

HAEMORRHAGE POST BIOPSY OF A BRONCHIAL CARCINOID

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ABSTRACT

Background: Bronchial carcinoid tumours are rare, indolent, malignant neuroendocrine tumours derived from Kulchitsky cells and are not related to smoking. As these tumours can be asymptomatic or present with nonspecific symptoms, a high index of suspicion is essential to make an early diagnosis which determines the prognosis. Surgery is curative and remains the mainstay of treatment.

Case presentation: A 41-year-old female with no background medical illness first presented with a spontaneous left sided pneumothorax requiring a chest tube insertion. High-resolution CT (HRCT) thorax detected an incidental solitary pulmonary nodule. Bronchoscopy revealed a smooth round tumour sitting at the ostium of the basal right lower lobe bronchus. Endobronchial biopsy was complicated with massive bleeding requiring emergency exploration via rigid bronchoscopy. Multiple attempts to secure haemostasis using Watanabe spigot and argon plasma coagulation failed. She was intubated with a double lumen tube to isolate the healthy left lung. An urgent CT pulmonary angiogram (CTA) was performed to look for collaterals and feasibility of embolization, but no collaterals were seen. She was then referred to the cardiothoracic surgeon for an emergency right lobectomy. Histopathological examination revealed typical carcinoid tumour. She was discharged from the hospital in a stable condition.

Discussion: Bronchial carcinoids embryologically originate from the foregut and patients rarely present with features suggestive of carcinoid syndrome and crisis. Mostly are asymptomatic resulting in late presentation and diagnosis. Majority of the typical carcinoids are centrally located and may present with obstructive symptoms and recurrent pneumonia. Bronchoscopists may face massive bleeding following endobronchial biopsy in bronchial carcinoids.

Conclusion: Massive bleeding after endobronchial biopsy can occur and therefore the bronchoscopist should have anaesthesia, interventional radiology, and cardiothoracic support to handle this complication. Using tumour markers may obviate the need for biopsy in typical bronchial carcinoids to prevent massive bleeding after endobronchial biopsy.

Keywords: Angiography, Arterial cannulation, Angioseal.

INTRODUCTION

Prior to the 1970s, bronchial carcinoids were coined as bronchial adenomas as they were postulated to be benign. Subsequently, these rare, indolent neuroendocrine tumours were recognised

for their malignant potential, local invasion as well as distant metastasis commonly to the lung, bone, liver, adrenal, and brain. Bronchial carcinoids which account for less than 2% of all lung tumours are derived predominantly from enterochromaffin

or Kulchitsky cells and are known for their potential to form and secrete a variety of chemical substances(1). Etiologically there is no association to smoking, ambient radiation or any known exposure to carcinogens(2). There has been reports 5% prevalence of bronchial carcinoid tumours in patients with multiple endocrine neoplasia type1 (MEN1) (3). Majority of these tumours are centrally located, arising from the major bronchi; only about 15% are in the periphery of the lung(2). Bronchial carcinoids can be asymptomatic or present with bronchial obstruction symptoms like haemoptysis, cough, pleuritic chest pain, recurrent infection, wheezing, and dyspnoea; as a result of complete or partial bronchial obstruction(2).² These symptoms should raise an index of suspicion essential to make an earlier diagnosis for better prognosis(4). Bronchoscopy is an important diagnostic tool for bronchial carcinoids as 75-77% are centrally located and easily accessible for endobronchial biopsy(5). However, bronchoscopists may face massive bleeding following endobronchial biopsy in bronchial carcinoids due to hypervascularity seen especially in patients with haemoptysis(6). Surgery is curative and remains the mainstay of treatment.

