Bronchial Leiomyoma with Presumptive Diagnosis of Lung Carcinoma: A Case Report and Review of the Literature

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Abstract
A case of bronchial leiomyoma arising from right middle lobe bronchus in a 44-year-old non-smoker woman with symptoms of cough and hemoptysis was presented. Bronchoscopy revealed complete obliteration of middle lobe bronchus by a soft tissue mass. Although an inferior bilobectomy was technically feasible, pneumonectomy was performed due to the small size of upper lobe, which was not expected to be fully expanded. The patient was discharged without any complications postoperatively. A well-demarcated lesion composed of spindle-shaped cells that showed reactivity for alpha-smooth muscle actin, desmin, and vimentin was observed. The patient was medically well 2 years after the operation.

Key words: Bronchopulmonary leiomyoma, clinicopathological features, treatment options, pathological differential diagnosis

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INTRODUCTION

Primary smooth muscle neoplasms of lung are the most rarely encountered tumors both in adults and children. To date, approximately 97 cases of bronchopulmonary leiomyomas have been reported in the world literature with a female predilection in adults and a male preponderance in children [1-21].

The purpose of this paper is to discuss a case diagnosed as bronchial leiomyoma with the emphasis of clinicopathological features and management of this tumor under the light of most recent literature review on this subject.

CASE REPORT

A 44-year-old non-smoker woman was referred to our hospital with symptoms of cough and hemoptysis of three weeks duration in February, 2005. Posteroanterior chest x-ray demonstrated a relatively well-defined opacity in the right paracardiac area that measured 6x4 cm in diameters (Fig. 1), which was revealed to be caused by an atelectatic right middle lobe on contrast-enhanced computed tomography (CT). The cause of atelectasis was a round hypodense soft tissue mass, 22 mm in diameter that obstructed the middle lobe bronchus (Fig. 2). Fiberoptical bronchoscopy confirmed complete obliteration of the middle lobe bronchus by a rather well-demarcated mass (Fig. 3). Because the mass was well vascularized, biopsy could not be taken due to the risk of hemorrhage. Right posterolateral thoracotomy was performed with the presumptive diagnosis of a lung carcinoma and a mass located centrally in the totally atelectatic middle lobe extending through the fissure to the hilum of lower lobe was detected. Although an inferior bilobectomy was technically feasible, pneumonectomy was performed due to the small size of upper lobe, which was not supposed to be fully expanded. The chest tube was pulled out on the first postoperative day and the patient was discharged without any complications. The patient was medically well 2 years after the operation.

Macroscopically, a well-demarcated nodular mass, 5x4x2 cm in dimensions, attached by a pedunculated stalk, obstructing the middle lobe bronchus and located 3 cm away from the bronchial resection margin was observed. The cut surface of the lesion was pinkish-gray, hard-to-elastic, smooth, and whorled. Microscopically, immediately beneath pseudostratified ciliated columnar epithelium, the neoplasm composed of bundles and whorles of spindle-shaped cells with fusiform nuclei displaying mild pleomorphism in some areas was observed (Fig. 4). Neither significant atypia nor mitotic activity was detected. The cytoplasm of the neoplastic cells was red with thrichrome stain. Immunohistochemically, the tumor showed strong diffuse cytoplasmic reactivity for alpha-smooth muscle actin (Fig. 5), desmin, and vimentin. The proliferation index detected by Ki-67 was found to be less than 5%. The immunostains for low and high molecular weight cytokeratin cocktail, S-100, chromogranin A, synaptophysin, and CD34 were negative. Transvaginal ultrasonography (USG) revealed no uterine leiomyoma. On the basis of morphological,

