

REVIEW ARTICLE

The challenge of pulmonary endobronchial chondromatous hamartomas

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Summary

Pulmonary chondromatous (or chondroid) hamartomas are common benign tumours of the lung and may be either parenchymal or endobronchial. The latter are only rarely encountered and have a variation in their clinical presentation related to the endobronchial obstructive lesion, including atelectasis, pneumonia, hemoptysis. If not diagnosed early and

treated properly, endobronchial hamartomas can cause irreversible lung damage. We present a review of the recent English literature over the diagnostic approach and management of pulmonary endobronchial chondromatous hamartomas.

Key words: chondromatous, endobronchial, hamartoma, pulmonary, resection

Introduction

Pulmonary chondromatous hamartomas (PCHs), which account for 5 to 8% of all pulmonary neoplasms [1], are the most common form of benign lung tumours (75%), with an incidence between 0.025 and 0.32% according to different post-mortem studies [2-4].

The vast majority of the patients with PCHs are males, asymptomatic at the time of diagnosis with a solitary circumscribed shadow in the lung fields on a routine radiography as the only feature. Less commonly, PCHs present as endobronchial masses with symptoms due to bronchial obstruction. In the largest review series published (N=215) only 1.4% of hamartomas were endobronchial, with the remainder situated within the parenchyma [5].

The management of PCHs depends on the presence or absence of symptoms, anatomical location and whether there is a need for differential diagnosis or not.

Endobronchial hamartomas (EHs) have been successfully removed both endoscopically and surgically without significant complications [6,7].

Surgical removal, which is the gold standard of treatment, includes wedge resection or enucleation in the case of peripheral lesions (through video-assisted thoracic surgery/ VATS or mini thoracotomy) and sleeve resection or endoscopic removal for endobronchial lesions [8].

Definition and incidence

The term hamartoma, which derives from Greek terms meaning "error" and "tumour", was coined by Albrecht in 1904 to describe tumour-like malformations resulting from a presumptive developmental abnormality [9,10].

In 1934, Goldsworthy applied this term to benign tumours located in the lung that were composed predominantly of a combination of fat and cartilage [11].

PCHs are benign lung tumours with a low risk to evolve into a malignancy. Slow growth is a characteristic feature [8]. Most patients are males (2-4 times more common than females) and present between the sixth and seventh decades of life [12,13]. In the majority of the cases the tumour is located intrapulmonary whilst endobronchial tu-

mours are rare [12]. EHs are frequently seen at the proximal bronchial tree and usually have a stalk [12].

Pathology

Cytogenetic studies have identified chromosomal bands of recombination located at positions 6p21 and 14q24, supporting the idea that hamartomas represent mesenchymal clonal neoplasms instead of a developmental abnormality [14].

PCHs derive from the peribronchial mesenchyme and are biphasic lesions (composed of a mixture of both stromal and epithelial cells). In such lesions, the High Mobility Group (HMG) proteins genetic alterations occur in the mesenchymal component and they involve the chromosomal region 12q14 through q15 [8,15,16].

Histologically, mixing of normal components including cartilage, fat, bone, smooth muscle, and respiratory endothelium may be seen [17].

Parenchymal hamartomas usually contain chondroid (80%), fibroblastic (12%), fatty (5%), and osseous tissues (3%). EHs can be chondroid (50%), fatty (33%), and fibroblastic (8%) [17].

Presentation-Clinical features

PCHs typically present as single, well circumscribed round nodules and only very few cases (only 17) have been presented with multiple nodules. The tumour diameter usually ranges from 1 to 2 cm [17]. Multiple PCHs, especially in young women, may be a manifestation of Carney triad and/or Cowden disease.

Cowden triad consists of gastrointestinal stromal tumors, paragangliomas and pulmonary chondromas. In fact, it is a multiple neoplasia syndrome and predisposes to a variety of tumors including adrenocortical adenomas (unilateral or bilateral) that are usually non functioning [18,19].

