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Thoracic Computed Tomography Scan and Bronchoscopy Appearance of Mounier-Kuhn Syndrome: A Case Report

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Abstract

Mounier-Kuhn syndrome (MKS) is a rare congenital disease with an autosomal recessive inheritance pattern, characterized by an enlargement of the trachea and bronchi. MKS is secondary to a thinning of the muscular mucosa and atrophy of the longitudinal muscle and elastic fibers of the tracheobronchial tree. As a consequence, tracheal diverticulosis and dilatations in the posterior membranous wall appear, along with bronchiectasis that tend to be cystic in appearance. Overall, there is an impairment of mucocilliary clearance, with an ineffective cough, which predisposes the patient to recurrent lower respiratory tract infections. Clinical manifestations vary from asymptomatic to respiratory failure and death, most patients being diagnosed between the third and fourth decades of life. It is an often undiagnosed disease, with a diagnostic algorithm that includes the use of radiological techniques, alone or in combination with bronchoscopy. Specific diagnostic criteria have been developed, based on patients' tracheal and main bronchi diameter on chest X-ray and thoracic computed tomography scan. We present the case of a 45-year-old African American man who presented with a history of multiples episodes of pneumonia that required management in the intensive care unit, on whom MKS was diagnosed.

Keywords

tracheobronchomegaly, Mounier-Kuhn syndrome, computed tomography, bronchoscopy, case report

Background

Mounier-Kuhn syndrome (MKS), also known as congenital tracheobronchomegaly (TBM), is a rare disease characterized by an enlargement of the trachea and bronchi. It was first reported by Czyhlarz in 1897 in an autopsy description, but it was not until 1932 that Mounier and Kuhn described its clinical presentation.[1] Evidence comes mainly from case reports and case series, with very few clinical trials; thus, epidemiologic data are scarce. However, there are approximately 300 reported cases in the literature, from where an estimated prevalence of 0.4% to 1.6% has been drawn with a male predominance of 8:1.[2] Little is known about the etiology of this disease, but it appears to be congenital, with an autosomal recessive inheritance pattern[3]; it has been reported in children who suffer from recurrent pulmonary infections or in conjunction with other congenital disorders.[2]

MKS is caused by a thinning of the muscular mucosa and atrophy of the longitudinal muscle and elastic fibers of the tracheobronchial tree. As a consequence, tracheal diverticulosis and dilatations of the posterior membranous wall develop, along with bronchiectasis that tend to be cystic in appearance. Overall, there is an impairment of mucocilliary clearance, with an ineffective cough, predisposing the patient to recurrent lower respiratory tract infections.[2,4] Clinical manifestations vary from asymptomatic to respiratory failure and death, most patients being diagnosed between the third and fourth decades of life.[5] Diagnostic algorithm includes chest radiography (X-ray), which is often overlooked, thoracic computed tomography (CT) scan, and bronchoscopy.[2] There is no specific treatment for MKS; management is focused on the optimization of comorbidities and supportive therapy such as physiotherapy and antibiotics for pulmonary infections. We believe awareness of this condition should be increased among physicians, to avoid delayed diagnosis and

