Original Article

Meta-analysis of a master mimicker: endobronchial lipoma

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Background: Endobronchial lipomas (ELs) are extremely rare benign tumors that account for 0.1–0.4% of all bronchial tumors. Our study aims to better characterize these lesions based on their baseline demographic characteristics, size, location, association with smoking and establish a treatment modality of choice for such tumors.

Methods: We conducted a retrospective meta-analysis of 29 studies of EL reported from 1994 till present. These 29 studies yielded 36 patient encounters which were included in our study. Categorical outcomes were compared between study groups using chi-square test. P value <0.05 was considered statistically significant.

Results: Our study has shown that smaller lesions more likely to be ELs or benign lung tumors. Eighty percent of ELs had a size <1.5 cm (P=0.056) and the other tumor types had a size ≥1.5 cm.

Conclusions: These tumors are difficult to diagnose due to their nonspecific presenting complaints unless pulmonologists maintain a high index of suspicion. Treatment options such surgical resection (SR) or bronchoscopic resection (BR) are available and interventions should be planned on a case-by-case basis by a multidisciplinary team.

Keywords: Endobronchial lipoma (EL); lung neoplasm; bronchoscopy; cough; bronchiectasis; chronic obstructive pulmonary disease (COPD)

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Introduction

A variety of benign and malignant tumors arise from the lung, around 95% are carcinomas, 5% are bronchial carcinoids, and 2% to 5% are mesenchymal in origin (1). Intrathoracic lipomas are tumors composed exclusively of mature adipose tissue which rarely occur within the lungs (0.1–0.5% of benign lung tumors) (2). Intrathoracic lipomas can be classified into five groups: endobronchial, parenchymal, pleural, mediastinal and cardiac (3). Endobronchial lipomas (ELs) originate from the fat cells located in the peribronchial tree and occasionally the submucosal tissue of main bronchi. These lesions usually are pedunculated with a narrow stalk and may extend between the cartilaginous rings into the peritracheal tissue (1,2,4). A lipoma consists of mature fatty tissue covered with normal bronchial epithelium (2). Squamous metaplasia, fibrous, glandular tissue, areas of cartilage or osseous metaplasia can also be found in the lipoma; a pathologist must use a variety of differentials to rule out atypical lipomatous tumors and well-differentiated liposarcomas (1).

ELs are rare tumors and hence can be missed easily (5). When missed, these rather benign lesions can cause a high degree of morbidity and mortality (6). The late diagnosis of benign neoplasms can lead to irreversible pulmonary damage (7). Symptoms may be generalized and mimic chronic pulmonary diseases, lowering our degree of suspicion and increasing the chances of missing such lesions. These tumors can present with signs and symptoms of productive cough, hemoptysis, wheezing, obstruction,

Table 1 Baseline characteristics and demographics of the adults in the study

Demographics	Percentages (%)
Age (years)	
≤40	8.3
≥41	91.7
Gender	
Male	72.2
Female	22.2
Histopathology	
EL	72.2
Other tumors	27.8
Location of tumor	
Right	47.2
Left	44.4
Bilateral	8.3
Size of tumor	
<1.5 cm	13.8
≥1.5 cm	38.8
Treatment	
SR	41.2
BR	58.8
Presenting complaints	
Recurrent pneumonia	11.1
Chest pain tightness	16.6
Thoracic pain	2.7
Palpitations	2.7
Acute cough	16.7
Persistent cough	27.8
Productive cough	30.6
Dry cough	19.4
Fever	22.2
Hemoptysis	16.7
Stridor	2.7
Exertional dyspnea	38.9
Acute pneumonia	13.8

EL, endobronchial lipoma; SR, surgical resection; BR, bronchoscopic resection.

recurrent pneumonias and bronchiectasis (6). These lesions can cause bronchial obstruction which can lead to distal parenchymal lung damage over months to years. They often present with a clinical picture of asthma and can be misdiagnosed as malignancies. These lesions can cause post-obstructive pneumonias in patients leading to multiple repetitive antibiotics (7). Given, the high degree of lung injury caused by these benign lesions, it is important to focus our efforts on maintaining a high degree of suspicion. Currently in literature, only case reports and case series are published, our study aims to better characterize these lesions based on their size, location, association with smoking and gender and establish a treatment modality of choice for such tumors.

