CHEST

Mounier-Kuhn Syndrome Mimicking Lymphangioleiomyomatosis

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We present the case of a man with Mounier-Kuhn syndrome (MKS), or tracheobronchomegaly, who was referred to the National Institutes of Health Clinical Research Center because of a potential diagnosis of lymphangioleiomyomatosis (LAM), a rare condition in men. The patient was evaluated using ongoing protocols and provided written informed consent. The case demonstrates the presence of chronic inflammation surrounding the dilated airways and histologic changes of the lung parenchyma with emphysematouslike disruption in areas adjacent to the dilated airways. This finding suggests that damage to the lung parenchyma is an ongoing phenomenon in MKS. Moreover, our analysis of CT images indicates similar abnormalities in areas remote from the dilated airways. Finally, because of increased anatomic dead space, calculation of lung diffusion capacity by the single-breath method yielded abnormally low values that required making a correction for the large anatomic dead space, which can be measured by the single-breath nitrogen washout test. CHEST 2018; 153(2):e19-e23

KEY WORDS: cystic lung diseases; fungus ball; lymphangioleiomyomatosis; tracheobronchomegaly

Case Report

A 40-year-old white man was referred with a potential diagnosis of lymphangioleiomyomatosis (LAM) and a history of recurrent low-grade hemoptysis and mild dyspnea. A CT scan revealed tracheomegaly (39 × 35 mm in transverse and anteroposterior diameters), large air-filled cystlike structures, and a 1.5-cm mass in the right upper lobe. The mass was suggestive of a "fungus ball" due to its attachment to the bronchial wall (Figs 1A-C). Aspiration of the mass revealed the presence of *Aspergillus fumigatus*.[1] Virtual bronchoscopy demonstrated that the cystlike structures were enlarged airways (Fig 1D). Fiberoptic bronchoscopy confirmed the presence of an enlarged tracheobronchial tree and redundancy of the airway mucosa (Fig 2).

The right upper lobe mass was removed by a right upper lobectomy. Pathologic tissue examination showed dilated airways containing mucus and fungus, with

ABBREVIATIONS: CPET = cardiopulmonary exercise tests; DCLD = diffuse cystic lung disease; DLCO = diffusion capacity for carbon monoxide; ECM = extracellular matrix; LAM = lymphangioleiomyomatosis; MKS = Mounier-Kuhn syndrome

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This work was presented at the 2016 American Thoracic Society Conference. May 13-18, 2016, San Francisco, CA.

FUNDING SUPPORT: This study was supported by the Intramural Research Program, National Institutes of Health, National Heart, Lung, and Blood Institute.

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DOI: https://doi.org/10.1016/j.chest.2017.10.024

