

However, age-related physiological decline and comorbidities such as primary hypertension, dyslipidaemia, and osteochondrosis of the spine may represent potential hurdles regarding long-term health and recovery. While these factors do not in themselves change tumour biology, they may

decrease functional reserve, raise surgical risk, and require an individualized rehabilitation protocol after resection.

Post-bilobectomy, ENETS and National Comprehensive Cancer Network (NCCN) guidelines favour formal surveillance. For lymph node-negative typical carcinoids, chest CT should be conducted every 6-12 months during the first 2 years and annually thereafter for a minimum of 5-10 years (NCCN, 2023). Pulmonary function tests may be helpful in determining lung capacity after resection, particularly in light of the extent of lobar resection in the patient. In conclusion, the patient's subsequent course after surgery and histology are consistent with an excellent long-term outcome. The individualized therapeutic plan—derived from early diagnosis, accurate histopathological classification, and proper surgical treatment—shows how effective the multidisciplinary approach is in handling pulmonary carcinoid neoplasms.

6.1 Patient Perspective and Quality of Life (QoL) After Treatment

The diagnosis and management of pulmonary carcinoid tumours, although often associated with favourable long-term outcomes, carry significant implications for the patient's quality of life (QoL), particularly in older individuals undergoing major thoracic surgery. In the present case, the patient—a 74-year-old woman—underwent a right bilobectomy for a typical carcinoid tumour. While the procedure was curative, the physical and psychological sequelae of diagnosis, hospitalization, and surgery must be carefully considered in her ongoing care.

6.1.1 Physical and psychological recovery

Physical recovery in elderly patients may be prolonged due to reduced cardiopulmonary reserve, sarcopenia, and comorbidities such as hypertension or dyslipidaemia. Pulmonary resection often leads to a measurable decline in forced expiratory volume (FEV1) and exercise tolerance, particularly when two lobes are resected, as in this patient’s case. Residual symptoms such as mild exertional dyspnea, chest wall discomfort, or persistent fatigue may persist for months and require active rehabilitation.

From the psychological perspective, the impact of a cancer diagnosis—even a well-differentiated, low-grade tumour like a typical carcinoid—can induce significant distress, anxiety, or depression, particularly in elderly individuals. Fear of recurrence, dependence on healthcare providers, and limitations in daily activities may reduce overall well-being. Moreover, post-hospital deconditioning and the experience of hemoptysis or respiratory distress prior to surgery can leave a lasting emotional imprint.

6.1.2 Quality of life assessment and Rehabilitation

It has been demonstrated that even in patients with favourable tumour biology, quality of life assessments with questionnaires like the EORTC QLQ-C30 (European Organisation for Research and Treatment of Cancer QoL questionnaire) indicate long-term effects on role function, fatigue, and emotional functioning [12]. They are helpful in surveillance of outcomes in survivors and in detection of patients who need psychosocial intervention or pulmonary rehabilitation.

Rehabilitation of the lungs and formal follow-up, such as physical therapy, breathing techniques, and psychological counselling, are necessary to optimize functional recovery and return of patients to day-to-day life. Personalized patient education—about the disease nature, recurrence risk, and recovery expectations—also enables patients and enhances follow-up adherence.

In this patient, early rehabilitation initiation, proper pain control, and formal outpatient follow-up were factors that contributed towards her stable status at six-month follow-up. Nevertheless, vigilant

monitoring of her QoL—noting particularly psychological distress and long-term pulmonary function—remains crucial towards providing holistic care to the survivor.

7. Recommendations for Future Research and Clinical Practice

With the changing knowledge regarding pulmonary carcinoid tumours, there are several areas that are worth pursuing in the future. Future studies should investigate the molecular heterogeneity between typical and atypical carcinoids, specifically regarding targetable mutations like MEN1, mTOR pathway abnormalities, and epigenetic dysregulation. Advancements in genomic characterization may help in the formulation of tailored treatment regimens and improved risk classification.

From the clinical perspective, earlier diagnosis is still challenging because of the nonspecific symptoms and slow growth pattern of the tumour. There is a need to promote greater recognition among primary care physicians, pulmonologists, and radiologists to decrease the delay in diagnosis. After diagnosis routine incorporation of functional imaging (e.g., PET/CT with Ga-68 DOTA-TATE) should be facilitated, particularly in the workup and planning of PRRT.