CASE PRESENTATION

A 41 year old female, para 3, a nurse by profession first presented to us in January 2021 for spontaneous left sided pneumothorax requiring a

chest tube. She had no previous admissions for similar problems but was involved in a motor vehicle accident in December 2020, one month prior. She is a non-smoker and there was no history of passive smoking or being exposed to biomass fuel. There were no clinical features to suggest Marfan syndrome or any cystic lung disease. A high-resolution CT (HRCT) thorax was done as part of the workup for the pneumothorax which incidentally detected a solitary pulmonary nodule over the right lower lobe. Brock risk estimation of the probability of the nodule being malignant was 21.5%. However, the initial HRCT thorax was not able to differentiate the solitary pulmonary nodule from a vessel, hence a CT pulmonary angiogram (CTPA) was performed within a month from the HRCT thorax which confirmed a mass measuring 2.4 cm anteroposterior diameter, 2.6 in width and 2.8 cm in intercommissural diameter (CC) over the anterior segment of the right lower lobe. The rest of the lung fields were clear and there were no hilar or mediastinal lymphadenopathy. If proven malignant, the clinical staging would be T1cN0M0 (Stage 1a). Flexible bronchoscopy was performed in May 2021 which revealed a smooth round tumour sitting at the ostium of the basal right lower lobe bronchus causing obstruction. Endobronchial biopsy was taken with a 2mm flexible forceps, complicated with massive bleeding requiring an emergency exploration via rigid bronchoscopy.

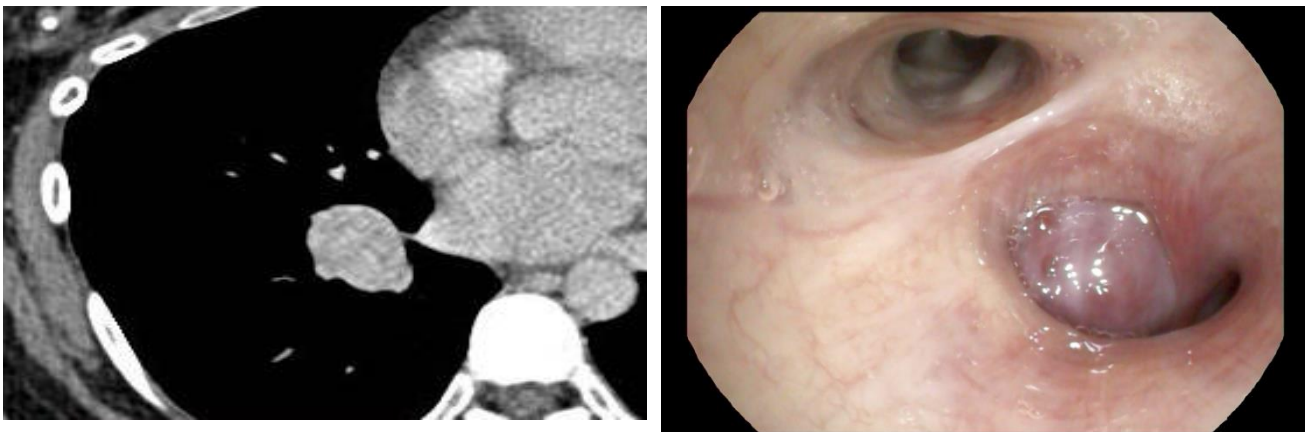


FIGURE 1: Computed tomography pulmonary angiography (CTPA) scan showing a mass over the anterior segment of the right lower lobe

