CASE REPORT

Bronchial Mucoepidermoid Carcinoma: A Rare Cause of Chronic Respiratory Symptoms in Children - Case Report

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Abstract

Primary pulmonary tumors are uncommon in children. Mucoepidermoid carcinoma accounts for approximately 10% of all primary pulmonary neoplasms. This study reported the case of a 6-year-old male patient who presented with fever, cough, and wheezing, and had a history of choking and recurrent respiratory infections. Chest radiography showed a hyperinflated left lung, and bronchoscopy revealed a friable polypoid mass obstructing more than 90% of the left primary bronchus. Moreover, a chest computed tomography scan showed no lymphadenopathies. Endoscopic resection of the mass and posterior surgical resection of its remainder were performed. Histological examination revealed a low-grade mucoepidermoid carcinoma. Due to its rarity and the non-specific nature of symptoms, the diagnosis of mucoepidermoid carcinoma is usually delayed. In the presence of chronic respiratory symptoms and signs of bronchial obstruction on imaging exams, mucoepidermoid carcinoma should be included in the differential diagnosis, along with other more frequent conditions.

Keywords: Bronchial Neoplasms; Bronchoscopy; Carcinoma, Mucoepidermoid/diagnosis; Carcinoma, Mucoepidermoid/surgery; Child; Cough/etiology; Diagnosis, Differential; Respiratory Sounds/etiology; Case Report

Keypoints

What is known:

- Primary pulmonary tumors and mucoepidermoid carcinoma are rare in pediatrics and have non-specific symptoms. Hence, diagnosis and treatment are often delayed and a high degree of suspicion is required for an early diagnosis.

What is added:

- When in the presence of chronic respiratory symptoms and signs of bronchial obstruction on the imaging exams, mucoepidermoid carcinoma should be included in the differential diagnosis, along with other more prevalent conditions.
- Despite the lack of guidelines for the diagnosis, management, treatment, and follow-up of these cases in children, complete resection by surgery seems to be the best approach.

Introduction

Primary pulmonary tumors are very rare entities in children. Studies have reported that in pediatric age, 95% of all malignant tumors and 80% of all lung tumors are metastatic diseases.[1] The primary to metastatic to benign lesions ratio in this population is 1:5:60.[1] Among primary pulmonary tumors, mucoepidermoid carcinoma accounts for approximately 10% of cases.[1-5] Due to its rarity and non-specific symptoms, the diagnosis of mucoepidermoid carcinoma is usually delayed.[1-4,6,7] and the tumor is only identified when obstructive symptoms or signs occur.[2] As such, for an early diagnosis, a high index of suspicion is required in the presence of recurrent respiratory symptoms. This case study aimed to report the case of a bronchial mucoepidermoid carcinoma in a 6-year-old male with a history of choking and chronic respiratory symptoms.

Case Report

A 6-year-old male patient with no known relevant past clinical history complained of fever, cough, and wheezing

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for three days. He was evaluated in primary care and empirically treated with amoxicillin 50 mg/kg/day and desloratadine. As the cough continued to deteriorate, he was revaluated. This time, he was referred to the hospital due to abnormal pulmonary auscultation.

At the time of admission, the patient was eupneic and had no apparent acute respiratory distress. Pulmonary auscultation was frankly asymmetric, with marked decreased breath sounds over the left lung. The remainder of the physical exam was unremarkable. The chest radiography revealed hyperinflation of the left lung with increased lung translucency (Fig. 1).

At this point, the medical history of the patient was reviewed. There was a history of frequent choking, although without any recent episodes. Similar abnormal pulmonary auscultation was described in two hospital admissions in the past five months. The chest radiography performed at that time had similar features to the present one. However, on the previous occasion, as there was also an opacity on the left lung, pneumonia was thought to be the issue and the patient was treated accordingly. Given the hypothesis of foreign body aspiration with recurrent secondary pneumonia, it was decided to continue antibiotic treatment (clavulanate was associated with amoxicillin) and a flexible bronchoscopy was performed. A friable polypoid endobronchial lesion was identified in the left main bronchus that obstructed more than 90% of its lumen (Fig. 2).

Chest computed tomography revealed a high-density lesion in the left primary bronchus, similar to a foreign body. The lesion had some apparent calcified content and was almost completely obstructing the bronchial lumen. The computed tomography scan also showed hyperinflation in the left lung. Moreover, no mediastinal or hilar lymphadenopathies were observed (Fig. 3).