Cowden disease is associated with benign findings of variable mucocutaneous lesions, such as trichilemmomas, papillomatosis, papules, pigmentations, macrocephaly, lipomas, neuromas, hemangiomas, fibromas and GI hamartomas, fibrocystic breast disease, uterine fibroids, thyroid lesions and malignancies (especially breast, thyroid, and endometrial cancers) [20]. Although the association between multiple pulmonary hamartomas and Cowden disease is not clear in the existing literature, their possible coexistence should be taken into account during the diagnostic set-up [21].

Gabrail and Zara proposed the name of pulmo-

nary hamartoma syndrome (pulmonary hamartomas accompanied by other benign tumours or congenital anomalies) as they consider it separate to Cowden's disease. This is because none of their patients with pulmonary hamartoma had the characteristic skin features of Cowden's disease, and there has been no reported association between Cowden's disease and pulmonary hamartoma [22].

The important conclusion that needs to be drawn is that PCHs are frequently accompanied by other developmental abnormalities and benign tumours.

PCHs are commonly asymptomatic and usually found incidentally with routine chest radiography as a single peripheral nodular lesion [12]. Gjevre and colleagues noted that only 3% were symptomatic [5].

However, in the case of endobronchial location, they often produce symptoms, manifesting as haemoptysis and obstructive pneumonia secondary to bronchial obstruction. Other symptoms such as cough, wheezing and dyspnoea can occur and may often be incorrectly diagnosed as asthma [23]. Most of the EHs occur as isolated lesions, however combinations of EHs with parenchymal hamartomas have been encountered. Clinically, the latter are usually asymptomatic [5-7].

Differential diagnosis for the single nodule should include metastatic disease as well as carcinoma of the lung. When multiple, Carney triad and Cowden syndrome should additionally be considered.

Diagnostic approach

The diagnostic approach consists of imaging (plain x-ray and computed tomography/CT or magnetic resonance imaging/MRI scan), bronchoscopy (flexible or rigid) and biopsy of the tumour, with the latter two being the best method for pre-operative diagnosis and management plan [12].

Pulmonary imaging of EHs shows endobronchial soft tissue space-occupying lesions leading to secondary signs, such as air entrapment, lung hyperinflation, bronchiectasis, collapse and recurrent pneumonia, all due to obstruction [12].

The lesions on CT scan are rounded and commonly exhibit calcification and fat density typical of adipose tissue [24,25]. Intranodular fat and popcorn-like chondroid calcifications are reliable indicators of hamartoma [4]. The distinction between benign and malignant nature of solitary lung nodules as detected by CT scan (mainly during the screening process of high-risk patients



Figure 1. Thoracic CT showing a lesion (circle) obstructing the left lower lobe bronchus in a 66-year-old female presented with unexplained cough persisting for several months, who underwent left lower lobectomy successfully, due to non-conclusive primary diagnosis. Histology revealed an endobronchial hamartoma.

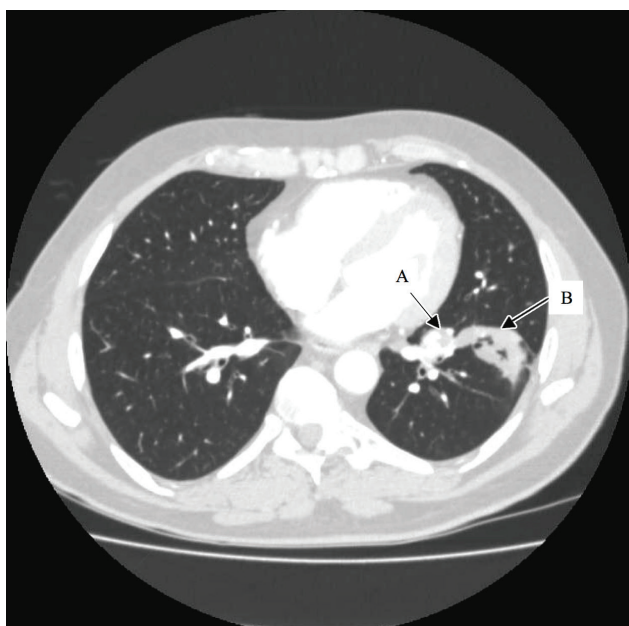


Figure 2. Thoracic CT showing a mass (arrow A) in the left lower lobe with parenchymal atelectasis (arrow B) in a 53-year-old male with haemoptysis, who underwent an uneventful anterior basal segmentectomy of the left lower lobe through a mini thoracotomy. The histology report was consistent with the report of the intraoperative frozen section biopsy, suggesting an endobronchial hamartoma.