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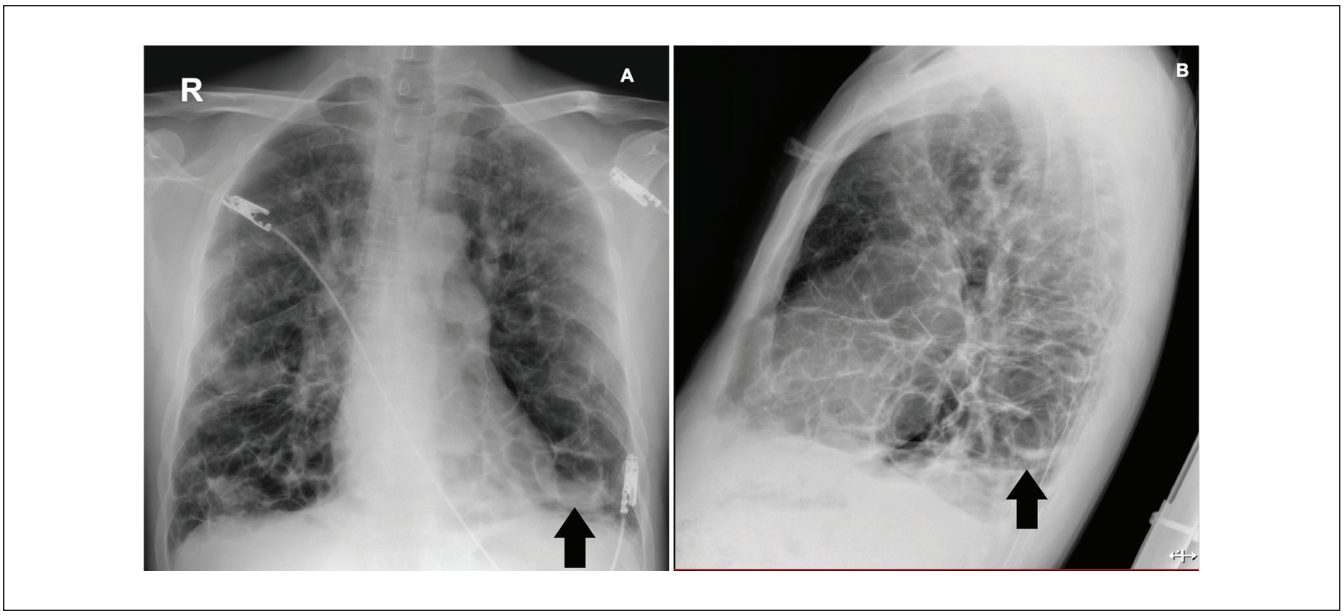

Figure 1. (A and B) Anteroposterior and lateral chest X-ray. Central trachea and cystic images with thin walls less than 4 cm in the lower two thirds of both lungs, some with presence of air fluid level (black arrow).

further complications. We present the case of a 45-year-old African American man who had a history of multiples episodes of pneumonia that required management in the intensive care unit, who was finally diagnosed with MKS.

Case Presentation

The case is of a 45-year-old African American male, nonsmoker, with a history of arterial hypertension, iron deficiency anemia, and auricular fibrillation. For the past 10 years, he had multiple episodes of community-acquired pneumonia, requiring admission to the intensive care unit on several occasions. Immunodeficiency virus (HIV), cystic fibrosis, tuberculosis, and several primary immunodeficiencies had been discarded and negative family history for similar diseases. He had chronic dry cough and dyspnea with modified Medical Research Council (mMRC) scale 3/4, requiring use of domiciliary oxygen. He consulted to our institution when his respiratory symptoms increased, presenting with productive cough with purulent secretion, functional class deterioration, and dyspnea with mMRC scale 4/4. At admission, physical examination reported the following vital signs: arterial tension 130/85 mm Hg, heart rate 100 beats per minute, respiratory rates 18 breaths per minute, SO_2 93%, and temperature 38 °C. He showed dyspnea at rest with use of accessory muscles; wet mucous membranes, without jugular ingurgitation or neck masses; regular and rhythmic tachycardic heart sounds, without murmurs; diminished respiratory sounds in both pulmonary fields; tubal murmur in bases; unremarkable abdomen; absence of edema in extremities; and presence of digital hippocratism.

Blood work with white blood cell count $7.4 \times 10^3/\mu L$, neutrophils $3.17 \times 10^3/\mu L$, lymphocytes $2.77 \times 10^3/\mu L$, hemoglobin 9 g/dL, hematocrit 34%, positive C-reactive protein 16.2 mg/dL, lactate 0.7, arterial blood gases with a pH 7.38, partial pressure of carbon dioxide ($PaCO_2$) of 76.6 mm Hg, PaO_2 46 mm Hg, oxygen saturation (SaO_2) 80%, and HCO_3 39 mg/dL.

Imaging Findings

Chest X-ray showed a central trachea and multiple thin-walled cystic images, occupying the lower two thirds of both hemithorax, no masses, or pneumothorax (Figure 1). Thoracic CT scan showed an increased tracheal diameter, measuring 28 × 33 mm (anteroposterior × transversal) 2 cm above the aortic arch, with atonic walls and presence of cylindrical and cystic bronchiectasis (Figure 2A). Enlarged mainstem bronchus with a right mainstem bronchus (RMB) and left mainstem bronchus (LMB) diameter of 22 and 17 mm, respectively (Figure 2B-F). On 3-dimensional coronal volumetric reconstruction and multiplanar reconstruction with digital subtraction, a gradual enlargement of the trachea and diffuse dilatation of the bronchi is observed, along with cystic bronchiectasis that give a cobblestone appearance (Figure 3).