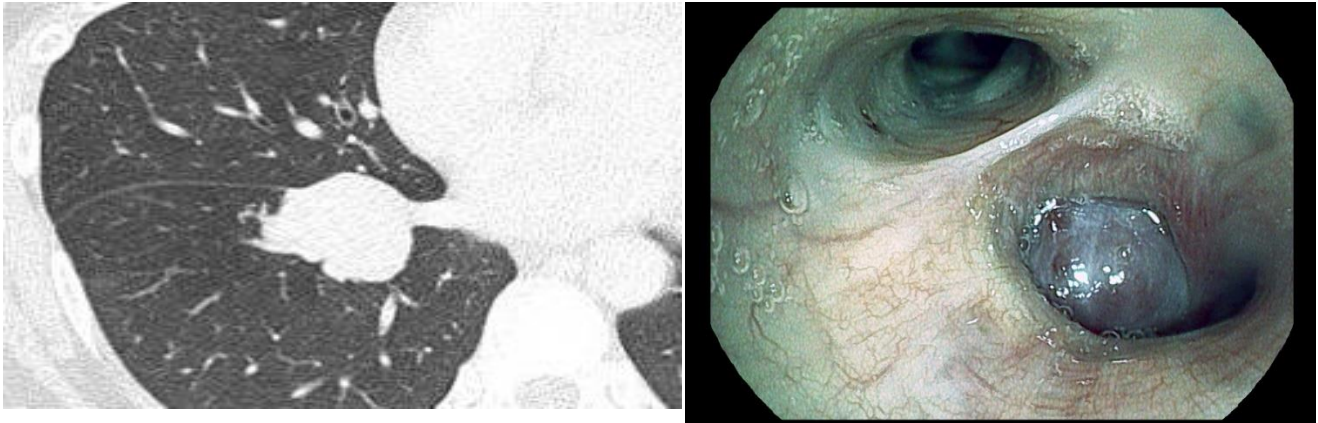


FIGURE 2: Initial bronchoscopy with smooth round tumour at the ostium of the basal right lower lobe bronchus.

Airway examination during rigid bronchoscopy revealed blood clots over right main bronchus with active bleeding. Blood clots were extracted using Erbe flexible cryoprobe 2.4mm and endobronchial biopsy was taken from the right lower lobe using 2mm flexible forceps. Multiple

attempts to secure haemostasis using adrenaline (1:1000) flush, Watanabe spigot and argon plasma coagulation failed. She was then reintubated with a 35F double lumen endotracheal tube to isolate the left healthy lung.

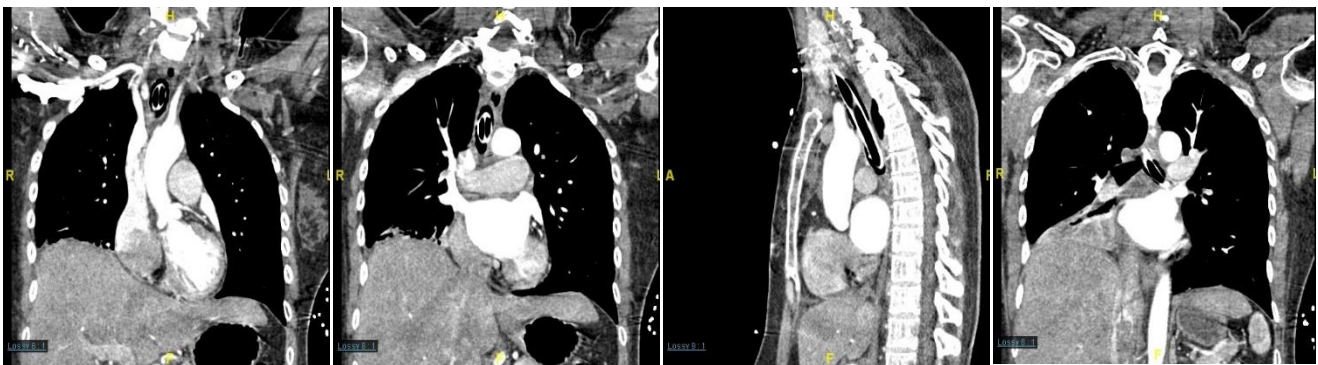


FIGURE 3: Double lumen endotracheal tube (bronchial limb pushed into left main bronchus).

Urgent CT pulmonary angiogram (CTA) was performed to look for collaterals and for feasibility of embolization of the collaterals; however, there were no collaterals visualised. She was then referred to the cardiothoracic surgeon for an emergency thoracotomy and lower lobectomy. Intraoperative findings of right lower endoluminal bronchial tumour which was almost completely obstructing the lumen with right paratracheal (4R)

and right interlobar (11R) lymph node. Post operatively, she was transferred to intensive care unit. She had a smooth post-operative recovery and was transferred back to surgical ward 2 days later. The output from chest tube was insignificant and minimal bubbling ceased gradually. Chest x ray taken on her 2nd post op day showed well expanded right upper lobe with no evidence of pneumothorax and the chest tube was removed.

