Case report

Pulmonary carcinoid presenting with persistent pneumothorax

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SUMMARY

Lung neuroendocrine tumours (Lung NETs) are a rare group of pulmonary neoplasms often characterised by insidious clinical behaviour. Lung NET account for ~1%–2% of all lung malignancies in adults and 30% of all NETs. Incidence ranges from 0.2 to 2/100 000 population per year. While some patients may be asymptomatic, others may present with obstructive symptoms due to mass effect. Incidence of spontaneous pneumothorax as a complication of lung neoplasms is rare (0.05%–1.4% of all pneumothoraces). In this report, we present a case of recurrent pneumothorax due to Lung NET that was refractory to conservative management. We also discuss the diagnostic methods as well as surgical management approach, which is considered the treatment of choice in such tumours.

BACKGROUND

Lung neuroendocrine (carcinoid) tumours are a rare group of pulmonary neoplasms often characterised by insidious clinical behaviour with a myriad of clinical syndromes, including carcinoid syndrome, Cushing's syndrome and acromegaly. However, the incidence of spontaneous pneumothorax as a presenting symptom of lung neuroendocrine tumour (Lung NET) is extremely rare, and may pose a diagnostic challenge. In this report, we present a case of recurrent pneumothorax due to Lung NET that failed conservative management. We also discuss histological features, diagnostic methods and surgical management.

CASE PRESENTATION

An 80-year-old man with history of asthma and type 2 diabetes mellitus presented to the emergency department with worsening cough and shortness of breath, and was found to have a left-sided spontaneous pneumothorax ([figure 1](#)). He was admitted to the hospital and chest tube was inserted. However, due to persistent leak, PleurX catheter was placed, and the patient was discharged home afterwards. However, he presented with subcutaneous emphysema on the same day and was subsequently readmitted. Recurrent pneumothorax was managed conservatively. PleurX catheter was attached to underwater seal with negative pressure and respiratory status was optimised given evidence of asthma exacerbation. Treatment with methylprednisolone

Figure 1 Chest X-ray demonstrates a large left-sided spontaneous pneumothorax.

40 mg intravenous two times per day was initiated for 3 days, and was later switched to prednisone 40 mg orally daily over the course of 2 days and subsequently tapered to 30 mg. Montelukast, tiotropium, mometasone furoate/formoterol inhalers, ceftriaxone/azithromycin and cough suppressants were initiated. However, air leak persisted despite conservative management for 13 days. CT scan of the chest without intravenous contrast was performed and revealed subcutaneous emphysema in the left chest wall, with minimal left pneumothorax and a left chest tube adequately located in the pleural space. After discussing in a multidisciplinary team settings, decision was made to proceed with video-assisted thoracoscopic surgery. During surgery, multiple wedge resections were performed along with partial pleurectomy, lysis of adhesions and decortication of left upper lobe.

Figure 2 Carcinoid tumour islands underlying the pleura, visualised under microscopy by H&E stain.

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Figure 3 Immunoperoxidase stains with positive chromogranin and synaptophysin in tumour, visualised under microscopy.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses include bullous lung disease as a cause of recurrent pneumothorax. However, no bullae were noted on CT scan of the chest, making this diagnosis unlikely. Other differential diagnoses include indolent lung malignancies or benign tumours such as pneumocytomas that are too small to be picked up on CT scan of the chest.

OUTCOME AND FOLLOW-UP

Pathology revealed a subpleural 5 mm carcinoid tumorlet (figure 2) with solid nests of cells along with lung tissue with emphysematous change, pleural scarring and bullous formation. No nuclear pleomorphism or mitotic figures were noted. Immunoperoxidase stains were positive for thyroid transcription factor-1 (TTF-1) (figure 3), synaptophysin, chromogranin (figure 4) and CD56 and negative for CK5/6, calretinin and P-40. Serum chromogranin A was elevated 431 ng/L. Postoperative course was uncomplicated and the patient was eventually discharged to an inpatient rehab facility.

DISCUSSION

Bronchial carcinoid or lung neuroendocrine tumours are a rare group of pulmonary neoplasms that are often characterised by insidious clinical behaviour. They are considered a low-grade malignant neoplasm that consist of a specialised bronchial cell which belongs to the group of neuroendocrine cells. Carcinoid tumours are usually classified as typical or atypical. Typical

Figure 4 Immunoperoxidase stains with positive TTF-1 in tumour, visualised under microscopy.