A fibrobronchoscopy was then performed revealing tracheal dilatation, with tracheal diverticula and moderate purulent secretions. Posterior to the right main bronchus giving the branches for the superior and intermediate lobe, the anatomy is altered giving rise to multiple cavitations, some of them occupied by abundant pus. Similarly, on the left main

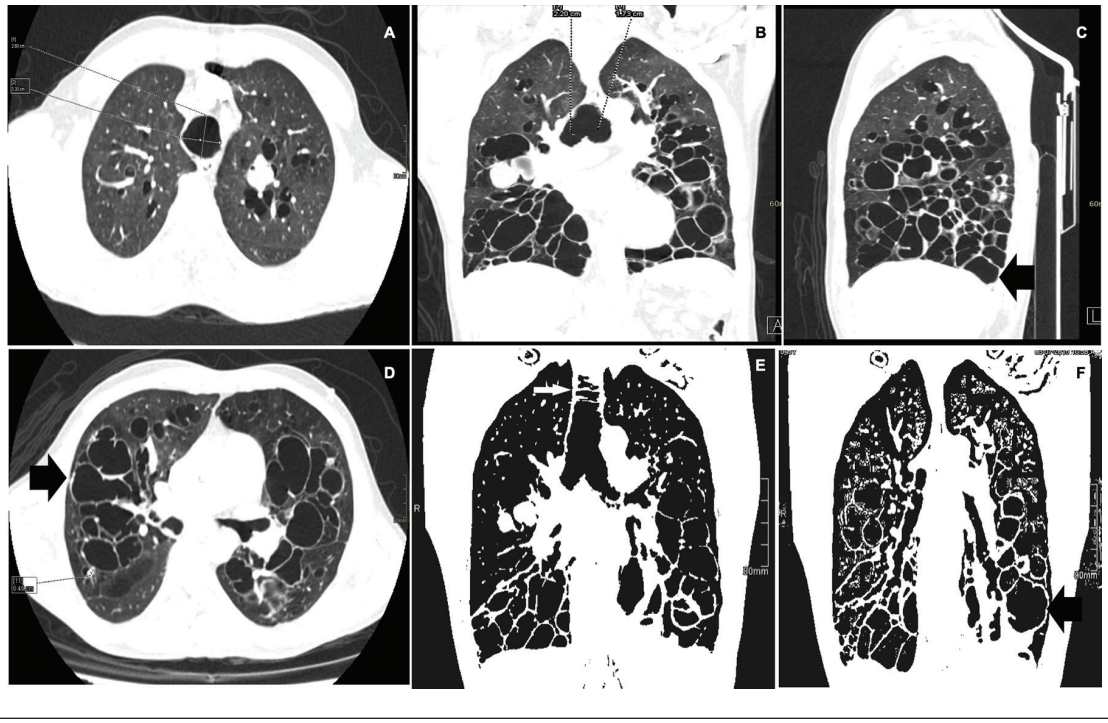

Figure 2. (A, B, C, and D) Thoracic computed tomography scan, coronal and sagittal planes. Dilated trachea of 28 × 33 mm (anteroposterior × transversal) and enlarged mainstem bronchi with a diameter of the right mainstem bronchus and left mainstem bronchus of 22 mm and 17 mm (pointed lines), respectively. Several peripheric thin-walled cysts are observed, which correspond to cystic bronchiectasis (thick black arrow), with partial sparing of pulmonary apices. (E and F) Coronal maximum intensity projection reconstruction. Scalloping of tracheal wall with presence of diverticula (thin white arrow) and peripheric cystic bronchiectasis with air fluid levels and apical sparing.