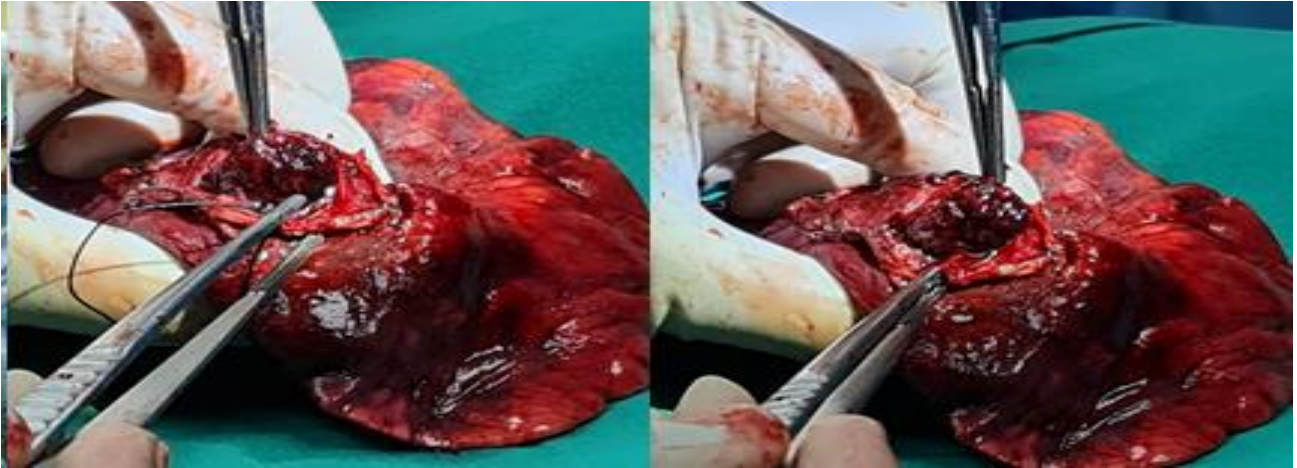


FIGURE 4: Intraoperative image showing obstructive right lower endoluminal bronchial tumour.

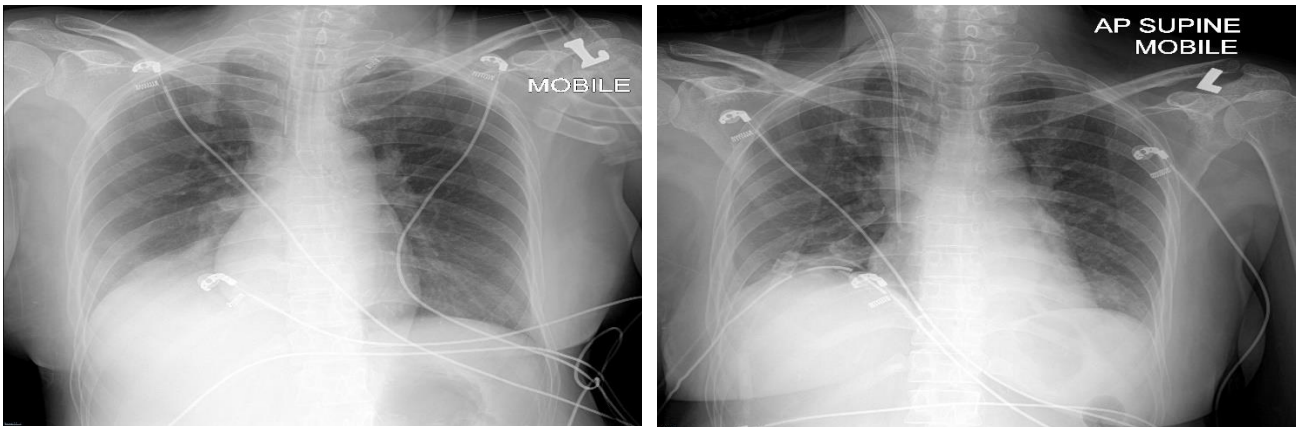


FIGURE 5: Chest radiograph pre and post right lower lobectomy.