Methods

Study selection

The literature and database searches identified 29 studies since 1994 for inclusion. An online search of MEDLINE and Ovid yielded a total of 161 records. Manual bibliographic searches of identified articles and publications resulted in an addition of 15 records. Manuscripts were screened following the removal of duplicates and applying the inclusion criteria. Keywords including 'EL, hamartoma, leiomyoma' were searched in the discussion and tumor histopathology sections. We selected 29 articles for our retrospective analysis after excluding 147 articles as per our exclusion criteria (e.g., incorrect tumor histopathology, unavailability of tumor histopathology reported). These 29 studies yielded 36 patient encounters which were included in our study.

Epidemiology

Baseline characteristics included age, gender, presenting complaints, size of the tumor, tumor histopathology, smoking history, history of pulmonary diseases [asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis] (*Table 1*). Additional variables such as chest radiographs, computed tomography (CT) scans, location of the tumor and treatment method were included. Follow-ups were studied as office visits, follow-up CT scans and chest radiographs done for suspicious disease recurrence.

Statistical methods

Descriptive analysis was carried out by mean and

standard deviation for quantitative variables, frequency and proportion for categorical variables. Non-normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data was also represented using appropriate diagrams such as bar graphs, pie charts and box plots. Categorical outcomes were compared between study groups using chi-square test. P value <0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY, USA).

Results

Clinical characteristics

A total of 36 patients were included in the final analysis. In our study we showed that 91.7% of our patients had an age greater than or equal to 41 and a majority of patients were male [n=26 (72.2%) males, n=8 (22.2%) females] as demonstrated by previous studies (6). We found 36.1% of patients with ELs were reported smokers, and only 5.6% of them were non-smokers/never smokers. Obesity and smoking are considered risk factors, although there are no conclusive studies showing a causative relation (8).

Presenting symptoms included productive cough (n=11, 30.6%), persistent cough (n=10, 27.8%), exertional dyspnea (n=14, 38.9%), fever (n=8, 22.2%), dry cough (n=7, 19.4%), acute cough (n=6, 16.7%) and hemoptysis (n=6, 16.7%). Cough is the most common form presentation and progressive dyspnea, hemoptysis, recurrent pneumonias were the other commonly seen presenting complaints (8). Patients are erroneously diagnosed with bronchial asthma, delaying the diagnosis of these types of lesions (4,5,8,9). A minority (n=6) of patients reported chest pain and chest tightness. A few (n=5) presented with acute and/or recurrent pneumonias. Atypical presentations such as thoracic pain, palpitations and stridor were reported too. Eighty percent of patients had abnormalities on chest radiograph (e.g., atelectasis, consolidation, or mass) and 58.3% of them got a chest radiograph prior to their diagnosis (3). Ninety-seven point two percent underwent a CT scan of the chest to establish diagnosis. As previously mentioned, CT scans are highly specific and sensitive to adipose tissue density helping with early diagnosis (*Table 2*).

Eleven point one percent reported a previous history of COPD while 8.3% reported a history of asthma. Others had a history of chronic cystic bronchiectasis (n=2, 5.4%) and pneumothorax (n=1, 2.8%) prior to diagnosis.

Majority of the tumor histopathology were ELs (n=26, 72.2%), hamartomas (n=5, 13.9%) and leiomyomas (n=3, 8.3%). Our study has shown that smaller lesions are more likely to be ELs or benign lung tumors. Eighty percent of ELs had a size <1.5 cm (P=0.056) and the other tumor types had a size ≥1.5 cm. Forty-seven point two percent ELs were found in the right lung (main bronchus, lobular bronchus and peripheral to segmental bronchus) in comparison 44.4% were discovered in the left lung. These lesions were found in the first three subdivisions of the tracheobronchial tree (6). Eight point three percent of ELs were interestingly seen in bilateral lung lobes.

Flexible bronchoscopy was used to locate the tumor in 77.8%, while 13.9% (n=5) underwent a rigid bronchoscopy. Fifty-eight point eight percent (n=20) underwent bronchoscopic resection (BR) of the EL with use of either argon plasma coagulation (APC) or Nd-YAG laser or electrocautery while 41.2% (n=14) ultimately underwent surgical resection (SR) for treatment of the EL (*Figure 1*).