for lung cancer) can be difficult. Even small (5-10 mm) nodules or those with smooth margins, as seen on CT scan, have relatively high risk (up to 28% and 20-30% respectively) of malignancy, and therefore must be removed [26]. Use of contrast may make it easier to distinguish benign from malignant nodules but prevents the measurement of density [27] (Figures 1,2).

The retrospective study by de Cicco et al. supports that the combination of multidetector CT scan and positron emission tomography (PET) scan is more efficient than CT alone in characterising solitary lung nodules. Out of 42 patients with pulmonary hamartomas who took part in that study, only 62% of the solitary nodules were identified as benign with the use of CT scan alone, compared to 81% when CT scan was combined with PET scan [4]. Yi et al. came to the same conclusion, suggesting the use of combined PET/CT as the first line method for evaluating solitary lung nodules, after they found that the combination was more sensitive and accurate at identifying malignancy than dynamic helical CT [28].

MRI study is an additional diagnostic tool and is especially useful when a discrete pulmonary nodule demonstrates neither fat nor calcification on CT. It identifies (particularly the T2-weighted images) the quite typical cleft-like structure of a pulmonary hamartoma and can provide confidence in the diagnosis [29].

In bronchoscopy, smooth, fleshy, pedunculated, polypoid mass lesions are seen, which may be tan to pink [30].

Convex probe endobronchial ultrasound may also have a role in diagnosis, serving to guide a transbronchial needle, as presented by Hata et al. [31].

Findings of transthoracic fine needle aspiration biopsy under CT guidance reveal cartilage, myxomatous connective tissue, smooth muscle and epithelial structures [32]. Various mesenchymal components are seen with adipose tissue usually predominating. Surgical resection is the mainstay of definitive diagnosis and treatment of symptomatic EHs.

Surgical treatment

The surgical management of EHs depends on their location, accessibility, size of the mass, associated symptoms and morbidity, diagnostic findings, availability of equipment and experience plus preference of the surgical team.

Successful removal of EHs by rigid or flexible bronchoscopy, laser excision, electrocautery and argon plasma ablation via fiberoptic bronchoscopy, have been reported, and the recurrence rate after the surgical treatment is generally low (0-2.8%), however, in the study by Cosio and colleagues it was found to be as high as 17% [5,10,12,23,33,34].

Bronchoscopy (rigid or flexible), beyond its diagnostic use, can also be performed as a tool for definitive treatment. Kim et al. in their retrospec-

tive study of 135 patients with pulmonary hamartomas, showed that bronchoscopic intervention, which was performed in 15 out of 17 patients with endobronchial hamartomas, appears to be both safe and effective in resecting EHs [35]. Compared to rigid bronchoscopy, flexible bronchoscopy may be preferred in some cases as it can be performed under local anesthesia and allows for interventions more distally in the bronchial tree. Additionally, fine manipulation is possible as magnified images of the bronchus can be obtained [36].

Endoscopic resection of EHs by laser (Neodymium-Yttrium aluminium garnet or diode laser) can be performed with a rigid or flexible bronchoscope. The role of endobronchial laser resection is especially important in patients who are not fit for or refuse surgery. Patients with fibrosis, cicatrization collapse and bronchiectasis of long duration are less likely to benefit and resection surgery is therefore preferential [18].

Electrocautery and argon plasma coagulation may represent an alternative method for resection of selected EHs, as successful and uneventful removal has been performed [25,34].

Additionally, resection by fiberoptic bronchoscopy electrosurgical snaring has been described in a case by Mondello and colleagues, which was carried out successfully and uneventfully [37].

Cryoablation has also been reported as a treatment option for EHs with effective outcomes. Indications include critical stenosis of the central respiratory tract with clinical symptoms and patient's ability to tolerate bronchoscopy, while cryotherapy should be avoided when tumour involvement of large vessels in the interventional area is evident on CT scan. Its advantage over laser therapy is that larger amounts of tissue can be removed and its more serious complication is injury of the bronchial wall [36].