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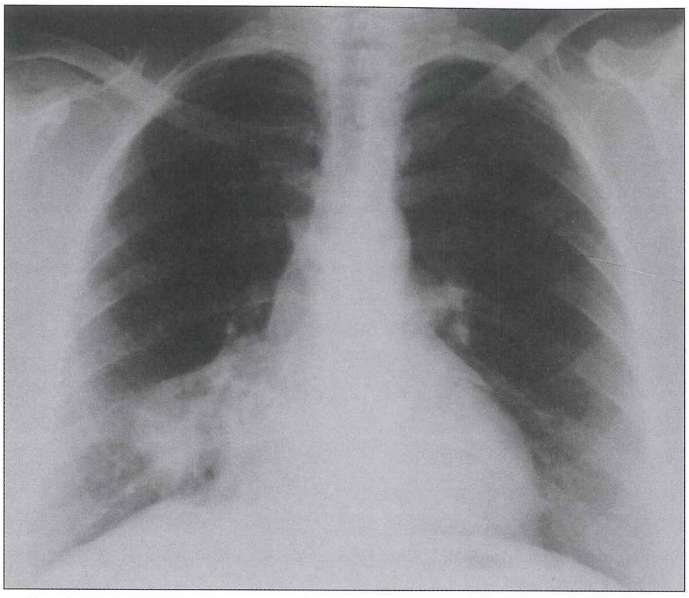

Figure 1. Posteroanterior chest x-ray of relatively well-demarcated opacity in the right paracardiac region

immunohistochemical, and transvaginal ultrasonographical findings, the lesion was diagnosed as bronchial leiomyoma arising from the right middle lobe bronchus.

DISCUSSION

Bronchial leiomyomas are thought to derive from smooth muscle layer of bronchial wall and peripheral leiomyomas may originate from the walls of arterioles, plain muscle tissue in the interstitial plane of the alveolar walls, or from primitive mesenchymal cells [6].

Primary leiomyoma is one of the most rarely encountered benign tumors of lung, accounting for 1.5-2% [22,23]. The updated total number of published cases of leiomyoma

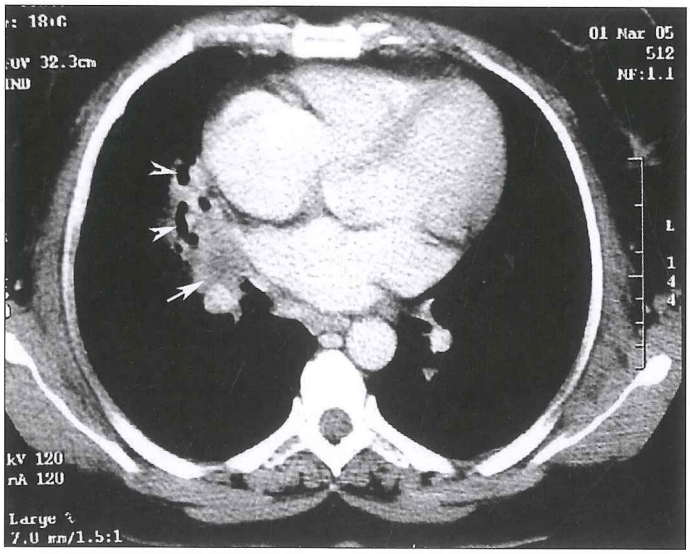

Figure 2. Contrast-enhanced computed tomography image of 22 mm soft tissue mass (arrow) obstructing the right middle lobe bronchus. Note the dilated bronchi (arrowheads) in the atelectatic middle lobe

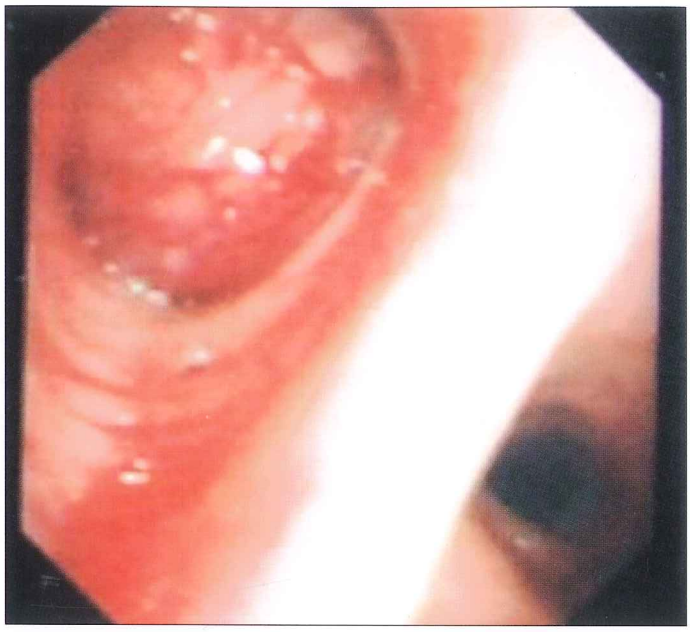

Figure 3. Fiberoptical bronchoscopy of endobronchial lesion located at the entrance of the right middle lobe bronchus