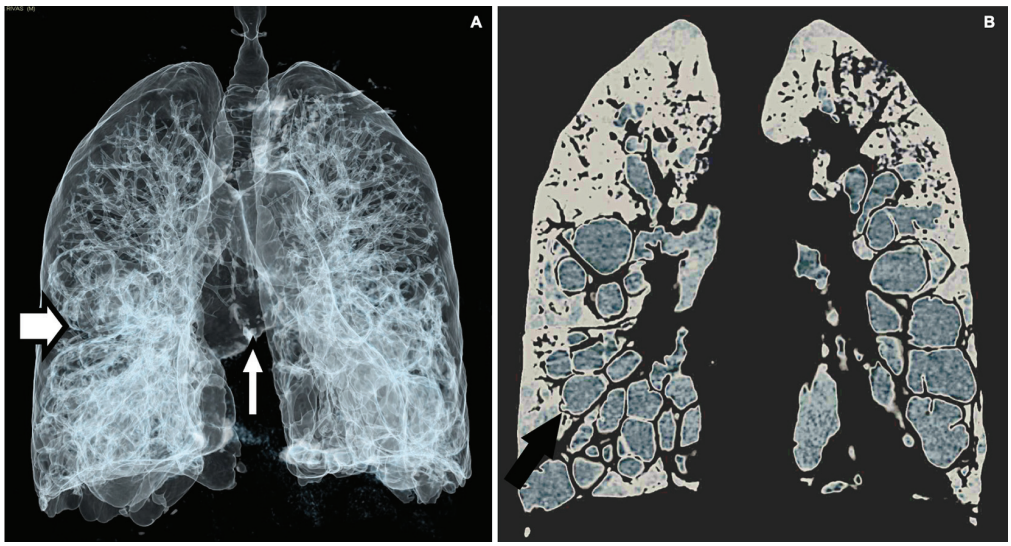

Figure 3. (A) Three-dimensional coronal volumetric reconstruction of the airway. A gradual dilatation of the trachea is observed (narrow white arrow), along diffuse enlargement of bronchi, predominantly showing basal predominance with presence of bronchiectasis (thick white arrow). (B) Coronal multiplanar reconstruction with digital subtraction. Compromise of intraparenchymal airway by cylindrical and cystic bronchiectasis that appear "blueish" giving a cobblestone appearance (black arrow), with surrounding normal "white" parenchyma. Black spaces correspond to subtractions of the remaining thoracic structures.

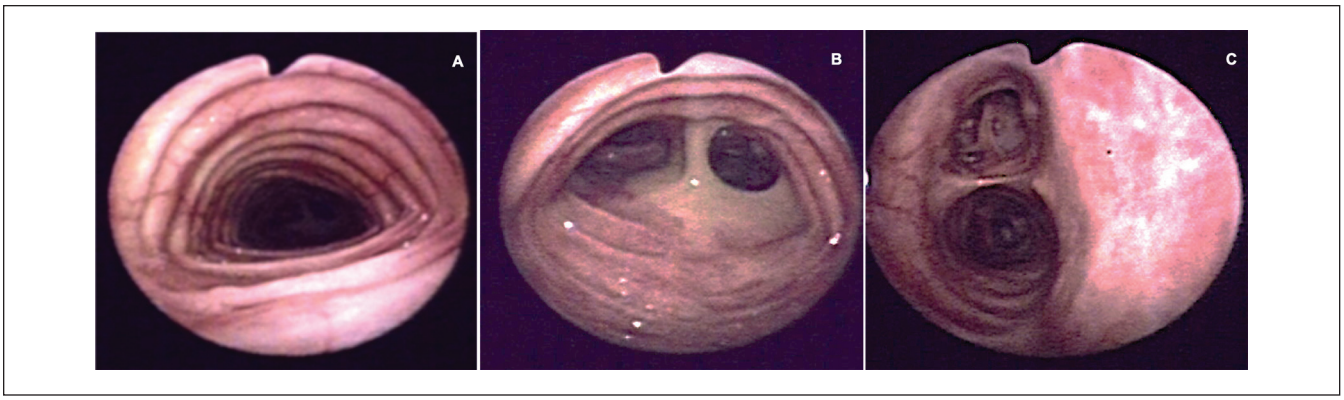

Figure 4. Bronchoscopy. (A) Dilated trachea with mucosal edema and diverticula causing the mucosa to protrude between cartilaginous rings. (B and C) Edematous mainstem bronchus with presence of purulent material.

bronchus, a loss of normal structure is seen, with multiple purulent filled cavitations (Figure 4). Bronchoalveolar lavage was performed, being positive for *Achromobacter xylosoxidans* spp (resistant to cefepime and ceftriaxone) and *Pseudomonas aeruginosa*. Taking into consideration the patient's clinical, imagenological, and endoscopical findings, MKS is diagnosed.