With this clinical picture, the hypothesis of foreign body aspiration gained relevance. It was thought that the foreign body could already be epithelialized due to the considerable length of time it was settled in the bronchus. Rigid bronchoscopy was performed and revealed no foreign body; however, a friable polypoid endobronchial lesion covered with normal mucosa was found.

The mass was biopsied and almost completely excised. Histological examination of the tissue revealed a salivary gland-type adenoma. The pathology slides were reviewed at a specialized international center with the final diagnosis of low-grade mucoepidermoid carcinoma. Subsequently, a fluorescence *in situ* hybridization analysis detected *MAML2* rearrangement in 68% of cancer cells.

Due to the rare nature of this entity, the case was discussed by a multidisciplinary team. It was decided to follow up on the case with frequent bronchoscopies. As there was a local relapse, the patient underwent surgical resection of the bronchus. The lesion, which was adjacent to the left secondary carina, was resected and intraoperative frozen section analysis confirmed mucoepidermoid carcinoma. A bronchoplasty with primary anastomosis was performed without complications. Pathological examination of the surgical specimen confirmed the existence of a residual lesion with clear margins and analysis of a pulmonary lymph

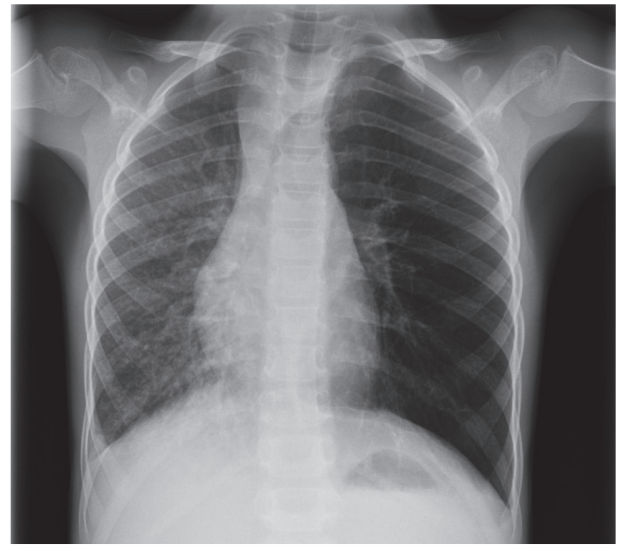

Figure 1. Posteroanterior chest radiography at hospital admission showed hyperinflated left lung with increased lung translucency.

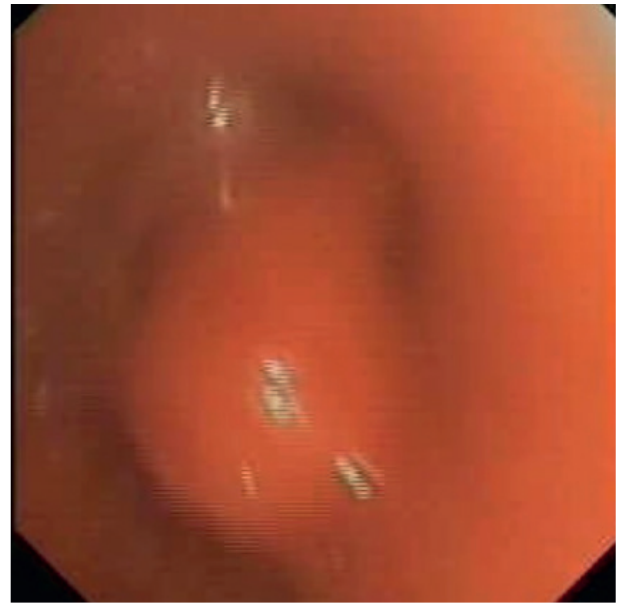

Figure 2. A polypoid friable mass obstructing more than 90% of the left primary bronchus was identified on bronchoscopy.

