# Resolution of lobe collapse in a child with cystic fibrosis with M. abscessus using serial intrabronchial rhDNase

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**Abstract**

An eight-year-old girl with cystic fibrosis (CF) developed a left upper lobe collapse failing to resolve with initial conventional antibiotic treatment, mucolytics and intensified physiotherapy. Mycobacterium abscessus was isolated from her sputum. Bronchoscopy revealed thick viscous mucus plugging of the left upper lobe bronchus with complete obliteration. Three bronchoscopies with saline lavage and Dornase alfa, a rhDNase, at the end of each procedure resulted in removal of this mucus plug and the re-inflation of the affected lobe, with clinical and radiological resolution. The use of flexible bronchoscopy as a 'secondary' treatment with 0.9% saline lavage and instillation of rhDNase is described sparsely in the literature. This is the first reported successful therapeutic resolution of a lung collapse in a CF patient with Mycobacterium abscessus, with sequential therapeutic bronchoscopies with instillation of Dornase alfa. This should be considered for lobar collapse in CF not responding to the standard therapeutic regime.

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### To the Editor

### Introduction

Lobar collapse is a common complication in cystic fibrosis (CF). We describe a case of unilateral left upper lobe collapse in a CF patient complicated by *Mycobacterium abscessus* (MABS), which responded to serial therapeutic bronchoscopies with instillation of Dornase alfa, a recombinant human DNase (rhDNase).

### Background

Patients with lobar collapse often respond to intravenous antibiotics, physiotherapy and mucoactive agents. The use of flexible bronchoscopy as a 'secondary' treatment with 0.9% saline lavage and instillation of rhDNase is described sparsely in the literature. Serial bronchoscopic clearance of a lung collapse with rhDNase is documented in only one case series report in CF patients with allergic bronchopulmonary aspergillosis (ABPA)[1].

*Mycobacterium abscessus* forms part of the Non-tuberculous Mycobacterium (NTM) group that can cause pulmonary disease resembling tuberculosis, especially in vulnerable hosts with underlying structural lung disease, such as cystic fibrosis and bronchiectasis[2].

### Case Presentation

An eight-year-old girl with cystic fibrosis (genotype Delta F508/G542X), presented with productive cough, associated with impaired exercise tolerance. Examination revealed decreased air-entry on the left upper zone,

with deterioration in lung function. Chest X-RAY showed collapse of the left upper lobe. She was treated with an empirical course of oral antibiotics, pending microbiological results, as per cystic fibrosis guidelines. She failed to respond, with persistence of clinical and radiological findings. A non-tuberculous Mycobacterium was isolated from her sputum, which was subsequently verified to be, *Mycobacterium abscessus complex* , detected by Mycobacterium DNA probe test and polymerase chain reaction by a reference lab.

She was admitted for three weeks of intravenous antibiotics (Amikacin, Meropenem, Cefoxitin), oral Azithromycin and nebulised Tobramycin, as well as intensive chest physiotherapy.

Initial Bronchoscopy revealed thick viscous mucus plugging of the left upper lobe bronchus with complete obliteration, making the prospects of clearance by conservative measures highly unlikely. Therapeutic bronchoalveolar lavage was attempted using normal saline (total volume of 50ml (2ml/kg). Dornase alfa 2.5mg was instilled at the opening of the left upper lobe bronchus at the end of the procedure. The patient underwent a total of 3 therapeutic bronchoscopies. Progress was slow but consistent with complete clearance of the bronchus with the final procedure.

**Outcome and Follow-up**

An improvement was noted progressively in her clinical condition, lung function parameters, bronchoscopy findings and radiologic findings.

Clinically the cough decreased drastically, and the exercise tolerance improved.

The FEV1 improved from 0.78L (53% Pred) to 1.39L (75% Pred) whilst FVC improved from 0.81L (47% Pred) to 1.59L (73% Pred).

There was radiological resolution of the left upper lobe collapse with complete and persistent re-inflation of the left upper lobe (*Image 1* ).

Unfortunately, despite 1$^{st}$, 2$^{nd}$ and 3$^{rd}$ line protocol guided anti-microbial treatment, the*Mycobacterium abscessus* was not eradicated.