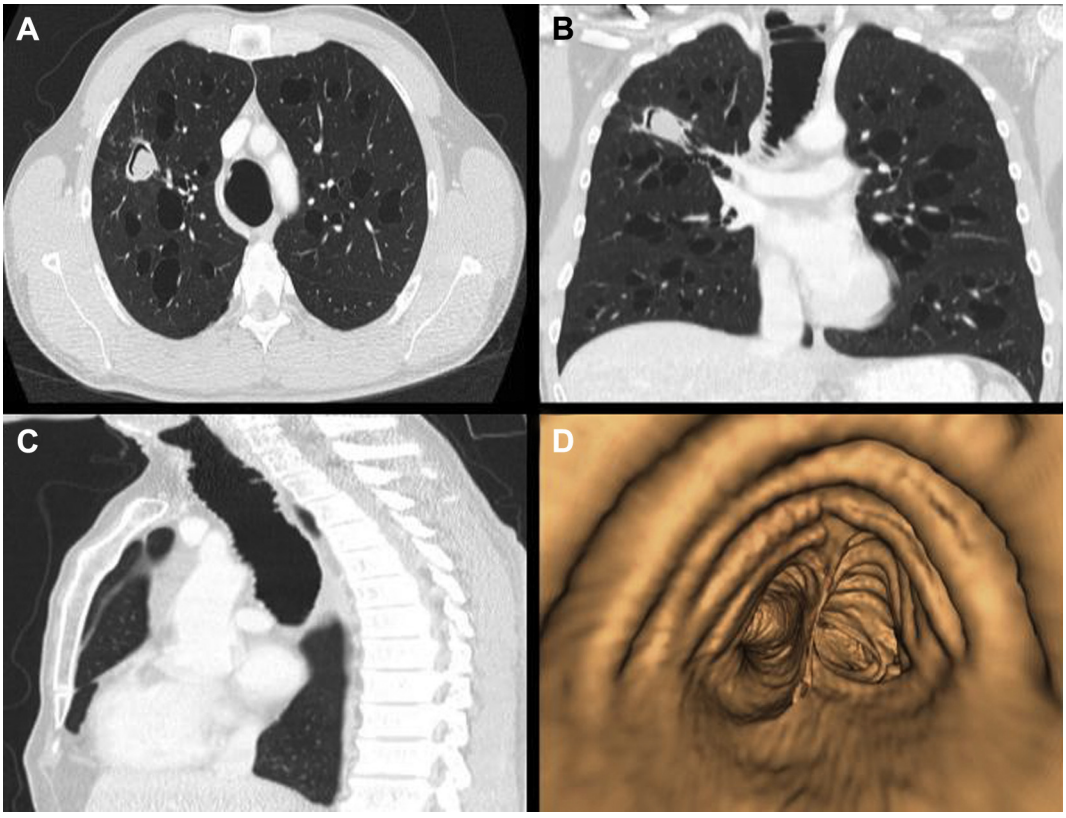

Figure 1 – *A, B, CT images of the lungs demonstrating multiple large "cystic cavities," sparing the periphery of the lung parenchyma. A solid mass within one of the cystic spaces in the right upper lobe is noted, which was found to be* Aspergillus fumigatus. *C, Of note is the enlarged trachea, which is best visualized on the anteroposterior CT image. D, A virtual bronchoscopy image of the dilated tracheobronchial tree.*

lymphocytic infiltration around the airways suggesting chronic inflammation (Fig 3B) and collagen deposition, which is consistent with peribronchial fibrosis (Fig 3A, 3B). Dilated bronchi were seen in other areas of the lung (Fig 3B). The normalized spatial dependency of pixel intensity in CT images of regions surrounding and away from the cystlike structures was examined by a CT technique described previously.[2] Areas away from the

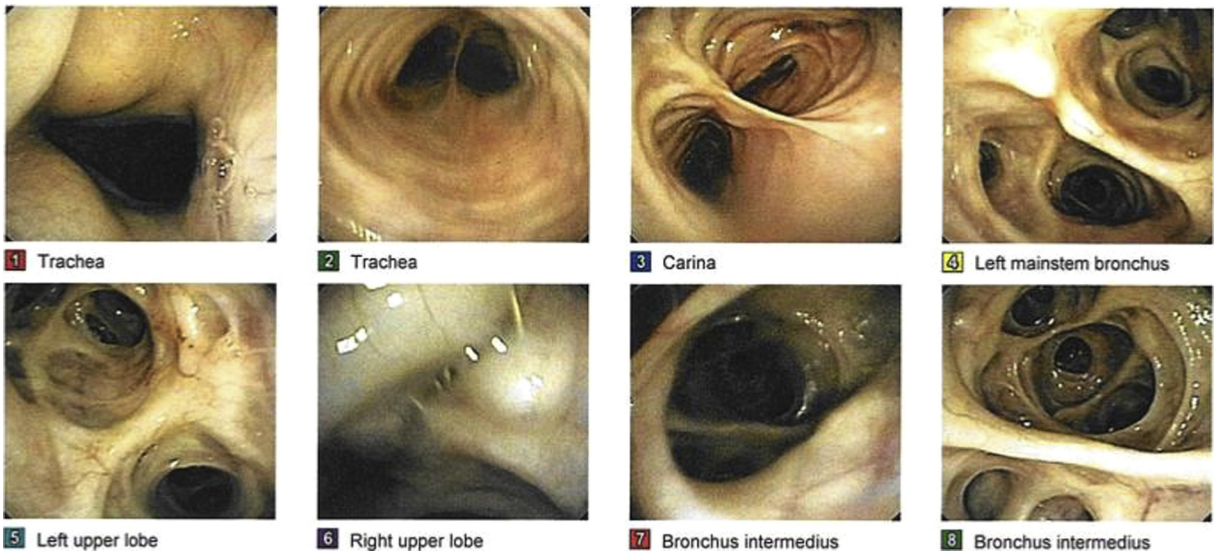

Figure 2 – *Images obtained during fiberoptic bronchoscopy showing a dilated trachea and dilated lobar bronchi.*