Resected specimens sent for urgent histopathological examination (HPE) showed a circumscribed, polypoid endobronchial tumour with neoplastic cells arranged in organoid nesting pattern and trabeculae. The cells had fine granular chromatin, inconspicuous nucleoli, moderate to abundant eosinophilic cytoplasm with mitosis seen at 7/2mm². The stroma is vascularised with areas of haemorrhage and no necrosis. The immunohistochemical stains were positive for

Chromogranin A, Synaptophysin, Ki-67. The resected right paratracheal and interlobar lymph nodes were free from malignancy. The final diagnosis was typical carcinoid tumour; pathological staging pT2a pN0. 24-hour urinary excretion of 5-Hydroxyindoleacetic acid (5-HIAA) was normal but serum Chromogranin A was significantly high. Other blood investigations done were unremarkable.

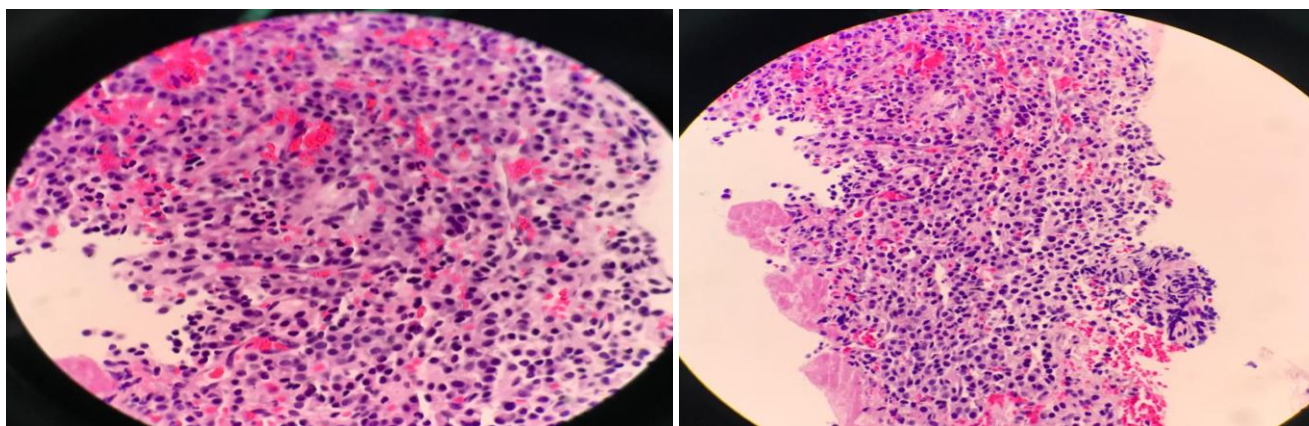


FIGURE 6: Histologic section showing neoplastic cells in organoid nesting pattern with fine granular chromatin and eosinophilic cytoplasm

Gallium-68 DOTATATE PET CT study showed a somatostatin receptor avid focus at right temporo-frontal region of the brain possibly due to meningioma. Otherwise, there was no avid local tumour recurrence in the lung, or any abnormal uptake seen elsewhere throughout the body. The patient showed a remarkable improvement and was discharged from the hospital in a stable condition. She is currently undergoing oncology follow-up at National Cancer Institute.

DISCUSSION

The varied presentation of bronchial carcinoids continues to intrigue and puzzle clinicians. Traditionally these tumours are classified according to their embryological origin as foregut carcinoid tumours. Histologically, the World Health Organization/The International Association for the Study of Lung Cancer (WHO/IASLC) has classified bronchial carcinoids into typical and atypical carcinoids based on cellular morphology, mitotic index, and necrosis(7, 8).

Table 1: Classification of carcinoid pulmonary tumours.

TYPE	PRESUMED CELL OF ORIGIN	HISTOLOGICAL OF FEATURES	CLINICAL CHARACTERISTICS	5-YEAR SURVIVAL RATE
TYPICAL CARCINOID	Epithelial endocrine cell	No necrosis, mitosis/2mm ²	<2 Usually indolent, may secrete corticotrophin, rarely secretes serotonin.	>90%
ATYPICAL CARCINOID	Epithelial endocrine cell	Focal areas of necrosis, mitosis/2mm ²	2-10 Usually aggressive, with incidence of metastases.	40-60%

Adapted from (7).