Outcome

BR was successful in 75.0%. For the one unsuccessful patient, the location of the tumor was the lobar bronchus of the left upper lobe (LUL) (4). Due to the acute angulation of the LUL of the patient, the mass could not be grasped with using any kind of endobronchial tools as reported (4). The patient underwent an open thoracotomy and LUL lobectomy (4). No mortality occurred in the 28 patient outcomes reported. We compared all the variables such as smoking, location, gender, age, presenting symptoms, tumor histopathology with final outcome and there was no significant difference.

Follow-up and recurrence

Duration of follow-up ranged from 1 to 38 months' post-resection. Relief of symptoms was noted post-resection/surgery on follow-up clinic visits. In one case recurrence in the form of leiomyoma was diagnosed by chest CT and bronchoscopy seventeen months post-resection.

As the lesion was in the proximal left main bronchus, the patient underwent left pneumonectomy. The pathology showed a leiomyoma confined within the bronchial cartilage. No complications were noted on 17-month follow-up post procedure. In one patient, the postoperative course was characterized by fever and purulent bronchial

Table 2 Composite results of study selection

Year	Age	Histopathology	Location	Tumor size	Treatment for the tumor	Outcome & follow-up
2008	62	EL	RLL	NR	SR	Successful, post-op pneumonia treated with Abx
1996	68	EL	RML	NR	BR	Successful
2013	63	EL	LLL	2.0 cm	SR	Successful
2007	56	EL	RUL	NR	BR	Successful
2009	41	EL	RLL	NR	BR	Successful
2009	73	EL	BI	NR	BR	Successful
2014	43	EL	RLL	NR	NR	NR
2015	64	EL	RUL	NR	SR	NR
2004	47	EL	RM	1.5 cm × 1.0 cm	SR	Successful, 5 months
2015	68	SEL	RLL	NR	SR	NR
2018	70	EL	LM	NR	BR	NR
2009	46	EL	LM	1.5 cm	SR	Successful, 36 months
2013	56	EL	LM	1.2 cm × 1.1 cm	BR	Successful, 12 months
2005	43	EL	RM	NR	SR	NR
2014	63	EL	RLL	NR	BR	Successful, 6 months
2013	35	EL	RM	2.0 cm	BR	NR
2016	60	MEL	RLL	1.2 cm	SR	Successful, 12 months
1999	62	EL	LLL	3.0 cm × 1.2 cm × 1.4 cm	SR	Successful
2014	61	EL	LLL	0.8 cm × 0.7 cm × 1.1 cm	BR	Successful, 3 months
2009	53	EL	BI	NR	SR	Successful, 6 months
2006	51	L	RUL	1.6 cm	BR	Successful, 38 months
2006	19	L	LM	2.1 cm	BR	Successful, 22 months
2006	17	L	RM	2.9 cm	BR	Successful,10 months
2006	50	H	LUL	3.5 cm	BR	Successful, 35 months
2006	59	H	LUL	1.6 cm	BR	Successful, 9 months
2006	58	H	LUL	1.5 cm	BR	Successful, 20 months
2006	63	EL	LUL	3.0 cm	SR	Failed, 56 months
2014	63	LH	RLL	1.5 cm × 1.0 cm	BR	Successful, 1 month
2017	63	EL	LM	NR	BR	Successful
2014	73	EL	LM	NR	BR	Successful, 1 month
2013	65	EL	RUL	2.2 cm × 1.8 cm × 1.1 cm	SR	Successful, 11 months
1994	68	EL	LUL	1.0 cm	SR	Successful
2004	56	LH	BI and RLL	NR	SR	NR
2011	48	EL	RM	NR	BR	Successful, 1 month
2017	63	EL	LLL	1.2 cm × 1.0 cm × 1.5 cm	Biopsy, no resection	NR
2013	62	EL	LUL	NR	BR	Successful, 1.5 months

BR includes APC, snare electrocautery, Nd-YAG laser therapy; SR includes thoracotomy, lobectomy, pneumonectomy, wedge resection, bronchotomy. EL, endobronchial lipoma; SEL, submucosal endobronchial lipoma; MEL, myxoid endobronchial lipoma; L, leiomyoma; H, hamartoma; LH, lipomatous hamartoma; RM, right maintstem bronchus; LM, left mainstem bronchus; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; BI, bronchus intermedius; LUL, left upper lobe; LLL, left lower lobe; NR, not reported; BR, bronchoscopic resection; APC, argon plasma coagulation; SR, surgical resection.