Therapeutic Intervention

The patient was successfully treated for this infectious episode, for which treatment with piperacillin/tazobactam was administered for 14 days. Respiratory therapy was initiated, consisting of inhalation therapy and mucus drainage using the Acapella airway clearance device. After 10 days, the patient was discharged home.

Outcomes

Typical out-of-hospital management includes domiciliary therapy using Venturi 50% per day, salbutamol and ipratropium bromide inhaler as needed, respiratory therapy, and inhalation of a hypertonic solution to mobilize mucous secretions. The patient has been hospitalized in approximately 17 occasions from 2015 until 2019 for pulmonary infections that have been managed efficaciously without further complications. On his last appointment with the pulmonologist, his baseline disease was stable with no further deterioration in functional class. A control chest X-ray showed an improvement in pulmonary radiolucency with decrease in air fluid levels (Figure 5).

Discussion and Conclusions

MKS is a rare but often undiagnosed disease; diagnostic algorithm includes the use of radiological techniques, alone or in combination with bronchoscopy. Clinical manifestations are nonspecific, ranging from asymptomatic to severe in patients who develop life-threating pneumonia, sepsis, respiratory insufficiency, and so on. On physical examination, it is common to find finger clubbing, hoarseness secondary to vocal cord paralysis, and, on cardiopulmonary auscultation, the presence of rales and even wheezing.[2] In fact, spirometry and body plethysmography can show an important degree of obstruction associated to an increased residual volume.[6]

The dilatation caused by MKS compromises the trachea and up to the fourth bronchial generation.[6] An anatomical classification for TBM of all causes was proposed in an review article published in 1973, taking into account the authors' experience and the available literature to that date, which can be easily applied to MKS: type 1 corresponds to a diffuse enlargement of both the trachea and bronchi; in type 2 (the most common), the dilatation primarily affects the trachea with pronounced diverticula and an abrupt transition to a normal bronchial diameter; and in type 3 (the least common), the diverticula and sacculation extend to the distal bronchi.[2,6]

Other classifications have been proposed, focusing not on anatomical involvement but on etiologic features. In 2015, Payandeh et al[7] published a literature review of MKS and proposed a description of TBM types with the purpose of framing diagnostic and therapeutic approaches. They classified TBM in types 1 to 4 as follows: type 1A and type 1B for infants who underwent fetal endoscopic tracheal occlusion and developed TBM and those with prolonged intubation who developed TBM, respectively; type 2A and type 2B for patients who develop TBM after multiple infections and after being diagnosed with pulmonary fibrosis, respectively; type 3 for patients with TBM and extrapulmonary elastolysis; and type 4 for patients with TBM and no predisposing factors. This classification could route physicians to a certain therapeutic approach, while allowing to somehow predict the patient's response to management and prognosis taking into consideration the underlying pathophysiology.