There is no gender predilection for typical carcinoid. There is a bimodal peak incidence during adolescence and 40-50 years of age(9). Although our patient belongs to the second peak of presentation, she likely had the tumour earlier as its indolent and remained asymptomatic till date. Approximately 70% of bronchial carcinoids are centrally located in the major bronchi; only one third of the tumours, mostly atypical carcinoid

tumours; are located peripherally in the segmental bronchi or beyond(10). There is a predilection for these tumours to occur in the right lung (61%) especially the middle lobe(10).

Most patients with bronchial carcinoid are asymptomatic or can present with nonspecific symptoms of airway obstruction such as wheezing, haemoptysis, dyspnoea, chest pain and recurrent infections resulting in misdiagnosis or

late diagnosis(9). Furthermore, as these tumours are rare, they are often not considered as a differential diagnosis especially in the young presenting with a myriad of vague symptoms. Bronchial carcinoids have the potential to form and secrete a variety of vasoactive substances into the systemic circulation especially serotonin, which may result in carcinoid syndrome in 1% of the patients(5). A high index of suspicion and a thorough work up including CT scan thorax and bronchoscopy is essential to clinch an accurate diagnosis early in patients with refractory symptoms.

Bronchoscopic biopsy is the gold standard modality for early tissue diagnosis as 75-77% are centrally located and easily accessible.(5) Well-vascularised, well circumscribed lesions that are raspberry coloured, which have a risk of bleeding are pathognomonic of bronchial carcinoids.(5) Bronchial washings or brushing are unrewarding in contrary to biopsy specimens due to the intact surface epithelium of the tumour(10). Bronchoscopists may face massive bleeding following endobronchial biopsy in bronchial carcinoids necessitating emergency pulmonary resection as seen with our patient. Bleeding is common and was found in 30 (71.4%) of 42 patients with typical carcinoid and only 3 (16.7%) of 18 patients with atypical carcinoid ($p<0.05$)(11). In a study by McCaughan et al., bronchoscopic biopsy was not routinely performed due to risk of haemorrhage(10, 12). Hence complication of bleeding post endobronchial biopsy should be well anticipated and the bronchoscopist should have anaesthesia, interventional radiology, and cardiothoracic support to handle this complication.

Rigid bronchoscopy and biopsy under anaesthesia in a controlled setting can reduce the risk of massive bleeding and result in a larger,

more reliable sample(10). Alternatively, chromogranin A(CgA) and neuron specific enolase(NSE) tumour markers may be utilised and may obviate the need for biopsy in typical bronchial carcinoids to prevent massive bleeding after endobronchial biopsy(13). CgA, specificity of 75% and sensitivity of 67.9%(14) could be used to detect bronchial carcinoids(15). A raise in NSE may be used to differentiate between carcinoids and small cell carcinoma(16-18). Non-small cell carcinoma, particularly squamous cell carcinoma was ruled out by the negative immunostaining to p63 and p40.

Surgical resection is the mainstay treatment in bronchial carcinoids even when mediastinal nodal metastasis is present(19). These tumours are generally unresponsive to chemotherapy or radiotherapy; the prognosis is excellent for both typical and atypical bronchial carcinoids post-surgical resection(19).

CONCLUSION

Clinical symptoms and imaging studies suggestive of obstructive endobronchial lesion with a raised CgA should raise a high suspicion of bronchial carcinoid tumour. The gold standard to diagnose this rare tumour is bronchoscopic biopsy. Massive bleeding after endobronchial biopsy can occur and therefore the bronchoscopist should have multidisciplinary support from anaesthesia, interventional radiology, and cardiothoracic to handle this complication. Plasma CgA is nonspecific but reliable marker with good correlation to tumour burden; is useful for diagnosis, follow up and even precede radiological evidence of progression(20). Using tumour markers may obviate the need for biopsy in typical bronchial carcinoids and prevent massive bleeding after endobronchial biopsy.

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