Table 1 Treatment recommendations of lung/bronchial NET based on disease progression, adopted from the North American Neuroendocrine Tumour Society (NANETS) consensus guidelines for the management and treatment of neuroendocrine tumours¹³

	Intervention	Recommendations
Local-regional disease	Surgical resection with hilar/mediastinal lymph node sampling is recommended	Recommend
Recurrent disease, resectable	Surgical resection	Recommend
Metastatic disease, unresectable	Everolimus	Consider
	Interferon alpha	Consider
	Radiation for unresectable disease	Consider
	Temozolomide	Consider

NETs, neuroendocrine tumours.

carcinoid tumours account for ~90% of carcinoid tumours which are well-differentiated, low-grade tumours with scarce mitoses and pleomorphism. They are slowly growing neoplasms which rarely metastasize to extrathoracic structures. Atypical carcinoid tumours account for the remaining 10% of tumours. Pathological criteria by the WHO include the presence of poor-differentiated neuroendocrine morphology and necrosis or increased mitotic activity. They are characterised by nuclear pleomorphism, disorganisation, and can behave aggressively with rapid tumour growth and early distant dissemination.¹⁻⁴ Immunohistochemical staining for neuropeptides like CD56, chromogranin and synaptophysin may help with the diagnosis. A high Ki-67 help distinguish small cell and large cell neuroendocrine carcinoma from pulmonary carcinoids.

Lung NETs makeup 1%–2% of all lung malignancies in adults and 30% of all neuroendocrinetumours (NETs). Incidence ranges from 0.2 to 2/100 000 population per year. While some patients may be asymptomatic, others present with obstructive symptoms due to mass effect, haemoptysis, dyspnea, wheezing or recurrent pneumonia. Clinical presentation includes carcinoid syndrome, Cushing's syndrome and acromegaly. Incidence of pneumothorax as a complication of lung neoplasms is low at 0.05%–1.4% of all pneumothoraces.^{5,6} In the literature, there are few similar cases where Lung NETs present with a spontaneous pneumothorax. Interestingly, the pathophysiological mechanism behind the association between the development of pneumothorax and carcinoid tumours remains unclear.

CT of the chest remains the most useful imaging modality and diagnosis is usually confirmed either by bronchoscopic biopsy (for central lesions) or by transthoracic needle biopsy (for peripheral lesions).⁶⁻⁸ For patients with localised Lung NETs, surgical resection is the preferred treatment approach with mediastinal lymph node sampling or dissection. Adjuvant platinum-based chemotherapy with or without radiation therapy is a reasonable option for patients with intermediate-grade (atypical) Lung NETs, although little evidence exist to support this practice (tables 1 and 2). Patients with low-grade (typical) tumours are unlikely to benefit from adjuvant systemic treatment as they are generally considered chemoresistant. The role of adjuvant therapy after complete resection of a Lung NET is undefined due to the lack of prospective randomised trials. Lung NETs have an excellent prognosis following surgical resection, with 5-year survival rates of 87%–100%.⁹⁻¹¹ Serum chromogranin A and urinary

Table 2 Comprehensive review of the management of localised pulmonary neuroendocrine tumours, mainly atypical carcinoids (AC) and typical carcinoids (TC) by different guidelines, adapted from Gosain *et al*¹⁴

Guidelines	NCCN	NANETS	ENETS	ESMO
Surgical approach	Lobectomy along with mediastinal node dissection or sampling.	Bronchial NETs—sleeve resection, along with lymph node sampling in well-differentiated bronchial NETs. Thymic NETs—median sternotomy approach with complete tumour resection and mediastinal lymphadenectomy.	Lobectomy/segmentectomy along with a minimum of six lymph nodes sampling, min of three to be mediastinal including subcarinal. Central airway tumour—lung parenchymal sparing surgery. Bronchial sleeve resection or sleeve lobectomy preferred over pneumonectomy. Systemic nodal dissection.	Inoperable—bronchoscopic laser excision of intraluminal typical bronchial NETs. Lobectomy/sleeve resection, along with systemic nodal dissection.
Adjuvant regimen	Stage IIIA/B ACs radiation ± chemotherapy.	No recommendations.	Consider adjuvant therapy in ACs with positive lymph nodes.	No recommendations.

EMSO, European Society of Medical Oncology; ENETS, European Neuroendocrine Tumour Society; NANETS, North American Neuroendocrine Tumour Society; NCCN, National Comprehensive Cancer Network; NETs, neuroendocrine tumours.

5-hydroxyindoleacetic acid are usually elevated and can be used as a marker to assess disease progression, response to therapy or recurrence after surgical resection.^{10–12}

Learning points

- Symptoms of lung neuroendocrine tumour (Lung NET) may vary and can present as a persistent pneumothorax despite prolonged conservative management.
- Surgical resection remains the cornerstone of treatment for Lung NETs.
- Serum chromogranin as well as urinary 5-hydroxyindoleacetic acid (5-HIAA) are typically elevated and can be helpful in monitoring response to therapy, disease progression and recurrence after surgery.
- Lung NETs are generally curable and carry an excellent prognosis.

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