of lung in adults is approximately 80 including collective series [1-3,6] and single case reports [7-11,13-15,19,20] from the world literature. To date, 17 cases of leiomyoma of lung in childhood have been reported [4,5,12,16-18,21]. There is a female predilection, the ratio of female to male being 1.6:1 in adults [1-3]. Contrary to female preponderance in adults, leiomyomas of lung in the pediatric age are mostly seen in males [12,16-18]. The age trends illustrate that these tumors are commonly encountered in middle-aged patients, mean age being approximately 36 years [1-3]. Leiomyomas of the lower respiratory tract can be separately termed as tracheal, bronchial, and parenchymal on the basis of anatomically affected locations. The distribution of such lesions favors

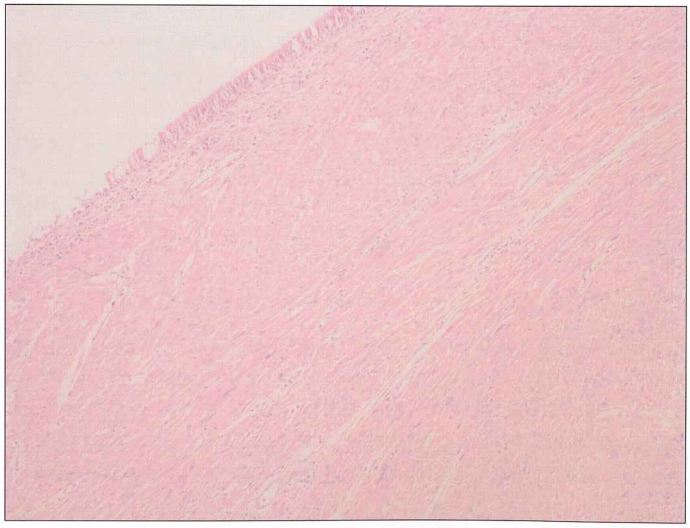

Figure 4. The neoplasm composed of bundles and whorles of spindle-shaped cells beneath the respiratory epithelium (Hematoxylin and eosin, x100)

Figure 5. TSpindle-shaped cells showing diffuse strong cytoplasmic reactivity for alpha-smooth muscle actin (Diaminobenzidine, x100)

the distal parts of the tracheobronchial tree. Although the ratio of bronchial versus parenchymal localization is 1.5:1 (60% endobronchial, 40% parenchymal) [3], nearly all the childhood leiomyomas are endobronchial [12,16-18].

The presence of symptoms is correlated with the location of the tumor within a lung. Patients with bronchial leiomyomas usually have respiratory symptoms due to partial or complete obstruction of the affected bronchus and superimposing infection resulting from atelectasis or bronchiectasis distal to obstruction. Therefore an endobronchial growth causes cough, wheezing, hemoptysis, shortness of breath, chest pain, fever, and chronic or recurrent episodes of pneumonitis in the same part of the lung. Parenchymal or peripheral leiomyoma most commonly presents as an asymptomatic solitary nodule because of absence of symptoms caused by obstruction of the tracheobronchial tree [3,6]. A recent onset of asthma in patients over 40 years of age, if accompanied by paroxysmal nocturnal dyspnea, precipitation of wheezing initiated by a change in position while a bronchodilator is useless as a treatment, or hemoptysis, should lead one to a suspicion of a tracheal obstruction, for which leiomyoma is a very rare cause [6]. In children clubbing of fingers could be the only presenting abnormality [3]. Similar to the endobronchial cases presented in the literature, the current case who was a non-smoker patient had symptoms of cough and hemoptysis of three weeks duration.