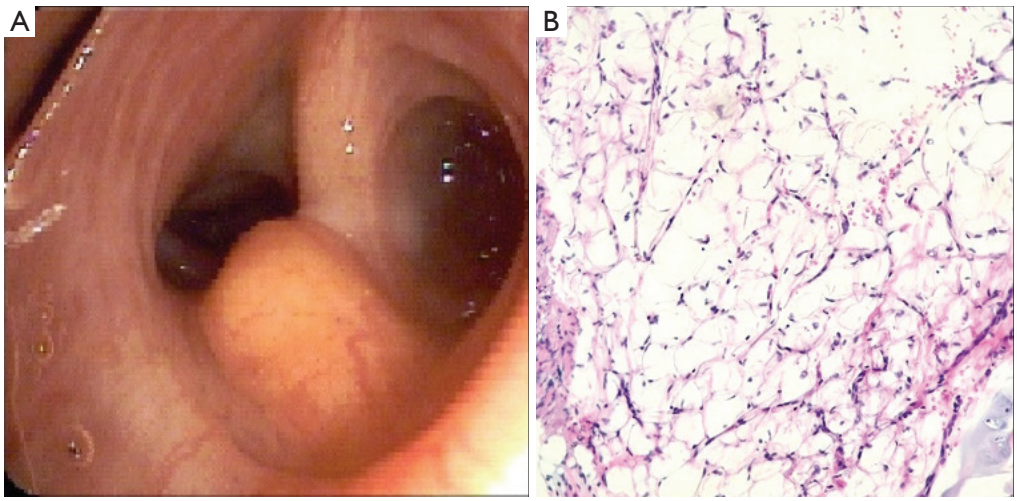

Figure 1 Bronchoscopic image and histopathology. (A) The finding of the lesion in situ via the bronchoscope, revealing a 3 mm polypoid tumor in the RLL bronchus and EL was suspected; (B) a pathological examination revealed a polypoid tumor, covered with stratified ciliated epithelial cells, which consisted of mature adipocytes; cell scale bar: 7.92 cm × 15.90 cm; dyeing method: black and white. RLL, right lower lobe; EL, endobronchial lipoma.

secretions, controlled with broad-spectrum antibiotics and discharged home after 6 days (9). In another patient, post-snare cautery of the lipoma, a coughing bout during the bronchoscopy caused the tumor to slip into the left mainstem bronchus. Hypoxemia ensued requiring endotracheal intubation, followed by a rigid bronchoscopy to extract the already resected tumor mass. Immediately after the extraction, oxygenation improved, the patient was extubated and discharged home the next day. At follow-up the patient had complete resolution of cough (10).

Discussion

ELs are rare benign tumors of the lung which arise from the submucosal layer of the bronchus. Only 5% of all lung tumors are benign. Ninety percent of benign lesions are adenomas or hamartomas. Although lipomas are a common tumor of the body, ELs are extremely rare. Their incidence has been reported to range from 0.1–0.5% in all lung tumors (3,6,11). These lesions have been reported to have no premalignant connotation (3).

In our study, 36% of the patients reported tobacco dependence prior to the diagnosis of the tumor. Case reports claim that smoking and obesity are significant risk factors (8,11). Our study comprised 72% male patients with EL which adheres to previous reports that mention a male predominance with this condition (8). Most of our study patients were aged 41 years or older. Studies have shown a peak incidence between the fifth and sixth decades of life (8). The most common presenting complaints in our study were exertional dyspnea (38.9%), sputum production (30.6%), persistent cough (27.8%), fevers (22.2%), hemoptysis (16.7%) and chest pain (16.6%) (3,6,7,9,12).