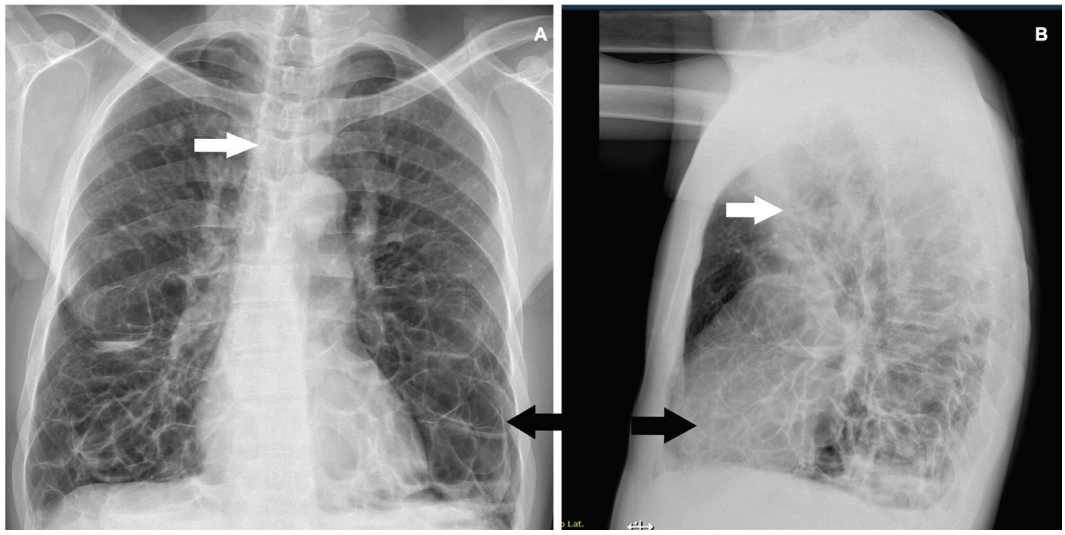

Figure 5. (A and B). Anteroposterior and lateral chest X-ray. Tracheal dilatation (white arrows) associated to thin-walled cystic images (black arrows) in the lower two thirds of both lungs, presence of several air fluid level, with improvement compared with initial chest X-ray.

Furthermore, specific diagnostic criteria are available, based on patients' tracheal and main bronchi diameter on chest X-ray and thoracic CT scan. On lateral chest X-ray, a tracheal diameter ≥30 mm, RMB diameter ≥24 mm, and LMB diameter ≥23 mm are diagnostic.[1] On thoracic CT scan, the diameter has been divided by gender.[2] Findings of transverse and anteroposterior tracheal diameter ≥25 and 27 mm in males, and 21 and 23 mm in females, respectively, are diagnostic of MKS. Findings of RMB and LMB diameter ≥21.1 and 18.4 mm in males, and 19.8 and 17.4 mm in females, respectively, are also diagnostic of MKS.[1] In our case, the patient has a type 1 MKS, evidenced by the enlargement of both the trachea and mainstem bronchi (Figure 2).

Other key features to look for on chest X-ray are a scalloped tracheal contour due to the protrusion of mucosa between the cartilage rings, which is seen anteriorly on the lateral projection, plus tracheal diverticula and bronchiectasis compromising the central bronchi.[8] If there is no superimposed pulmonary infection, peripheral airways should appear normal. Although this syndrome is often overlooked on chest X-rays, retrospectively, it is easier to observe the changes due to tracheal enlargement. We encourage physicians to do so in order to train themselves and achieve an opportune diagnosis in future patients with recurrent pulmonary infections.

However, the gold standard to diagnosed MKS remains thoracic CT scan, in which a marked enlargement of the trachea and main bronchi is observed. While tracheal scalloping is more difficult to see as compared with chest X-rays, the presence of diverticula on the posterolateral walls of the trachea is one of the diagnostic hallmarks. Large and central cystic bronchiectasis are commonly found, with bullae in the peripheric parenchyma. Using dynamic CT is an alternative to look for tracheobronchomalacia on expiratory scans,[8,9] defined as an airway collapse greater than 50%[10] that presents as a consequence of the tracheal anatomic alterations.

On the other hand, on bronchoscopy, a marked tracheal dilatation and the presence of expiratory collapse due to excessive dynamic airway collapse or tracheobronchomalacia are the most common findings. The structures flaccidity may even obstruct the view with the bronchoscope. It is also very common to find diverticula filled with purulent material.[2]

Being a rare condition, MKS is of outmost importance that diagnosis is made after ruling out other pathologies, including acquired causes of TBM such as mechanical ventilation in preterm babies, pulmonary fibrosis, radiotherapy, and some immunodeficiencies syndromes in children.[2] Diseases that present with bronchiectasis should also be considered, such as immotile cilia syndrome and cystic fibrosis, in which not only radiological findings overlap with type 3 MKS but they could also coexist with TBM.[6,11] Additionally, as previously mentioned, a consequence of TBM is tracheobronchomalacia, which can be congenital or acquired. Within the congenital causes appear dyschondroplasias, polychondritis, Ehlers-Danlos syndrome, Pierre-Robin syndrome, and Williams-Campbell syndrome (WKS) among others.[10] It is important to note that there have been several case reports of patients with MKS associated to Ehlers-Danlos syndrome, cystic fibrosis, Marfan's syndrome, and cutis laxa.[2,8] Among

Table 1. Involvement of Lung Structures in the Differential Diagnosis of Pathologies That Cause Tracheobronchomegaly and/or Cystic Bronchiectasis[a].