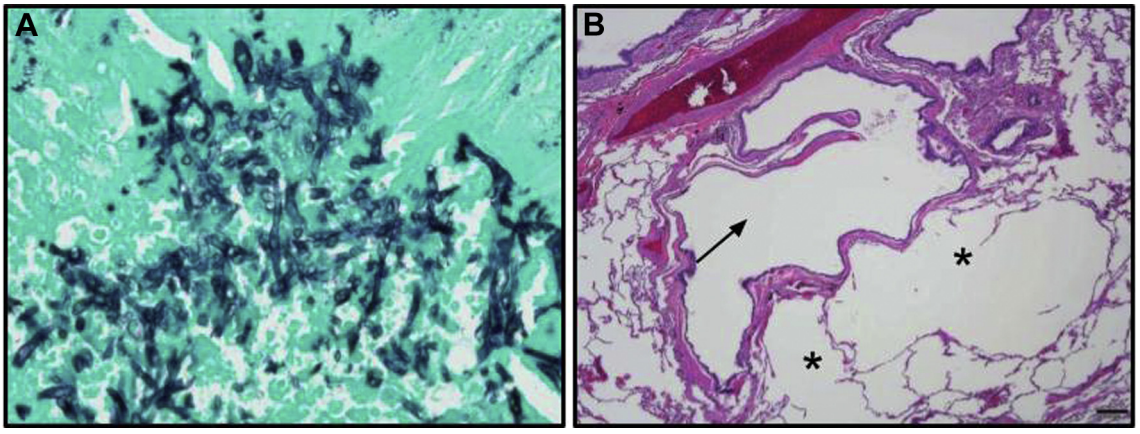

Figure 3 – *Lung histopathologic findings. A, A small intraparenchymal necrotizing granuloma with septate fungal hyphae, consistent with* Aspergillus *species (Gomori methenamine silver, ×600). B, Dilated thin-walled bronchiole (arrow) is shown next to an area of cystic emphysematous change (asterisk) (H&E, ×4).*

cystlike structures showed similarly high normalized spatial dependency of pixel intensity both before (−562.2) and after (−557.7) the lobectomy (Table 1). The normalized spatial dependency of pixel intensity is a measure of changes in the texture of the lung parenchyma, with higher scores being indicative of heterogeneous texture. Areas surrounding the cystlike structures showed overall lower scores than areas far from the cystlike regions (Table 1).

Tracheal volume was estimated at 152 mL, and the percentage of lung parenchyma occupied by enlarged airways was estimated at 16% of the total lung volume. Pulmonary function tests were performed using a computerized Master Screen pulmonary function test system (Erich Jaeger). Lung volumes and flow rates were normal (Table 2). Lung diffusion capacity for carbon monoxide (DLCO), however, was decreased significantly (34% predicted) (Table 2). Results of a cardiopulmonary exercise test (CPET) were normal, showing no evidence of oxygen desaturation at peak exercise. Thus, we assessed the effect of the enlarged tracheobronchial tree on the measurement of DLCO. Accordingly, we measured the anatomic dead space by the single-breath nitrogen washout test.[3] We found that the anatomic dead space was approximately 450 mL or about 300% predicted. After adjusting for the large anatomic dead space, the DLCO corrected to normal values (88% predicted) (Table 2).

TABLE 1] Normalized Spatial Dependency of Pixel Intensity in CT Images From Patient With MKS Expressed as Hounsfield Units (HU)

Right Upper Lobe	Area Surrounding Airway	Area Far From Airway
Before lobectomy	−646.9	−562.2
After lobectomy	−782.6	−557.7
Healthy volunteer	−453.6	−440.4

Discussion

MKS is a rare chronic airway disease with a poorly understood cause. MKS is predominantly found in men and is characterized by tracheobronchomegaly, eccentric diverticula, and muscular and elastic tissue atrophy of the tracheobronchial tree.[4,5] Patients often present with recurrent infections, breathlessness, and hemoptysis.[5]

Diffuse cystic lung disease (DCLDs) are characterized by thin-walled, air-filled spaces within normal lung parenchyma.[6] DCLDs include some rare lung diseases,

TABLE 2] Pulmonary Function Studies in a Patient With Mounier-Kuhn Syndrome

Pulmonary Function Test	Actual	% Predicted
TLC, L	7.32	118
FRC, L	4.3	127
RV, L	2.24	124
RV/TLC	0.3	105
FVC, L	5.16	118
FEV_1, L	4.19	125
FEV1/FVC	0.81	106
DLCO, mL/min/mm Hg	9.7	34
Anatomic dead space, mL	500	300
Corrected DLCO, mL/min/mm Hg	24.9	88