Almost all of the parenchymal leiomyomas are discovered by chest radiographic examinations and are seen as rounded shadows lacking special features. Calcifications are detected within the lesion in a few cases. The obstructive nature of endobronchial leiomyomas is expressed in their radiological appearances. Thus the corresponding chest radiographic findings range from pneumonic infiltration, mediastinal shift, and collapse of lung to unilateral emphysema or hyperlucency according to obstructive sequelae of bronchus due to the tumor [6,11,17]. Additional CT helps to define the location of the tumor in the bronchus. In the current case, posteroanterior chest x-ray demonstrated a well-defined opacity in the right paracardiac area. The contrast-enhanced CT findings showed that this opacity was caused by an atelectatic right middle lobe and that the cause of atelectasis was a round hypodense soft tissue mass which obstructed the middle lobe bronchus.

The definitive diagnosis of leiomyoma of the lower respiratory tract is made by bronchoscopy, which at the same time provides visualization and localization of the tumor and enables one to obtain a biopsy material for histological examination as in this case in which fiberoptical bronchoscopy confirmed complete obliteration of the middle lobe bronchus by a rather well-demarcated mass.

A classical problem concerning smooth muscle tumors is faced when deciding whether the tumor is benign or malignant. In general, mitotic activity is the principal criterion used to evaluate malignancy in smooth muscle neoplasms in which the treshold is supposed to depend on the location of the lesion where the threshold level is well fitted in uterine smooth muscle tumors. However, mitoses vary considerably from less than 5 per 10 high power fields (HPFs) to as many as 40 per 10 HPFs in leiomyosarcomas of the lower respiratory tract [6]. Although nuclear pleomorphism, cellularity, and growth pattern of the lesion have also been regarded as aids in the evaluation of malignancy, all these criteria including mitotic activity do not always permit a definitive diagnosis.

Before designating a tumor as pulmonary leiomyoma, the possibility of extrapulmonary leiomyoma/leiomyosarcoma most often originating in uterus or soft tissues metastasizing to lung [24] should be excluded even for bronchial leiomyomas, as in our case who had no uterine leiomyoma revealed by transvaginal USG. However, metastatic leiomyosarcomas could be differentiated from their pulmonary counterparts by their tendency being multiple, having frequent mitoses, entrapment of reactive pulmonary epithelium, and a previous history of a resected smooth muscle neoplasm originating from uterus or soft tissue.

Bronchial leiomyoma should be differentiated from epithelial and mesenchymal spindle cell tumors and tumor-like lesions such as spindle cell carcinoid, neurogenic tumor, particularly schwannoma, inflammatory myofibroblastic tumor (IMFT), and inflammatory polyp. Finely granular nuclear chromatin and immunoreactivity for cytokeratin and neuroendocrine markers can distinguish spindle cell carcinoid from leiomyoma. The pattern of Antoni A and B areas and staining for S-100 protein help to differentiate schwannoma from leiomyoma. IMFT should be considered in the differential diagnosis of bronchial leiomyoma, especially in children. The admixture of an inflammatory infiltrate, often obscuring the spindle cell proliferation in IMFT, containing plasma cells, lymphocytes, and histiocytes, including Touton type giant cells (particularly in IMFT) is an important feature in separating IMFT and inflammatory

polyp from leiomyoma. Lymphangioleiomyomatosis, another smooth muscle related lesion of lung, although does not have an endobronchial localization could enter into the differential diagnosis of parenchymal leiomyoma due to presence of immature short spindle cells resembling smooth muscle cells expressing alpha-smooth muscle actin and desmin. Although microscopical findings can help to discriminate these lesions, immunohistochemistry becomes an important tool in challenging cases where a panel consisting of smooth muscle, neural, vascular, epithelial markers, and a marker showing proliferation index may be required. Despite the fact that the current case was not a challenging one, we performed an immunohistochemical panel including all of the aforementioned markers in order to document the immunoprofile of this case completely.