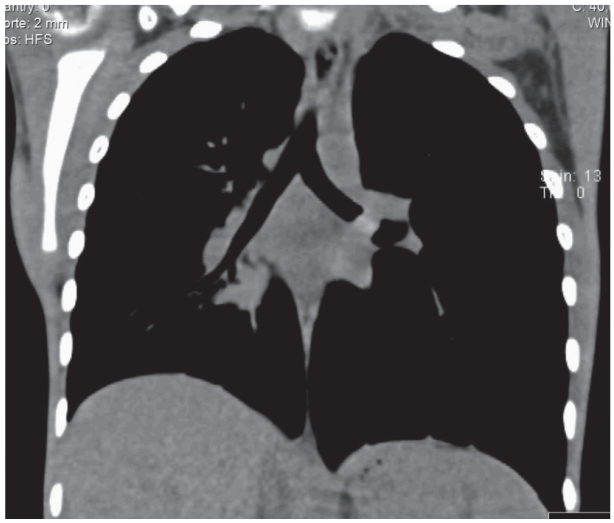

Figure 3. Chest computed tomography scan in mediastinal window coronal plan showed a tumor lesion with some apparent calcified content in the left primary bronchus.

node showed no signs of tumor invasion.

Currently, the patient is well and symptom-free. He is under clinical, endoscopic, and radiological surveillance with periodic flexible bronchoscopies and computed tomography scans, with no signs of apparent recurrence.

Discussion

Primary pulmonary tumors are extremely rare during pediatric age. A vast majority of lung neoplasms in this age are due to metastasis from a distant tumour.[1,4] Studies have reported that mucoepidermoid carcinomas are the second most common primary pulmonary tumors in children[1,2] and account for approximately 10% of all cases.[1-5] The mean age at diagnosis is around 10 years old[3] and there is a 1:1 female-to-male ratio,[3,7] with an average diagnosis delay of 11 months after the onset of symptoms.[4]

The mucoepidermoid carcinomas are typically localized in the primary bronchi or the proximal portion of the lobar bronchi.[7] Location at the left primary bronchus seems to be slightly more frequent than the right side.[3] The tumor of our patient was located at the left primary bronchus and the symptoms began approximately 5-6 months prior to the diagnosis.

Exposure to carcinogens from the environment and abnormal pulmonary development may participate in the pathogenesis of mucoepidermoid carcinoma.[4] It should be mentioned that smoking does not seem to be related to this lesion.[5] Tracheobronchial mucoepidermoid carcinoma originate from salivary / mucus glands.[1-4,6,7] They are composed of three major cell types, namely mucous cells, Malpighian cells, and intermediate cells.[5]

Based on the histological features (mitotic index, presence of cystic structures, predominant cellular group, and cellular pleomorphism) mucoepidermoid carcinoma are classified as low-, intermediate-, and high-grade tumours.[2-4,6,7] It is noteworthy that most of these lesions in pediatric age are low-grade tumours.[1] The tumor in the present case was primarily composed of mucinous cells with a mitotic index of less than 5%; therefore, it was classified as a low-grade tumor.

Due to its rarity and the non-specific nature of its symptoms, the diagnosis is challenging and treatment of tracheobronchial mucoepidermoid carcinoma is often delayed. As the tumor grows, the tracheal or bronchial obstruction may develop.[2,7] Symptoms originate either from inflammation of the tracheobronchial mucosa or airway obstruction.[7] Patients usually present with cough (50%), pneumonia (43%), fever (30%), and hemoptysis (20%).[1-4,7] Constitutional symptoms, such as weight loss, fatigue, malaise, and night sweats may also occur. Nonetheless, some children with lung masses remain asymptomatic until diagnosis.[4]

In the diagnostic workup, a chest radiography is usually the first exam to be performed[3] and the tumor is observed in 30% of cases[7]; however, a chest computed tomography scan is mandatory.[2] It is useful to assess tumor location and extension, evaluate ganglia involvement, and search for metastases.[7] Imaging exams typically show signs of bronchial obstruction, such as air trapping or atelectasis,[3,4] congruent to the presentation of our patient.

On computed tomography scans, mucoepidermoid carcinomas are often lobulated or oval masses[2,3] with calcifications on the inside in 50% of cases.[2,7] It should be mentioned that the mass of our patient also had some calcified content. Endoscopic evaluation, with flexible and/or rigid bronchoscopy, is another diagnostic procedure that must be performed.[2,3,7] The goal is not only to characterize the lesion but also to obtain a biopsy for a definitive diagnosis.