Lobectomy may also need to be performed in EHs, in the case of non-endobronchial approach, as reported by Lien et al. [38].

Bronchoplasty or bronchial sleeve-resection has been reported as an alternative surgical method for removal of EHs [39]. When the definitive diagnosis confirms the benign nature of endobronchial tumours, bronchoplasty should be the operation of choice whenever possible [39]. The type of bronchoplastic procedure should be chosen on an individual basis after careful assessment of the location and extension of the lesion [39].

Tomos et al. described a technique of transverse bronchoplasty of the membranous wall after

resection of an EH and they claimed it is a safe procedure ensuring an adequate bronchial lumen at the site of the procedure [40].

Surgical treatment in cases of parenchymal pulmonary hamartomas can include wedge resection, enucleation, segmentectomy, lobectomy, and pneumonectomy, depending on the size of the mass, anatomical location and accessibility, and related features [10].

Surgical resection can be performed with VATS, mini thoracotomy and robotic surgery [38,41].

Guo and colleagues, in their retrospective study, presented their 20-year experience in surgical resection of PHs (30 patients), with wedge resection being their main choice. However, this method was impossible in patients with multiple or huge tumours, involvement of the deep part of pulmonary lobes and severe adherence of the tumour to the hilum, and where the distal lung tissue was non-functional. In these cases, lobectomy or pneumonectomy had to be used [10].

Some controversy still exists about the indications and timing of surgery of PCHs, with Guo et al. recommending surgery to be performed when: 1) there is a solitary lung nodule larger than 2.5 cm; 2) psychic burden makes removal necessary; 3) tendency of expansion or recurrence exists; 4) there are coexistent pulmonary symptoms not responding to medical therapy; and 5) most importantly malignancy cannot be excluded [10].

The same indications apply for EHs with primary priority being the coexistent pulmonary symptoms and the definitive diagnosis.

The same authors highlight the importance of follow-up, due to potential recurrence or malignancy development [10].

Minimally invasive techniques, such as wedge resection via a thoracoscopic approach, reduce procedure-related morbidity, patients leave the hospital earlier and return to daily activities sooner compared to operations involving thoracotomy [8]. They also make it less important to avoid removing a mass that may be benign as risks and complications are significantly reduced [8].

Although both bronchoscopic and surgical removal of PHs is associated with good prognosis and low risk of recurrence, adverse cases have been reported. Tomiyasu and colleagues encountered a hamartoma that extended beyond the visceral pleura and after surgical resection, bronchial carcinoma had arisen at the same location [42]. Kato et al. and Guo et al. reported postoperative

recurrence in a patient with multiple PHs and regional recurrence postoperatively three times, respectively, after wedge resection [10,43].

Multiple intrapulmonary and EHs that recurred three times after the surgical technique of “shelling out” (via thoracotomy) have been reported by Laroche et al., who suggested that a wedge excision with a margin of normal lung may be necessary to prevent further recurrences in similar patients [44].

In their retrospective study of 43 patients with EHs, Cosio et al. describe non-complete resolution of the mass in 4 out of 17 patients who underwent resection with right bronchoscopy and LASER therapy. Two of those needed a second endoscopic procedure. Follow-up was performed in 23 out of 43 patients (mean 17 months, range 1-73) which revealed recurrence in 4 patients [12]. Finally, Long et al. reported a rare case of an EH

that resulted in recurrent necrotizing pneumonia and needed thoracotomy and left lower lobectomy for definitive treatment [45].

As most EHs are identified following onset of symptoms, post obstructive pneumonia may occur, which can lead to chronic inflammation/empyema and destruction of the distal lung parenchyma. In such cases, segmental or wedge resection, lobectomy or even pneumonectomy may be necessary (through thoracotomy, VATS or Robot-assisted lung resection).

Conclusion

PCHs with endobronchial location appear to be a challenge regarding the diagnostic approach and successful management. Surgical resection, independently of the type of the procedure, remains the gold standard for definitive diagnosis and treatment.

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