	Type 1 MKS	Type 2 MKS	Type 3 MKS	Williams-Campbell syndrome	Immotile cilia syndrome	Cystic fibrosis
Trachea	Enlarged Presence of diverticula in posterolateral walls Scalloped tracheal wall TBM	Enlarged Pronounced diverticula Scalloped tracheal wall TBM	Normal or TBM	TBM	Normal	Normal
Mainstem bronchi	Diffuse enlargement Presence of bronchial cartilages	Abrupt transition to normal bronchi diameter Presence of bronchial cartilages	Normal mainstem bronchi Presence of bronchial cartilages	Normal mainstem bronchi	Normal	Cylindrical bronchiectasis Bronchial thickening
Lobar bronchi onward	Dilatation stops at fourth bronchial generation Central cystic bronchiectasis	Normal Central cystic bronchiectasis	Enlargement of distal bronchi Central cystic bronchiectasis	Altered or absent bronchial cartilages in mid-order subsegmental airways (can compromise from first to eighth generation) Cystic bronchiectasis	Varicoid bronchiectasis in middle and lower lobes	Right upper lobe is the first involved Varicoid and cystic bronchiectasis Bronchial thickening
Lung parenchyma	Mosaic attenuation pattern Peripheric bullae	Mosaic attenuation pattern Peripheric bullae	Mosaic attenuation pattern Peripheric bullae	Air trapping	Diffuse tree-in-bud nodules	Large lung volumes Atelectasis Air trapping on expiration Centrilobular opacities

Abbreviations: MKS, Mounier-Kuhn syndrome; TBM, tracheobronchomalacia.
[a]Adapted from Webb and Higgins[8] and Webb WR, Mulier NL, Naidich DP. *High-Resolution CT of the Lung*. 5th ed. Wolters Kluwers; 2014. Chapter 19.

the acquired etiologies, posttraumatic, specially post tracheostomy stand out. Other causes are emphysema, asthma, chronic infections, and external compression of the trachea,[10] which can also be present in patients with MKS.

Furthermore, WKS is the main differential diagnosis of MKS; they share similarities in clinical presentation, presence of bronchial wall abnormalities, and bronchiectasis.[8] WKS is also a rare disease, characterized by altered or absent bronchial cartilages in subsegmental bronchi, causing distal collapse and bronchiectasis. Although it usually affects bronchi from the fourth generation onward, a point where MKS findings are no longer seen, there have been cases where the compromise has extended between the first and eighth bronchial generation, which overlaps with the findings of type 3 MKS. Additionally, these patients also suffer from recurrent pulmonary infections, functional class deterioration, and clubbing.[12] On thoracic CT, distal cystic bronchiectasis are found with expiratory collapse on dynamic CT. A useful tool to differentiate among WKS and MKS is virtual bronchoscopy, where the absence of cartilage rings is clearly seen.[13,14] In this case, the differentiation between these 2 entities is easy since our patient's compromise began on the trachea plus there is evidence of normal bronchial cartilage rings (Figure 2E and F). Taking into account diseases that can overlap with MKS, it is useful to analyze the involvement of different lung structures of the pathologies that cause TBM and/or cystic bronchiectasis (Table 1).

In conclusion, MKS is a rare and congenital disease that causes marked dilatation of the trachea and main bronchi. Patients usually present with a history of years of duration of recurrent pulmonary infections and in some occasions are misdiagnosed with other pulmonary diseases such as chronic obstructive pulmonary disease or chronic bronchitis. MKS is often overlooked on chest X-rays, and we believe physicians, especially emergency medicine physicians and radiologists, must be trained to recognize the subtle changes seen on plain radiographs, in order to make an opportune diagnosis and avoid further complications. The main findings on thoracic CT scans are TBM, tracheal diverticula, changes of tracheobronchomalacia, and cystic

bronchiectasis that can be filled with purulent material. Bronchoscopy can assist in the diagnosis, showing tracheal dilatation, presence of multiple diverticula, and expiratory collapse. Although there is no specific therapy for these patients, it is crucial to reach the diagnosis so the treating physician can establish supportive measures and be attentive to possible complications.

Authors' Note

This article has not been published and is not under consideration for publication elsewhere. Additionally, all of the authors have approved the contents of this article and have agreed to the journal's submission policies. All data and material are available for sharing if needed.

Author Contributions

All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Declaration of Conflicting Interests

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Ethics Approval

This report was prepared in accordance with the ethical standards of the institutional ethics committee and with the 1964 Helsinki Declaration. We have approval letter of Ethics Committee in biomedical research IRB/EC No. 217-2016 of the Fundación Valle del Lili to publish this article.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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