There are no published guidelines regarding the management, treatment, and follow-up of this tumor in the pediatric age; however, surgical resection and lymph node sampling are considered the treatment of choice to avoid recurrence.[2,3] Chemotherapy and radiotherapy are usually not indicated, except in case of recurrence or metastasis.[3,7] There have been some reports of using endothelial growth factor receptor tyrosine kinase inhibitors (TKI) in high-grade tumors since endothelial growth factor receptor is frequently overexpressed in mucoepidermoid carcinoma of salivary

gland origin.[8] Furthermore, some mucoepidermoid carcinoma present with translocation t(11;19) (q21;p13) (fusion gene *MECT1-MAML2*) and may be susceptible to tyrosine kinase inhibitors even in the absence of endothelial growth factor receptor mutation.[5]

The effectiveness of bronchoscopic therapy in the eradication of bronchial low-grade mucoepidermoid carcinoma in children is reported.[6] However, endoscopic resection of mucoepidermoid carcinoma is usually not recommended, considering the risk of incomplete resection[7] and the possible complications and limitations of the procedure *per se*.[2] In addition, bronchoscopy does not allow extraluminal lymph node sampling for staging.[3] In the present case, rigid bronchoscopy and partial excision of the mass were initially performed due to the suspicion of foreign body aspiration. At that time, it was assumed that an aspiration episode might have occurred a few months earlier and the foreign body would have already been epithelialized, given how long it was lodged in the bronchus.

Bronchial mucoepidermoid carcinoma generally have an excellent prognosis, with a survival rate of 87%-100%.[2,3,5] With a risk of distant metastasis of about 5%,[5] mucoepidermoid carcinoma rarely spread to lymph nodes or distant organs.[1] Favorable prognostic factors are low stage at presentation (early diagnosis), low histological tumor grade, the possibility of complete surgical resection, and the presence of the translocation t(11;19) (q21;p13).[3,6]

In the present case, the tumor was not detected at an early phase. It was occluding more than 90% of the bronchial lumen at the moment of diagnosis; however, it was a low-grade tumor with no metastases. After confirmation of the diagnosis, surgical resection of the remainder lesion was performed. The fluorescence *in situ* hybridization analysis of the tissue detected *MAML2* rearrangement in 68% of cancer cells.

Patients with this translocation have been reported to have a favorable prognosis regardless of pathological type,[6] with longer overall survival and disease-free survival.[9] Given the slow growth rate and the possibility of recurrence, a long-term follow-up strategy is recommended.[7]

Author Contribuitions

JNC participated in acquisition of data. JNC, MJ, CP and TRS participated in the analysis or interpretation of data. JNC participated in the drafting of the manuscript. MJ, CP and TRS participated in the critical revision of the manuscript. All authors approved the final manuscript and 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.

Conflicts of Interest

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Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Consent for publication

Consent for publication was obtained.

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Carcinoma Mucoepidermoide Brônquico: Uma Causa Rara de Sintomas Respiratórios Crónicos em Crianças

Os tumores primários pulmonares são raros em idade pediátrica, correspondendo o carcinoma mucoepidermoide a cerca de 10% das neoplasias primárias pulmonares. Descrevemos o caso de um doente do sexo masculino de 6 anos com queixas de febre, tosse e pieira, e com histórico de engasgamentos frequentes e infeções respiratórias de repetição. A radiografia do tórax revelou hiperinsuflação pulmonar esquerda. A broncofibroscopia revelou uma lesão polipoide, friável, que ocupava mais de 90% do lúmen do brônquio principal esquerdo. A tomografia computorizada excluiu a presença de adenopatias. Foi feita excisão endoscópica da massa e posterior ressecção cirúrgica da lesão remanescente. O exame histológico confirmou tratar-se de um carcinoma mucoepidermoide de baixo grau. Atendendo à sua raridade e sintomatologia pouco específica, o diagnóstico de carcinoma mucoepidermoide é, geralmente, tardio. Na presença de sintomas respiratórios crónicos e sinais de obstrução brônquica nos exames imagiológicos, é importante considerar esta entidade no diagnóstico diferencial, em conjunto com outras doenças mais frequentes.

Palavras-Chave: Broncoscopia; Carcinoma Mucoepidermoide/diagnóstico; Carcinoma Mucoepidermoide/cirurgia; Criança; Diagnóstico Diferencial; Neoplasias Brônquicas; Sons Respiratórios/etiologia; Tosse/etiologia; Caso Clínico