Operation is the mainstay of treatment for bronchial leiomyoma. The type of operation depends on the location of tumor and the presence of secondary lung destruction. Treatment of bronchial leiomyoma should be conservative since the purpose of therapy is to reduce the loss of intact parenchyma to a minimum in such benign tumors with rare recurrences. Although the term conservative also refers to localized resection, bronchotomy and segmental resection in the literature [7], the most conservative method for teratment seems to be bronchoscopical removal of the lesion [17]. Bronchoscopical resection should be attempted if a mass is strictly confined to bronchial lumen, especially if it has a pedunculated nature and distal lung parenchyma does not have destruction [11]. However, it should be kept in mind that bronchoscopical removal could be accompanied by hemorrhage [25], perforation, and a residual tumor especially in cases with broad-based polypoid mass due to bronchial wall origin of leiomyoma or distant extension along bronchial lumen [11,17]. There is also the possibility of endobronchial dissemination since a mass can be resected in pieces [11]. Thus, bronchoscopical resection should be limited to suitable selected cases, and patients must be carefully followed-up periodically. Bronchial leiomyomas could be safely treated by YAG laser via bronchoscopy [26], or electrocautery technique [27], too. Both tecniques may reduce the incidence of hemorrhage complicated by bronchoscopical removal. However, most bronchial leiomyomas have been treated by lobectomy or pneumonectomy which might be required as a result of chronic infection or advanced parenchymal destruction [3,6]. A transthoracic operation is required if a tumor can not be diffrentiated from a leiomyosarcoma or any other malignancy; if a lesion is of undetermined nature because of the small size of the biopsy specimens obtained through a bronchoscope especially with frozen sections, or if distal lung parenchyma is destructive [6,23]. Transthoracic approaches, including bronchoplastic operation are also attempted if a lesion can not be removed bronchoscopically because it is extensive in bronchus [23], has a broad bronchial base [7,23], or extends into opposite lumen [28] and if incomplete resection and recurrences are noticed after endoscopical resection [11]. Parenchymal leiomyomas usually require a less radical procedure and some of them have been treated by segmental resection [6,7]. In the current case, a conservative approach such as localized or bronchoschopical resection could not be attempted because of the localization and the size of lesion as well as the presumptive diagnosis of lung carcinoma. Although a more conservative operation like inferior bilobectomy was technically feasible, pneumonectomy was performed due to the small size of upper lobe, which was not expected to be fully expanded.

Smooth muscle neoplasia has recently been recognized as a complication of acquired immunodeficiency syndrome (AIDS), particularly in children [29,30] in whom bronchopulmonary involvement has also been documented [16,18,31-33]. Epstein-Barr virus has also been detected in almost all AIDS-related smooth muscle neoplasms [34-36]. To date, little has been written about the management of AIDS-related smooth muscle tumors. In particular, the number of reported bronchopulmonary cases is very limited and no guides to management can be provided at this time, but it seems that one of the most problematical locations of smooth muscle proliferations is the bronchopulmonary region. Chadarévian et al. [16] do not advocate bronchoscoping every one of these cases until wheezing persists, when this symptom does not respond to bronchodilators, and especially when wheezing and air trapping are clinically and radiologically unilateral. According to these authors, only those leading to critical obstruction should be pursued as these smooth muscle neoplasms are usually multiple and in such cases, lobectomy or bronchial sleeve resections may be indicated.

CONCLUSION

Bronchopulmonary leiomyomas are among the rarest of benign neoplasms of the lower respiratory tract. The diagnosis of these neoplasms should be made with the knowledge of recently introduced concepts of smooth muscle proliferations in the lung and the possibility that a metastatic leiomyoma/leiomyosarcoma is to be excluded. AIDS-related bronchial leiomyomas should be added to the differential diagnosis of causes of wheezing of recent onset with radiological evidence of air trapping in immunocompromised patients, particularly in children. Treatment of bronchial leiomyoma should be as conservative as possible. Bronchoscopical resection should be limited to suitable selected cases and transthoracic operation should be attempted if distal lung parenchyma is destructive, if the lesion can not be removed bronchoscopically, and if incomplete resection and recurrences occur after endoscopical resection.

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