Regarding treatment, increased availability of targeted therapies–such as the use of somatostatin analogues, PRRT, and mTOR inhibitors–will necessitate supporting national and institution-level policies to allow affordable delivery. Long-term follow-up protocols need to be standardized and applied systematically, with focus on patient-centred outcomes, quality of life, and rehabilitation efforts.

Lastly, interdisciplinary collaboration among oncologists, pulmonologists, surgeons, radiologists, and pathologists is essential to providing the optimum outcomes. Organizing specialized neuroendocrine tumour boards in reference centres may facilitate more uniform decision making and enable earlier planning for advanced therapies.

7.1 The Role of Lung Cancer Screening Programs in Early Detection

Besides enhancing clinical detection, the integration of lung cancer screening programs is also crucial for early detection of pulmonary carcinoid tumours. These programmes mostly comprise low dose computed tomography scans at regular intervals, which are carried out mainly for the detection of early lung cancers within populations at risk.

Based on the United States Preventive Services Task Force guidelines (USPSTF, 2021), smokers with a history of 20 pack-years and ages 50 to 80 years who smoke or have a history of smoking within the last 15 years should be screened with low dose computer tomography (LDCT) annually. Likewise, the NHS Targeted Lung Health Check programme provides biennial or annual scans of those smokers with a history of smoking between the ages of 55 and 74 years.

European guidelines support this strategy. The European Commission's Scientific Advice Mechanism, in a 2022 statement, advised introducing LDCT lung cancer screening for persons at risk throughout EU states on a member-by-member basis. The European Respiratory Society and European Society of Radiology endorse similar screening, with an emphasis on ensuring programs are quality-controlled and contain standardized pulmonary nodule management protocols and smoking cessation support programs.

These programs are aimed mainly at early detection of non-small cell lung cancer, although they also have the additional benefit of allowing incidental detection of pulmonary carcinoid tumours, which can occur as solitary pulmonary nodules. These tumours tend to be slow-growing and

clinically occult and may only be found incidentally on screening examinations. Early detection ensures earlier investigation and curative surgery.

ENETS recommends that clinicians put carcinoid tumours on the list of differential diagnoses when considering imaging for pulmonary nodules. Additionally, the BTS (2015) states that patients older than 40 years who present with unexplained hemoptysis or persistent radiological abnormalities should be investigated with chest CT within two weeks, with a follow-up bronchoscopy when necessary.

In summary, routine screening with LDCT, as advised by UK and European guidelines, provides a worthwhile opportunity not just to find aggressive lung cancers but also to discover less common conditions like pulmonary carcinoids. Incorporation of such knowledge into screening programs and radiological interpretation could minimize delayed diagnoses and help optimize patient outcomes.

8. Conclusion

Summary of the Case

This thesis chronicled and examined the clinical course of a 74-year-old female patient who presented with a classic pulmonary carcinoid tumour. Her progressive hemoptysis, in combination with extensive smoking and comorbidities, precipitated the usual cascade of diagnosis through imaging, bronchoscopy, and histology. The patient's case emphasized how subtle presentations in older patients are often indicative of underlying cancer and necessitate a high index of suspicion.

Diagnostic Key Points

Contrast-enhanced CT and bronchoscopy revealed a central endobronchial tumour with distal atelectasis. Functional evaluation by SPECT demonstrated no pathologic uptake of somatostatin, in keeping with the typical carcinoid. The diagnosis was verified by histology using characteristic morphology and immunohistochemical stains like synaptophysin, chromogranin A, and low Ki-67 index (<2%).

Treatment and Outcome

Surgical treatment by lower bilobectomy was successful, with histology showing complete removal and no metastases to the lymph nodes. Recovery from surgery was uneventful, and follow-up studies revealed no recurrence, confirming the favourable prognosis associated with usual carcinoids if treated early and properly.

Clinical Implications

This case supports the role of the multidisciplinary approach in the diagnosis and treatment of lung carcinoids. It also serves to highlight the value of early bronchoscopy in unexplained hemoptysis and the histological grading in directing treatment strategy.

Concluding Remarks

Finally, this report is part of the overall knowledge of pulmonary carcinoids and shows how meticulous clinical assessment, evidence-based diagnosis, and early surgery can lead to very

favourable patient outcomes. It also highlights the importance of comparing real-life findings with current literature to fine-tune the diagnosis and treatment techniques.

9. Literature

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