**Discussion**

*Mycobacterium abscessus* is a ubiquitous, rapidly growing mycobacterium. It frequently infects the lung tissue, notably in susceptible hosts with structural lung disease, such as cystic fibrosis[2]. In fact Nontuberculous mycobacteria (NTM), especially the subspecies *Mycobacterium abscessus subsp. abscessus* has emerged as the leading and worrisome pathogen in cystic fibrosis patients. Over the past twenty years the NTM incidence among cystic fibrosis patients has increased from 3.3% to 22.6%. The isolation of NTM was associated with increased morbidity and mortality[3].

Untreated it causes slow but progressive deterioration resulting in long-term symptoms, declining pulmonary function and impaired quality of life. Occasionally it can also cause fulminant acute respiratory failure[2].

Patients with *Mycobacterium abscessus complex* are not considered as candidates for lung transplant in many centers, but it is not considered as a definite contraindication for lung transplantation. However, one may anticipate a higher incidence of post-operative complications in these patients[4].

The organism's resistance to antimicrobials and multiple adverse effects of these treatment options, makes the treatment of *Mycobacterium abscessus* particularly challenging[2].

In the case described above, the child was not responding to conventional treatment options; including a combination of antibiotic regimes, mucoactive agents and extensive physiotherapy[5].

Therapeutic bronchoscopic lavage with normal saline and instilment of Dornase alfa cleared the left upper lobe bronchus with re-inflation of the affected lung. This was accompanied with improvement in the child's symptoms, clinical findings, lung function parameters (FEV1 and FVC) and radiological resolution of the airway collapse.

The use of sequential therapeutic bronchoscopies with installation of recombinant human DNase was reported previously in one case series in cystic fibrosis patients with allergic bronchopulmonary aspergillosis[1]. There were no studies or reports in the literature pertaining to *Mycobacterium abscessus* which could have guided us on the extent to which therapeutic bronchoscopies should be repeated. We were encouraged by the fact that small improvements were made with each procedure. Overall, we feel that the removal of some of the plug at bronchoscopy with installation of Dornase alfa paved the way for a better therapeutic result with sequential procedures. This is the first reported successful therapeutic resolution of a lung collapse in a Cystic fibrosis patient with *Mycobacterium abscessus* , using bronchoscopic lavage with installation of recombinant human DNase.

**Conclusion**

The repercussions of persistent lung collapse in cystic fibrosis patients can be significant and it is associated with a poor prognosis[1]. Sequential therapeutic bronchoscopies with instillments of recombinant human Dnase can be effective in*Mycobacterium abscessus* lobar collapse caused by mucus plugging and should be considered for cystic fibrosis patients who do not respond to the standard initial therapeutic regime for lobar collapse.

**References**

1. Whitaker P, Brownlee K, Lee T, Conway S, Etherington C, Peckham D. Sequential Bronchoscopy in the Management of Lobar Atelectasis Secondary to Allergic Bronchopulmonary Aspergillosis. J Bronchology Interv Pulmonol 2011;18(1):57-60. doi:10.1097/lbr.0b013e318206ea63
2. Griffith D, Aksamit T, Brown-Elliott B, Catanzaro A, Daley C, Gordin F, Holland S, Horsburgh R, Huitt G, lademarco M et al. An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases. Am J Respir Crit Care Med 2007;175(4):367-416. doi:10.1164/rccm.200604-571st
3. Degiacomi, Sammartino, Chiarelli, Riabova, Makarov, Pasca. Mycobacterium abscessus, an Emerging and Worrisome Pathogen among Cystic Fibrosis Patients. Int J Mol Sci 2019;20(23):5868. doi: 10.3390/ijms20235868
4. Benwill J, Wallace R. Mycobacterium abscessus. Curr Opin Infect Dis 2014;27(6):506-510. doi:10.1097/QCO.0000000000000104
5. Nagakumar P, Hilliard T. Recurrent lobar atelectasis in a child with cystic fibrosis. J R Soc Med 2012;105(suppl 2):50-52. doi:10.1258/jrsm.2012.12s010

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**Abbreviated Title:**

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