Radiological modalities such as chest radiographs and CT chest play a key role in establishing diagnosis. In our study, 80% of patients had abnormalities on chest radiograph (e.g., atelectasis, consolidation, or mass) and 58.3% of them got a chest radiograph prior to their diagnosis. CT scan is highly specific and sensitive for adipose density in the lesion (13). 97.2% of our study patients underwent a CT scan of the chest to establish diagnosis. These tumors are often diagnosed late, due to their slow growth and unspecific symptoms, of which cough is the most common. A delayed diagnosis leads to late treatment, increasing morbidity due to the distal obstruction caused by the lesion. Presenting complaints and physical examination findings can be nonspecific, cross-sectional imaging modalities such as a CT chest can help decisions about further management strategies (14). Conventional radiography is often nonspecific and shows post-obstructive changes such as atelectasis, pneumonia and bronchiectasis (15,16). Multidetector CT (MDCT) scan with isotropic resolution and thin slice thickness is the imaging modality of choice. It defines intraluminal and extraluminal extent well along

with the tumor density (17). The presence of fat attenuation narrows down the differential diagnoses to: pure EL, which has homogeneous fat attenuation, fibrolipomatous tumour, which has soft tissue attenuation with islands of fat; and hamartomas, which show fat density alternating with calcific foci (2,17). Ahn *et al.* reported that hamartomas can have connective tissue stroma, lymphoid tissue and smooth muscle components within the soft tissue attenuation suggesting a hamartoma (2,18-20).

Current therapeutic interventions include SR and endoscopic/BR (4,21-23). The majority of ELs occur in the first three subdivisions of the tracheobronchial tree where there is abundant cartilage and adipose tissue (24). In our study, 47.2% of ELs were found in the right lung (main bronchus, lobular bronchus and peripheral to segmental bronchus) while 44.4% were discovered in the left lung. SR with bronchoplastic reconstruction has long been the standard treatment (4). Forty-one point two percent (n=14) of study patients underwent SR for treatment of the EL. Flexible bronchoscopy is essential as it identifies the location of lesion and facilitates the collection of tissue for histopathology (13). Flexible bronchoscopy was used to locate the tumor in 77.8% of our study patients, while 13.9% (n=5) underwent a rigid bronchoscopy for the collection of tissue for histopathology. After the Nd-YAG laser was first applied by Toty and colleagues in 1978, bronchoscopic excision has seen new techniques applied to treat ELs (25). Fifty-eight point eight percent (n=20) of study patients underwent BR of the EL with use of either APC or Nd-YAG laser or electrocautery. Generally, bronchoscopic removal of endobronchial tumor is preferable when the tumor is small or pedunculated (26,27). Our study has shown that smaller lesions are more likely to be ELs and we showed that 80% of ELs have a size <1.5 cm (P=0.056). Early recognition and diagnosis of these benign lesions may allow for conservative treatment and excellent patient outcome in the long run (2). None except one patient was reported to have a recurrence of the lesion. Options include laser ablation, APC, electrocauterization, cryo-recanalization and electrosurgical snaring (24). Removal of an EL using a flexible bronchoscopic electrosurgical snaring does not require general anesthesia and is less invasive than a surgical excision (23). There are, however, several instances where SR is preferred such as difficult definite diagnosis, complicated peripheral destructive lung disease due to long-term atelectasis or pneumonia, subpleural lipomatous disease or expected technical difficulty due to multidirectional development of the tumor (4). While many treatment options are available, intervention should be planned on a case-by-case basis by a multidisciplinary team.

Conclusions

EL is a benign and rare neoplasm of the respiratory tract. Despite its benign nature, high degree of suspicion is required due to nonspecific symptoms. If missed can lead to deleterious and irreversible complications like bronchial occlusion, recurrent pneumonias, bronchiectasis and permanent damage to lung parenchyma. ELs are generally managed by endoscopic or SR. Endoscopic resection being less invasive, and both diagnostic and therapeutic, is the primary treatment of choice. Complete surgical excision is reserved for tumors which outgrows bronchial walls and becomes irresectable endoscopically. Therefore, a multidisciplinary approach is crucial for successful management.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/cco.2019.08.17). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by Saint Vincent Hospital, Department of Medicine, Worcester, MA 01608.

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