DLCO = diffusion capacity for carbon monoxide; FEV_1/FVC = ratio of FEV_1 to FVC; FRC = functional residual capacity; FVC = forced vital capacity; RV = residual volume; RV/TLC = ratio of RV to TLC; TLC = total lung capacity.

such as LAM, which primarily affects women and is characterized by infiltration of the lung parenchyma with neoplastic smooth musclelike cells.[6,7] CT scans show diffuse thin-walled cysts throughout the lungs.[8] Diagnosis of LAM in a man is rare.[8]

The patient in our study presented with a history of possible LAM and hemoptysis caused by an aspergilloma located in a dilated bronchus. CT findings were thought to mimic the cystic LAM structures.[4] However, bronchoscopy with histopathologic examination showed that the cystic structures represented dilated bronchi, not lung cysts, thereby leading to a diagnosis of MKS.

CT assists with the diagnosis of both DCLDs and MKS.[4,6] However, similarities in the appearance of cysts and enlarged airways on CT imaging could result in the initial mislabeling of MKS as a DCLD, such as LAM or Williams-Campbell syndrome (tracheobronchomalacia).[8–10] Although current literature reports no other cases of misdiagnosis of MKS as LAM, the prevalence of MKS is suspected to be higher than reported.[4] This case illustrates the potential for misdiagnosis of DCLDs and MKS based on only CT imaging evaluation.

Histopathologic evidence of chronic inflammation and dense peribronchial fibrosis supports previous descriptions of MKS as a chronic inflammatory disease.[11] Immunohistologic studies reported a reduction of elastic fibers in the submucosal connective tissue, an inflammatory infiltrate composed of $CD4^+$ cells, and increased matrix metalloproteinase expression surrounding the dilated airways.[11] In this case, normalized spatial dependency of pixel intensity in CT images of regions far from the enlarged airways showed a higher score in areas surrounding the airways. Higher scores indicate a greater likelihood that pixels in a certain direction have similar intensity and are suggestive of better lung tissue structure. Therefore, areas in the parenchyma far from the enlarged airways have better structure than those near the airways. However, such areas far from the airways in patients with MKS still show reduced structure compared with those in a healthy individual, indicating that parenchymal changes were present in areas both distant from and near to the dilated airways (Table 1). Studies reported a correlation between a low normalized spatial dependency of pixel intensity in CT images of the lung parenchyma in LAM and emphysematouslike changes.[2] Similarly, pathologic examination of the lung in the patient with MKS confirmed the presence of emphysematouslike changes and breakdown of the extracellular matrix (ECM). Although studies in patients with MKS suggested ECM breakdown of areas near the dilated airways, this case presents evidence of changes to the lung parenchyma in areas remote from the airways.[11] Therefore, the increased compliance of the airways and ineffective cough reported in MKS could be due to ECM breakdown in both the lung epithelium surrounding the airways and areas distant from the dilated airways.

CT images showed that 16% of the lung parenchyma was occupied by enlarged bronchi, initially perceived as cysts, and an abnormally large tracheobronchial tree for a subject who was only 167 cm in height. Therefore, we suspected that the reduced D_{LCO} (34%) was due to the large anatomic dead space, which precluded the accurate collection of a true alveolar gas sample during measurement of the D_{LCO}. Indeed, the gas sample collected included anatomic dead space gas with a high carbon monoxide content, resulting in an underestimation of the diffusion capacity. By measuring the anatomic dead space by means of the single-breath nitrogen washout test and accounting for the markedly increased dead space in the D_{LCO} measurement, we found that the D_{LCO} was normal, a finding that was consistent with the CPET results. We demonstrated that in conditions associated with tracheobronchomegaly, the measurement of D_{LCO} is affected by a large anatomic dead space.[3]

This case illustrates a unique presentation of dilated airways in a patient with MKS mimicking cystic structures in LAM on CT imaging. Our texture feature analysis of the lung parenchyma and correction of single-breath D_{LCO} for a very large anatomic dead space introduce novel methods for evaluating patients with MKS.

Acknowledgments

Author contributions: The manuscript has been seen and approved by all authors. All authors take responsibility for the integrity of the data and the data analysis and for the integrity of the submission. The objectives and procedures undertaken are honestly disclosed.

Financial/nonfinancial disclosures: None declared.

Role of sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

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